Scopus

Documents

1) Arya, P., Sharma, M.R., Raghav, N.
Carboxymethyl β-cyclodextrin: Box-behnken model optimized synthesis, modification with cetyltrimethylammonium bromide and usage as sustained release system for curcumin
(2023) *Journal of Molecular Structure*, 1277, art. no. 134820, .

Abstract
Development of novel drug delivery systems is one of the major thrust areas in medicinal chemistry so as to localize, enhance and extend the action of the drug. To achieve maximum degree of Carboxymethylation of β-cyclodextrin in the present work, we first report the optimization of reaction conditions using box-behnken model of Response Surface Methodology. Thus synthesized Carboxymethylated β-cyclodextrin was modified using CTAB surfactant and again optimized for maximum binding efficiency for curcumin. The synthesis was confirmed using FT-IR, SEM, X-Ray Diffraction and Particle Size Analysis. Curcumin binding, release & solubility studies, anti-oxidant, Serum Protein protecting and anti-Cathepsin studies were executed for the modified support. The prepared support acted as a promising carrier for curcumin delivery with enhanced aqueous solubility. © 2022

2) Brockmueller, A., Samuel, S.M., Mazurakova, A., Büsselberg, D., Kubatka, P., Shakibaei, M.
Curcumin, calebin A and chemosensitization: How are they linked to colorectal cancer?
(2023) *Life Sciences*, 318, art. no. 121504, .

Abstract
Colorectal cancer (CRC) is one of the leading malignant diseases worldwide with a high rate of metastasis and poor prognosis. Treatment options include surgery, which is usually followed by chemotherapy in advanced CRC. With treatment, cancer cells could become resistant to classical cytostatic drugs such as 5-fluorouracil (5-FU), oxaliplatin, cisplatin, and irinotecan, resulting in chemotherapeutic failure. For this reason, there is a high demand for health-preserving re-sensitization mechanisms including the complementary use of natural plant compounds. Calebin A and curcumin, two polyphenolic turmeric ingredients derived from the Asian Curcuma longa plant, demonstrate versatile anti-inflammatory and cancer-reducing abilities, including CRC-combating capacity. After an insight into their epigenetics-modifying holistic health-promoting effects, this review compares functional anti-CRC mechanisms of multi-targeting turmeric-derived compounds with mono-target classical chemotherapeutic agents. Furthermore, the reversal of resistance to chemotherapeutic drugs was presented by focusing on calebin A's and curcumin's capabilities to chemosensitize or re-sensitize CRC cells to 5-FU, oxaliplatin, cisplatin, and irinotecan. Both polyphenols enhance the receptiveness of CRC cells to standard cytostatic drugs converting them from chemoresistant into non-chemoresistant CRC cells by modulating inflammation, proliferation, cell cycle, cancer stem cells, and apoptotic signaling. Therefore, calebin A and curcumin can be tested for their ability to overcome cancer chemoresistance in preclinical and clinical trials. The future perspective of involving turmeric-ingredients curcumin or calebin A as an additive treatment to chemotherapy for patients with advanced metastasized CRC is explained. © 2023

3) Monika, P., Chandraprabha, M.N., Murthy, K.C.
Gene expression studies in primary human acute and chronic wound fibroblasts treated with most popular wound healing phytoextracts
(2023) *South African Journal of Botany*, 155, pp. 205-213.

Abstract
Background: Impact of chronic wounds in terms of quality of life and financial burden for patients is huge and it remains as a major clinical challenge throughout the world. In order to address chronic wounds effectively, it is at most important to understand wound biology at molecular level in clinically distinct wounds. Fibroblasts are the most common cells present in all types of wounds and are critical to regain the normal tissue homeostasis. Several plant-based extracts and compounds have shown significant wound healing activity in various experimental models. Objective: To identify the best phytoextract that regulate genes that can increase fibroblast proliferation, enhance angiogenesis, increase anti-inflammatory and antibacterial properties, decrease MMP degradation activity. Methods: mRNA expression of TNF-α, TGF-β, FGF-1, MMP-2, MMP-9 and VEGF in human primary Acute wound fibroblasts (AWFs) and Chronic wound fibroblasts (CWFs) treated with phytoextracts such as catechin, epicatechin, curcumin, garlic, pomegranate peel and neem. Results: Gene expression analysis showed that, catechin, epicatechin, curcumin, garlic, pomegranate peel and neem had significant influence on AWFs and CWFs treated cells by up regulating wound healing promoting genes or down regulating wound healing resistance genes. Among six test phytoextracts, epicatechin was found to be the best as it significantly ($P<0.05$) reduced the mRNA expression of TNF-α, TGF-β, MMP-2 and MMP-9 and neem was found to be the best phytoextract in terms of its influence on the mRNA expression of FGF-1 and VEGF genes in both AWFs and CWFs. Conclusion: Epicatechin extract was found to be the best phytoextract, which significantly reduced the mRNA expression of wound healing resistance

genes. On the other hand, treatment of neem extract significantly increased the mRNA expression of wound healing promoting genes in both AWFs and CWFs. Use of phytoextracts to target fibroblasts in wounds can be an economical, safe and efficient approach to treat non-healing chronic wounds. © 2023 SAAB

4) Porro, C., Panaro, M.A.
Recent Progress in Understanding the Health Benefits of Curcumin
(2023) *Molecules*, 28 (5), art. no. 2418, .

5) Laha, B., Suresh, A., Namboothiri, I.N.N.
Regio- and stereoselective synthesis of functionalized tetrahydro-benzochromenes and hexahydrochromenochromenones via [4 + 2] annulation of curcumins with nitrochromenes
(2023) *Organic and Biomolecular Chemistry*, 21 (9), pp. 1872-1877.

Abstract
A base-mediated regio- and stereoselective synthesis of functionalized tetrahydro-6H-benzo[c]chromenes and hexahydro-1H,6H-chromeno[6,5-c]chromenone is disclosed here. It involves a [4 + 2] annulation via cascade double and triple Michael reactions between curcumins and nitrochromenes in the presence of Cs2CO3 and DBU, respectively, at room temperature, and it offers a diverse array of products as single regio- and diastereomers in excellent yields under mild conditions. Preliminary studies towards developing an enantioselective version under organocatalytic conditions met with only limited success but revealed a potentially interesting kinetic resolution pathway. © 2023 The Royal Society of Chemistry.

6) Smirnova, E., Moniruzzaman, M., Chin, S., Sureshbabu, A., Karthikeyan, A., Do, K., Min, T.
A Review of the Role of Curcumin in Metal Induced Toxicity
(2023) *Antioxidants*, 12 (2), art. no. 243, .

Abstract
Metal toxicity poses a potential global threat to the environment and living beings. Their numerous agricultural, medical, industrial, domestic, and technological applications result in widespread distribution in the environment which raises concern on the potential effects of metals in terms of health hazards and environmental pollution. Chelation therapy has been the preferred medical treatment for metal poisoning. The chelating agent bounds metal ions to form complex cyclic structures known as ‘chelates’ to intensify their excretion from the body. The main disadvantage of synthetic chelators is that the chelation process removes vital nutrients along with toxic metals. Natural compounds are widely available, economical, and have minimal adverse effects compared to classical chelators. Herbal preparations can bind to the metal, reduce its absorption in the intestines, and facilitate excretion from the body. Curcumin, a bioactive substance in turmeric, is widely used as a dietary supplement. Most studies have shown that curcumin protects against metal-induced lipid peroxidation and mitigates adverse effects on the antioxidant system. This review article provides an analysis to show that curcumin imparts promising metal toxicity-ameliorative effects that are related to its intrinsic antioxidant activity. © 2023 by the authors.

7) Debnath, S., Kant, A., Bhowmick, P., Malakar, A., Purkaystha, S., Jena, B.K., Mudgal, G., Rahimi, M., Helal, M.M.U., Hasan, R., Chen, J.-T., Azam, F.
The Enhanced Affinity of WRKY Reinforces Drought Tolerance in Solanum lycopersicum L.: An Innovative Bioinformatics Study
(2023) *Plants*, 12 (4), art. no. 762, .

Abstract
In the scenario of global climate change, understanding how plants respond to drought is critical for developing future crops that face restricted water resources. This present study focuses on the role of WRKY transcription factors on drought tolerance in tomato, Solanum lycopersicum L., which is a significant vegetable crop. WRKY transcription factors are a group of proteins that regulate a wild range of growth and developmental processes in plants such as seed germination and dormancy and the stress response. These transcription factors are defined by the presence of a DNA-binding domain, namely, the WRKY domain. It is well-known that WRKY transcription factors can interact with a variety of proteins and therefore control downstream activities. It aims to simulate the effect of curcumin, a bioactive compound with regulatory capacity, on the protein–protein interaction events by WRKY transcription factors with an emphasis on drought stress. It was found that curcumin binds to WRKY with an energy of −11.43 kcal/mol with inhibitory concentration (Ki) 0.12 mM and has the potential to improve fruit quality and reinforce drought tolerance of S. lycopersicum, according to the results based on bioinformatics tools. The root means square deviation (RMSD) of the C-α, the backbone of 2AYD with ligand coupled complex, displayed a very stable structure with just a little variation of 1.89 Å. MD simulation trajectory of Cα atoms of 2AYD bound to Curcumin revealed more un-ordered orientation in PC1 and PC10 modes and more toward negative correlation from the initial 400 frames during PCA. Establishing the binding energies of the ligand–target interaction is essential in order to characterize the compound’s binding affinity to the drought transcription factor. We think we have identified a phyto-agent called curcumin that has the potential to enhance the drought tolerance. Compared to the part of the mismatch repair-base technique that can be used to fix drought related genes, curcumin performed better in a drop-in crop yield over time, and it was suggested that curcumin is a potential candidate factor for improving drought tolerance in tomatoes, and it needs future validation by experiments in laboratory and field. © 2023 by the authors.

8) Wendorff-Tobolla, L.M., Wolgin, M., Wagner, G., Klerings, I., Dvornyk, A., Kielbassa, A.M.
A Systematic Review and Meta-Analysis on the Efficacy of Locally Delivered Adjunctive Curcumin (Curcuma longa L.) in the Treatment of Periodontitis
(2023) *Biomedicines*, 11 (2), art. no. 481, .

Abstract
This meta-analysis intended to assess evidence on the efficacy of locally delivered curcumin/turmeric as an adjunctive to scaling and root planing (SRP), on clinical attachment level (CAL) and probing pocket depth (PPD), compared to SRP alone or in combination with chlorhexidine (CHX). RCTs were identified from PubMed, Cochrane Library, BASE, LIVIVO, Dentistry Oral Sciences Source, MEDLINE Complete, Scopus, ClinicalTrials.gov, and eLibrary, until August 2022. The risk of bias (RoB) was assessed with the Cochrane Risk of Bias tool 2.0. A random-effects meta-analysis was performed by pooling mean differences with 95% confidence intervals. Out of 827 references yielded by the search, 23 trials meeting the eligibility criteria were included. The meta-analysis revealed that SRP and curcumin/turmeric application were statistically significantly different compared to SRP alone for CAL (−0.33 mm; p = 0.03; 95% CI −0.54 to −0.11; I2 = 62.3%), and for PPD (−0.47 mm; p = 0.024; 95% CI −0.88 to −0.06; I2 = 95.5%); however, this difference was considered clinically meaningless. No significant differences were obtained between patients treated with SRP and CHX, compared to SRP and curcumin/turmeric. The RoB assessment revealed numerous inaccuracies, thus raising concerns about previous overestimates of potential treatment effects. © 2023 by the authors.

9) Mishra, A., Pathak, Y., Mishra, S.K., Prakash, H., Tripathi, V.
Natural compounds as a potential modifier of stem cells renewal: Comparative analysis
(2023) *European Journal of Pharmacology*, 938, art. no. 175412, .

Abstract
Cancer stem cells (CSCs) are indispensable for development, progression, drug resistance, and tumor metastasis. Current cancer-directed interventions target targeting rapidly dividing cancer cells and slow dividing CSCs, which are the root cause of cancer origin and recurrence. The most promising targets include several self-renewal pathways involved in the maintenance and renewal of CSCs, such as the Wnt/β-Catenin, Sonic Hedgehog, Notch, Hippo, Autophagy, and Ferroptosis. In view of safety, natural compounds are coming to the front line of treatment modalities for modifying various signaling pathways simultaneously involved in maintaining CSCs. Therefore, targeting CSCs with natural compounds is a promising approach to treating various types of cancers. In view of this, here we provide a comprehensive update on the current status of natural compounds that effectively tune key self-renewal pathways of CSCs. In addition, we highlighted surface expression markers in several types of cancer. We also emphasize how natural compounds target these self-renewal pathways to reduce therapy resistance and cancer recurrence properties of CSCs, hence providing valuable cancer therapeutic strategies. The inclusion of nutraceuticals is believed to enhance the therapeutic efficacy of current cancer-directed interventions significantly. © 2022 Elsevier B.V.

10) Boretti, A.
Evidence for the use of curcumin in radioprotection and radiosensitization
(2023) *Phytotherapy Research*, .

Abstract
Curcumin has antineoplastic properties and is considered a chemotherapeutic and chemopreventive agent. Curcumin may be associated with radiation therapy (RT) as a radiosensitizer for cancer cells and a radioprotector for normal cells. In principle, it may result in a reduction of RT dosage for the same therapeutic effect on cancer cells, and further reduced damage to normal cells. Though the overall level of evidence is modest, limited to in vivo and in vitro experiences and practically no clinical trials, as the risks of adverse effects are extremely low, it is reasonable to promote the general supplementation with curcumin during RT targeting the reduction of side effects through anti-inflammatory mechanisms. © 2023 John Wiley & Sons Ltd.

11) Pavan Kumar, V., Harikrishnan, N.
Nano-Phytoconstituents and its recent advancement in Anticancer efficacy
(2023) *Research Journal of Pharmacy and Technology*, 16 (1), pp. 447-452.

Abstract
Cancer is intense fitness trouble that is still considered to be the main reason for its demise worldwide. Nanotechnology considered as rising disciplines in technology and generation, which may be implemented to synthesize new materials on the nanoscale level. The application of nanotechnology in the treatment of several types of cancers has acquired a significant interest in current years. Cancer nanotechnology is an upcoming unique technique with vast application towards most cancers thru in time diagnosis, estimation and inhibition with the help of personalized medications. Plant occurring natural compounds considered as phytochemicals, crucial assets for most cancers remedy. Some traditional examples consist of curcumin, resveratrol, flavonoids, celastrol, berberine, camptothecins, vinca alkaloids (vincristine and vinblastine), taxol derivatives, and podophyllotoxin derivatives. These phytoconstituents directly act on molecular pathways that are

inhibiting in increase and development of several cancers. Phytochemicals used in foods, supplements, and prescribed drugs is inadequate because of lower bioavailability, low solubility, less therapeutic efficacy, and stability problem. To get rid of these issues a modern and advanced novel delivery technique has been developed. These naturally occurring phytochemicals can be incorporated in the form of liposomes, niosomes, nanosomes, nanoparticles, and nanoemulsions to produce better therapeutic efficacy against cancer. This review focuses on the recent advancement and development of nanophytoconstituents in cancer therapy.

12) Guo, H., Li, Z., Yang, X.-G.
Crystal structure, photophysical properties, and DFT calculations of a boron difluoride curcumin complex
(2023) *Zeitschrift fur Naturforschung - Section B Journal of Chemical Sciences*, .

Abstract
The crystal structure of a curcumin-BF2 complex has been successfully refined from single-crystal X-ray diffraction data of crystals with one molecule of co-crystallized dichloromethane. The complex has a nearly coplanar structure. The molecules form a mesh structure by intermolecular multiple hydrogen bonds, as well as weak hydrogen bonds with CH2Cl2 molecules. An investigation of the photo-physical properties has indicated that the curcumin-BF2 complex possesses a wide absorption band and an intense red emission in the solid state due to a strong electron-withdrawing effect of the BF2 groups. DFT calculations of a single molecule verify the relationships between the photo-physical properties and its intrinsic electronic features, but neglect the role of hydrogen bonding. © 2023 Walter de Gruyter GmbH, Berlin/Boston 2023.

13) Lan, C., Qian, Y., Wang, Y., Chen, Y., Lin, C., Zhang, Y., Huang, X.
The protective role of curcumin in human dental pulp stem cells stimulated by lipopolysaccharide via inhibiting NF-κB p65 phosphorylation to suppress NLRP3 inflammasome activation
(2023) *Clinical Oral Investigations*, .

Abstract
Objectives: This study aims to investigate the anti-inflammatory effect of curcumin and underlying mechanisms regarding the modulation of the nod-like receptor pyrin domain containing 3 (NLRP3) inflammasome in human dental pulp stem cells (hDPSCs). Materials and methods: The impact of curcumin on the viability of hDPSCs was evaluated. The effect of curcumin on the expression of IL-1β and NLRP3 in hDPSCs stimulated by lipopolysaccharide (LPS) was assessed. Then, LPS-primed hDPSCs were pre-treated with curcumin before ATP triggering NLRP3 inflammasome activation, and NLRP3 inflammasome-related mediators were assessed. The mechanism of curcumin inactivation of LPS plus ATP-induced inflammasome associated with NF-κB pathway was explored. The NF-κB pathway related pro-inflammatory mediators at mRNA and protein levels were evaluated. The expression of NF-κB p65 and phosphorylation p65 was visualized after curcumin or NF-κB inhibitor administrating respectively in hDPSCs with an activated NLRP3 inflammasome. Statistical analysis was performed. Results: While curcumin at the concentration of 0.5–5 μM showed no obvious impact on the viability of hDPSCs, it significantly decreased IL-1β and NLRP3 mRNA expression in LPS-induced hDPSCs in a dose-dependent manner. Curcumin significantly inhibited the LPS plus ATP-primed NLRP3 inflammasome activation in hDPSCs (NLRP3, ASC, caspase-1, and IL-1β). Curcumin evidently attenuated the LPS plus ATP-induced expression of NF-κB pathway-related pro-inflammatory mediators (IL-6, IL-8, TNF-α, and COX-2). Furthermore, curcumin effectively reduced p65 phosphorylation, which acts as an NF-κB inhibitor in hDPSCs with an activated NLRP3 inflammasome. Conclusions: Curcumin pre-treatment may exert an anti-inflammatory role via inactivation of the NLRP3 inflammasome by inhibiting NF-κB p65 phosphorylation in cultured hDPSCs. Clinical relevance: Curcumin may have therapeutic potential in pulp inflammation. © 2023, The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature.

14) Osali, A., Rostami, A.
Effect of 6 weeks of aerobic training with nanocurcumin consumption on IL1β, nitric oxide, and depression in women with metabolic syndrome
(2023) *International Journal of Diabetes in Developing Countries*, .

Abstract
Backgrounds and Objectives: The use of anti-inflammatory supplements is important in improving the executive function of obese people. This research aims to investigate the effect of 6 weeks of aerobic exercise with moderate intensity as well as the consumption of nanocurcumin on IL1β, nitric oxide (NO), and depression in women aged 60–65 with metabolic syndrome. Materials and Methods: Fourty-four women with metabolic syndrome were randomly selected and divided into four groups of 10 based on their use of nanocurcumin supplement. The treatment included the training (T), nanocurcumin (N), training + nanocurcumin (TN), and the control groups. The groups exposed to training performed aerobic exercise for 6 weeks (three sessions per week). Blood samples were obtained before and after the training period for antioxidant indicators and lipid degradation measurement. Also, the Beck anxiety questionnaire was used for evaluating levels of anxiety. T-test and one-way analysis of variance (ANOVA) tests were used for the assessment of within-group and between-group differences, respectively. Results: There was a significant difference in IL1β, NO, and depression before and after exercise in all three experimental groups ($p \leq 0.05$). Also, the results showed a significant difference in the level of NO and depression in the experimental groups. The highest decrease in these variables was observed in the T and TN groups ($p \leq 0.05$). Conclusion: These findings indicated that 6-week nanocurcumin supplementation with aerobic training is a suitable method for reducing IL1β, NO, and depression, preventing metabolic, cardiovascular, and inflammatory diseases in women with metabolic syndrome. Name of the registry: IR.SEMUMS.REC.1396.107 Trial registration number: IRCT2017082335857N1. © 2023, The Author(s), under exclusive licence to Research Society for Study of Diabetes in India.

15) More, S., Pawar, A.
Brain Targeted Curcumin Loaded Turmeric Oil Microemulsion Protects Against Trimethyltin Induced Neurodegeneration in Adult Zebrafish: A Pharmacokinetic and Pharmacodynamic Insight
(2023) *Pharmaceutical Research*, .

Abstract
Purpose: Aromatic turmerone, a major constituent of turmeric oil, has been recently reported for proliferation of neural stem cell showing great potential for effective treatment in neurodegenerative disorders. However, its effect as oral brain targeted formulation for neuroprotection has not yet reported. The objective of the study was to investigate the pharmacokinetic of curcumin loaded turmeric oil microemulsion for brain targeting and probing the protective effect against trimethyltin induced neurodegeneration in adult zebrafish. Methods: Initially, in vivo plasma and brain pharmacokinetics was performed to determine improvement in relative bioavailability in rats followed by biodistribution and histopathological evaluation. Furthermore, the neuroprotective effect of the formulation was assessed in trimethyltin induced neurodegeneration model using adult zebrafish by behavioral analysis and biochemical analysis. Results: The in vivo plasma and brain pharmacokinetics showed 2-fold and 1.87-fold improvement respectively. Biodistribution study revealed significantly lower concentration in organs other than brain. Furthermore, curcumin microemulsion exhibited improved spatial memory by remembering the training and made correct choices after curcumin microemulsion treatment than other treatment groups. Histopathological evaluation confirmed neuroprotective effect on zebrafish brains. The biochemical analysis revealed reduced oxidative stress in curcumin microemulsion treated group. Conclusions: Overall results showed a great potential of curcumin microemulsion for brain targeting in the effective treatment of neurological ailments. © 2023, The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

16) Bilajac, E., Mahmutović, L., Glamočlija, U., Osmanović, A., Hromić-Jahjefendić, A., Tambuwala, M.M., Suljagić, M.
Curcumin Decreases Viability and Inhibits Proliferation of Imatinib-Sensitive and Imatinib-Resistant Chronic Myeloid Leukemia Cell Lines
(2023) *Metabolites*, 13 (1), art. no. 58, .

Abstract
Chronic myeloid leukemia (CML) is a myeloproliferative haematological malignancy characterized by constitutive activation of BCR-ABL1 tyrosine kinase in the majority of patients. BCR-ABL1 expression activates signaling pathways involved in cell proliferation and survival. Current treatment options for CML include tyrosine kinase inhibitors (TKI) with resistance as a major issue. Various treatment options for overcoming resistance are being investigated. Among them, phytochemical curcumin could play an important role. Curcumin has been found to exhibit anti-cancerous effects in various models, including CML, through regulation of multiple molecular signaling pathways contributing to tumorigenesis. We have evaluated curcumin's effects on imatinib-sensitive LAMA84S and K562, as well as imatinib-resistant LAMA84R cell lines. Our results indicate a significant dose-dependent decrease in cell viability and proliferation of imatinib-sensitive and imatinib-resistant cell lines after curcumin treatment. Suppression of key signaling molecules regulating metabolic and proliferative events, such as Akt, P70S6K and NF-kB, was observed. Increased expression of caspase-3 suggests the potential pro-apoptotic effect of curcumin in the imatinib-resistant CML model. Additional in silico molecular docking studies revealed binding modes and affinities of curcumin with different targets and the results are in accordance with in vitro findings. Altogether, these results indicate the potential role of curcumin in the treatment of CML. © 2022 by the authors.

17) Franck, T., Ceusters, J., Graide, H., Niesten, A., Duysens, J., Mickalad, A.M., Serteyn, D.
Equine Muscle Derived Mesenchymal Stem Cells Loaded with Water-Soluble Curcumin: Modulation of Neutrophil Activation and Enhanced Protection against Intracellular Oxidative Attack
(2023) *International Journal of Molecular Sciences*, 24 (2), art. no. 1030, .

Abstract
We investigated the antioxidant potential of equine mesenchymal stem cells derived from muscle microbiopsies (mdMSCs), loaded by a water-soluble curcumin lysinate incorporated into hydroxypropyl-β-cyclodextrin (NDS27). The cell loading was rapid and dependent on NDS27 dosage (14, 7, 3.5 and 1 µM). The immunomodulatory capacity of loaded mdMSCs was evaluated by ROS production, on active and total myeloperoxidase (MPO) degranulation and neutrophil extracellular trap (NET) formation after neutrophil stimulation. The intracellular protection of loaded cells was tested by an oxidative stress induced by cumene hydroperoxide. Results showed that 10 min of mdMSC loading with NDS27 did not affect their viability while reducing their metabolism. NDS27 loaded cells in presence of 14, 7 µM NDS27 inhibited more intensively the ROS production, the activity of the MPO released and bound to the NET after neutrophil stimulation. Furthermore, loaded cells powerfully inhibited intracellular ROS production induced by cumene as compared to control cells or cyclodextrin-loaded cells. Our results showed that the loading of mdMSCs with NDS27 significantly improved their antioxidant potential against the oxidative burst of neutrophil and protected them against intracellular ROS production. The improved antioxidant protective capacity of loaded mdMSCs could be applied to target inflammatory foci involving neutrophils. © 2023 by the authors.

18)

Sideek, S.A., El-Nassan, H.B., Fares, A.R., ElMeshad, A.N., Elkasabgy, N.A.
Different Curcumin-Loaded Delivery Systems for Wound Healing Applications: A Comprehensive Review
(2023) *Pharmaceutics*, 15 (1), art. no. 38, .

Abstract
Curcumin or turmeric is the active constituent of Curcuma longa L. It has marvelous medicinal applications in many diseases. When the skin integrity is compromised due to either acute or chronic wounds, the body initiates several steps leading to tissue healing and skin barrier function restoration. Curcumin has very strong antibacterial and antifungal activities with powerful wound healing ability owing to its antioxidant activity. Nevertheless, its poor oral bioavailability, low water solubility and rapid metabolism limit its medical use. Tailoring suitable drug delivery systems for carrying curcumin improves its pharmaceutical and pharmacological effects. This review summarizes the most recent reported curcumin-loaded delivery systems for wound healing purposes, chiefly hydrogels, films, wafers, and sponges. In addition, curcumin nanoformulations such as nanohydrogels, nanoparticles and nanofibers are also presented, which offer better solubility, bioavailability, and sustained release to augment curcumin wound healing effects through stimulating the different healing phases by the aid of the small carrier. © 2022 by the authors.

19) Abidin, N.A.Z., Kormin, F., Abidin, N.A.Z., Bakar, M.F.A., Iwansyah, A.C.
Anti-tyrosinase Activities of Curcumin-Chitosan Gold Nanoparticles Synthesized from Beetle (Oryctes rhinoceros)
(2023) *Asian Journal of Chemistry*, 35 (1), pp. 79-82.

Abstract
A breakthrough in cosmeceuticals by utilizing insects as major ingredients in cosmetic products is gaining popularity. Therefore, the interest in rare sources of ingredients, for instance, from the Oryctes rhinoceros beetle, can bring huge benefit in turning pest to wealth. In this study, curcumin was chosen as the active ingredient loaded into chitosan-gold nanoparticles (CCG-NPs). However, curcumin is unstable, has poor absorption, a high rate of metabolism and high sensitivity to light. These are all factors that contribute to the lower bioavailability of any substance to reach the target cells. Therefore, chitosan extracted from O. rhinoceros acts as a drug carrier and incorported in gold nanoparticles are used to overcome these problems. The CCG-NPs were successfully synthesized at 70°C for 60 min under optimal conditions of reactant ratio of 2:0.5 (0.5 mM HAuCl4:0.1% curcumin). The tyrosinase enzyme inhibition of CCG-NPs from O. rhinoceros was 66.385 ± 3.0%. Thus showing a good inhibition trait for the anti-tyrosinase assay as it is almost double the tyrosinase inhibition percentage when being compared to CCG-NPs from the commercial chitosan. Therefore, CCG-NPs from O. rhinoceros has a high potential in cosmeceutical applications as whitening agent. © 2023 Chemical Publishing Co.. All rights reserved.

20) Ezati, M., Ghavamipour, F., Khosravi, N., Sajedi, R.H., Chalabi, M., Farokhi, A., Adibi, H., Khodarahmi, R.
Synthesis and Potential Antidiabetic Properties of Curcumin-Based Derivatives: An In Vitro and In Silico Study of α-Glucosidase and α-Amylase Inhibition
(2023) *Medicinal Chemistry*, 19 (1), pp. 99-117.

Abstract
Background: Over the past twenty years, the prevalence of diabetes as one of the most common metabolic diseases has become a public health problem worldwide. Blood glucose control is important in delaying the onset and progression of diabetes-related complications. α-Glycosidase (α-Glu) and α-amylase (α-Amy) are important enzymes in glucose metabolism. Diabetic control through the inhibition of carbohydrate hydrolyzing enzymes is established as an effective strategy. Methods: In this study, curcumin-based benzaldehyde derivatives with high stability, bioavailability, and favorable efficiency were synthesized. Results: The results showed that L13, L8, and L11 derivatives have the highest inhibitory effect on α-Glu with IC50 values of 18.65, 20.6, and 31.7 μM and, also L11, L13, and L8 derivatives have the highest inhibitory effect on α-Amy with IC50 value of 14.8, 21.8, and 44.9 μM respectively. Further-more, enzyme inhibitory kinetic characterization was also performed to understand the mechanism of enzyme inhibition. Conclusion: L13, compared to the other compounds, exhibited acceptable inhibitory activity against both enzymes. The L13 derivative could be an appropriate candidate for further study through the rational drug design to the exploration of a new class of powerful anti-diabetic drugs considering the antioxidant properties of the synthesized compounds. The derivative helps reduce the glycemic index and limits the activity of the major reactive oxygen species (ROS) producing pathways. © 2023 Bentham Science Publishers.

21) Bissacotti, B.F., Copetti, P.M., Bottari, N.B., Palma, T.V., Pillat, M.M., de Andrade, C.M., Morsch, V.M.M., Ulrich, H., da Silva, A.S.
Curcumin modulates neurogliogenesis and purinergic receptor expression in neural precursor cells infected with Toxoplasma gondii
(2023) *Parasitology Research*, 122 (1), pp. 77-84.

Abstract
Toxoplasma gondii is an obligate intracellular parasite that causes toxoplasmosis, and its congenital transmission is of paramount concern. During embryonic development, infection with the parasite causes irreversible damage to the still-forming fetus's central nervous system (CNS). In the pathogenesis of neurotoxoplasmosis, purinergic receptors prejudice neuroprotection, neuroinflammation, and activation of microbicide mechanisms against the parasitic vacuole. This study used curcumin as a treatment for neural precursor cells (NPCs) infected with T. gondii. The congenital toxoplasmosis induction consisted of maternal infection with the VEG strain, and NPCs were obtained from the telencephalon of mouse

embryos. Curcumin at increasing concentrations was administered in vitro to analyze NPC metabolic activity, cell number, and size, as well as neurogliogenesis, proving to be effective in recovering the size of infected NPCs. Curcumin partially re-established impaired neurogenesis. Purinergic A1, A2A, and P2X7 receptors may be related to neuroprotection, neuroinflammatory control, and activation of mechanisms for inducing the parasite's death. ERK 1/2 was highly expressed in infected cells, while its expression rates decreased after the addition of the treatment, highlighting the possible anti-inflammatory action of curcumin. These findings suggest that curcumin treats neurological perturbations induced by toxoplasmosis.

22) Yusuf, M., Sadiya, Ahmed, B., Gulfishan, M.
Modern perspectives of curcumin and its derivatives as promising bioactive and pharmaceutical agents
(2022) *Biointerface Research in Applied Chemistry*, 12 (6), pp. 7177-7204.

Abstract
In the current era of eco-preservation, global research has focused on using raw and sustainable natural products with new clean technologies. New pharmaceutical or pharmaceutical agents from renewable sources are considered as essential as pure chemicals or certified fragments. A variety of natural phytoconstituents have been shown to reduce the risk of certain diseases and disorders, for example, diabetes, heart disease, cancer, neoplastic, and other health disorders. And, therefore, ongoing efforts to identify specific chemicals in these foods may contribute to their positive effects on beans/grains, fruits, vegetables, etc. Many of the phytochemicals that occurred as natural products in medicinal plants offer many opportunities in natural product research due to their versatile uses and various formulation. Curcuminoids are polyphenols found in the under-soil rhizome of Curcuma longa L. and have been used for centuries for spice, culinary, and food coloring purposes, and description also documented in the alternative system of medicines such as Indian Ayurveda, Sidha, Unani, and Chinese medicine system. It has been observed from the literature that the C. longa rhizome or commonly known as turmeric has several phytochemicals to possess anti-inflammatory, hepatoprotective, neuroprotective, antioxidant, anticancer, cardioprotective properties, and many more. The review highlights the recent progress of curcumin and its derivatives as promising bioactive and pharmaceutical agents with emphasis on future research dimensions required to propose curcuminoids as promising candidates for therapeutic and pharmacology-related sectors. © 2021 by the authors.

23) Hussain, Y., Abdullah, Khan, F., Alsharif, K.F., Alzahrani, K.J., Saso, L., Khan, H.
Regulatory Effects of Curcumin on Platelets: An Update and Future Directions
(2022) *Biomedicines*, 10 (12), art. no. 3180, .

Abstract
The rhizomatous plant turmeric, which is frequently used as a spice and coloring ingredient, yields curcumin, a bioactive compound. Curcumin inhibits platelet activation and aggregation and improves platelet count. Platelets dysfunction results in several disorders, including inflammation, atherothrombosis, and thromboembolism. Several studies have proved the beneficial role of curcumin on platelets and hence proved it is an important candidate for the treatment of the aforementioned diseases. Moreover, curcumin is also frequently employed as an anti-inflammatory agent in conventional medicine. In arthritic patients, it has been shown to reduce the generation of pro-inflammatory eicosanoids and to reduce edema, morning stiffness, and other symptoms. Curcumin taken orally also reduced rats' acute inflammation brought on by carrageenan. Curcumin has also been proven to prevent atherosclerosis and platelet aggregation, as well as to reduce angiogenesis in adipose tissue. In the cerebral microcirculation, curcumin significantly lowered platelet and leukocyte adhesion. It largely modulated the endothelium to reduce platelet adhesion. Additionally, P-selectin expression and mice survival after cecal ligation and puncture were improved by curcumin, which also altered platelet and leukocyte adhesion and blood–brain barrier dysfunction. Through regulating many processes involved in platelet aggregation, curcuminoids collectively demonstrated detectable antiplatelet activity. Curcuminoids may therefore be able to prevent disorders linked to platelet activation as possible therapeutic agents. This review article proposes to highlight and discuss the regulatory effects of curcumin on platelets. © 2022 by the authors.

24) Liu, Z., Lansley, A.B., Duong, T.N., Smart, J.D., Pannala, A.S.
Increasing Cellular Uptake and Permeation of Curcumin Using a Novel Polymer-Surfactant Formulation
(2022) *Biomolecules*, 12 (12), art. no. 1739, .

Abstract
Several therapeutically active molecules are poorly water-soluble, thereby creating a challenge for pharmaceutical scientists to develop an active solution for their oral drug delivery. This study aimed to investigate the potential for novel polymer-surfactant-based formulations (designated A and B) to improve the solubility and permeability of curcumin. A solubility study and characterization studies (FTIR, DSC and XRD) were conducted for the various formulations. The cytotoxicity of formulations and commercial comparators was tested via MTT and LDH assays, and their permeability by in vitro drug transport and cellular drug uptake was established using the Caco-2 cell model. The apparent permeability coefficients (Papp) are considered a good indicator of drug permeation. However, it can be argued that the magnitude of Papp, when used to reflect the permeability of the cells to the drug, can be influenced by the initial drug concentration (C0) in the donor chamber. Therefore, Papp (suspension) and Papp (solution) were calculated based on the different values of C0. It was clear that Papp (solution) can more accurately reflect drug permeation than Papp (suspension). Formulation A, containing Soluplus® and vitamin E TPGs, significantly increased the permeation and cellular uptake of curcumin compared to other samples, which is believed to be related to the increased aqueous solubility of the drug in this formulation. © 2022 by the authors.

25) Le-Tan, H., Jaeger, H.
Impact of Cell Disintegration Techniques on Curcumin Recovery
(2022) *Food Engineering Reviews*, 14 (4), pp. 655-672.

Abstract
In recent years, the improvement of curcumin recovery from turmeric by cell and tissue disintegration techniques has been gaining more attention; these emerging techniques were used for a reproducible and robust curcumin extraction process. Additionally, understanding the material characteristics is also needed to choose the optimized technique and appropriate processing parameters. In this review, an outlook about the distribution of different fractions in turmeric rhizomes is reviewed to explain matrix challenges on curcumin extraction. Moreover, the most important part, this review provides a comprehensive summary of the latest studies on ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), enzyme-assisted extraction (EAE), high-pressure-assisted extraction (HPAE), pulsed electric field-assisted extraction (PEFAE), and ohmic heating-assisted extraction (OHAE). Lastly, a detailed discussion about the advantages and disadvantages of emerging techniques will provide an all-inclusive understanding of the food industry's potential of different available processes. © 2022, The Author(s).

26) Nanavati, K., Rutherfurd-Markwick, K., Lee, S.J., Bishop, N.C., Ali, A.
Effect of curcumin supplementation on exercise-induced muscle damage: a narrative review
(2022) *European Journal of Nutrition*, 61 (8), pp. 3835-3855.

Abstract
Curcumin, a natural polyphenol extracted from turmeric, is a potent antioxidant and anti-inflammatory agent. In the past few decades, curcumin's ability to impact chronic inflammatory conditions such as metabolic syndrome, arthritis, and cancer has been widely researched, along with growing interest in understanding its role in exercise-induced muscle damage (EIMD). EIMD impacts individuals differently depending on the type (resistance exercise, high-intensity interval training, and running), intensity, and duration of the exercise. Exercise disrupts the muscles' ultrastructure, raises inflammatory cytokine levels, and can cause swelling in the affected limb, a reduction in range of motion (ROM), and a reduction in muscular force-producing capacity. This review focuses on the metabolism, pharmacokinetics of various brands of curcumin supplements, and the effect of curcumin supplementation on EIMD regarding muscle soreness, activity of creatine kinase (CK), and production of inflammatory markers. Curcumin supplementation in the dose range of 90–5000 mg/day can decrease the subjective perception of muscle pain intensity, increase antioxidant capacity, and reduce CK activity, which reduces muscle damage when consumed close to exercise. Consumption of curcumin also improves muscle performance and has an anti-inflammatory effect, downregulating the production of pro-inflammatory cytokines, including TNF-α, IL-6, and IL-8. Curcumin may also improve oxidative capacity without hampering training adaptations in untrained and recreationally active individuals. The optimal curcumin dose to ameliorate EIMD is challenging to assess as its effect depends on the curcumin concentration in the supplement and its bioavailability. © 2022, The Author(s).

27) Maddheshiya, S., Ahmad, A., Ahmad, W., Zakir, F., Aggarwal, G.
Essential oils for the treatment of skin anomalies: Scope and potential
(2022) *South African Journal of Botany*, 151, pp. 187-197.

Abstract
Skin diseases contribute significantly to worldwide morbidity and mortality. It is the most common of all human diseases which can affect people of any age group. Most importantly, it is seen that the COVID-19 pandemic have further detrimentally contributed to dermatological manifestations. Due to the enormous socioeconomic burden created by skin disorders, the dermatological treatments have been added in the WHO List of Essential Medicines. Some of the major predominant diseases are acne, psoriasis, eczema, fungal infections and skin carcinoma. As a matter of fact, focus on treatment of skin diseases should be arguably considered as a matter of global urgency. Although treatments are available, they face numerous challenges which limit patient acceptability. Essential oils have a long history of pharmacological use; however their role in the treatment of dermatological disorders is vague. Therefore, in this review, the potential and mechanism of different essential oils obtained from various sources in the treatment of major dermal disorders has been summarized. This will help the formulation scientists and the clinicians to develop suitable formulation strategies for the prevention and cure of skin diseases. © 2021 SAAB

28) Nyankson, E., Awuzah, D., Tiburu, E.K., Efavi, J.K., Agyei-Tuffour, B., Paemka, L.
Curcumin loaded Ag-TiO2-halloysite nanotubes platform for combined chemo-photodynamic therapy treatment of cancer cells
(2022) *RSC Advances*, 12 (51), pp. 33108-33123.

Abstract
The use of naturally occurring anticancer materials in combination with doped metal oxide has emerged as one of the most promising ways for improving anticancer treatment efficacy. In this study, the anticancer potential of curcumin-loaded Ag-TiO2-halloysite nanotubes (curcumin-loaded Ag-TiO2-HNTs) was examined. Ag-TiO2-HNTs with different wt% of Ag-TiO2

were synthesized and characterized using XRD, TGA, FT-IR, UV-Vis spectroscopy, and SEM-EDX. The XRD results revealed the presence of crystalline TiO2. However, the presence of Ag was detected through the SEM-EDX analysis. Cyclic voltammetry measurements suggested the enhancement of the release of ROS from TiO2 upon deposition with Ag. FT-IR and TGA analysis confirmed the successful loading of curcumin inside the nanotubes of the halloysite. In vitro drug released studies revealed the release of approximately 80-99% curcumin within 48 hours. Kinetic model studies revealed that the release of curcumin from HNT and Ag-TiO2-HNT followed the first-order and Higuchi models, respectively. The light irradiated curcumin-loaded Ag-TiO2-HNTs samples exhibited considerable anticancer potential as compared to the free curcumin, irradiated Ag-TiO2 NPs samples, and unirradiated curcumin loaded Ag-TiO2-HNTs samples. The obtained results revealed that combined chemo- and photodynamic therapy using curcumin-loaded Ag-TiO2-HNTs nanomaterial has the potential as an effective anticancer treatment method. © 2022 The Royal Society of Chemistry.

29) Ramezani, M., Zainodini, N., Nosratabadi, R., Yousefpoor, Y., Taghipour, Z., Abbasifard, M., Rahmani, M.R.
Phytosomal curcumin alleviates collagen-induced arthritis by downregulating Th17 and upregulating Treg cell responses in rats
(2022) *Asian Pacific Journal of Tropical Biomedicine*, 12 (11), pp. 466-474.

Abstract
Objective: To explore the effects of a nano-formulation of curcumin (phytosomal curcumin) on the clinical and pathological symptoms of collagen-induced arthritis (CIA) in rats. Methods: Forty male Wistar rats were immunized with an emulsion containing bovine type II collagen and incomplete Freund's adjuvant and then administered phytosomal curcumin post-immunization. Clinical symptoms and histological analysis of the synovial tissues were performed. The effect of phytosomal curcumin on Th17 and Treg parameters was also evaluated. Results: Phytosomal curcumin reduced the clinical severity and paw swelling in CIA-induced rats, which was accompanied by a reduction in the number of inflammatory cell infiltration in the synovial tissue. Additionally, treatment with phytosomal curcumin significantly inhibited CIA-associated mediators as well as increased the anti-inflammatory mediators in comparison to the control groups. Conclusions: Phytosomal curcumin could improve CIA autoimmune responses and can be considered a potential candidate for the treatment of rheumatoid arthritis.

30) Rambaran, V.H., Singh, N.K.
Alternative medicines for diabetes management: Advances in pharmacognosy and medicinal chemistry
(2022) *Alternative Medicines for Diabetes Management: Advances in Pharmacognosy and Medicinal Chemistry*, pp. 1-218.

Abstract
Apart from diet and exercise, the strategic use of different classes of prescribed or non-prescribed xenobiotic compounds for the restoration of euglycemic levels in the body is well known. The ongoing rivalry between the recommended usage of allopathic medicines versus ayurvedic remedies has encouraged many researchers to focus their studies on thoroughly isolating and characterizing the extracts from different parts of plants and then evaluating their relative activities via in vitro, in vivo and in some cases clinical studies. Alternative Medicines for Diabetes Management: Advances in Pharmacognosy and Medicinal Chemistry provides a holistic view of all oral therapies for diabetes mellitus that are available to the public by removing the silos and stigmas that are associated with both allopathic and ayurvedic medicines. Additional Features Include: • Highlights the potential role of dietary and medicinal plant materials in the prevention, treatment, and control of diabetes and its complications. • Educates readers on the benefits and shortcomings of the various present and potential oral therapies for diabetes mellitus. • Allows quick identification and retrieval of material by researchers learning the efficacy, associated dosage and toxicity of each of the classes of compounds. • Presents the history, nomenclature, mechanisms of action and shortcomings for each of the various sub-classes of allopathic therapeutants for diabetes mellitus and then introduces ayurvedic medicines. • Section C discusses various metallopharmaceuticals and provides a holistic view of all available and potential therapies for the disease.

31) Goodman, J.F., Wang, M.B.
Complementary and Integrative Medicine in Head and Neck Cancer
(2022) *Otolaryngologic Clinics of North America*, 55 (5), pp. 993-1006.

32) Vavilala, P., Deo, A., Prakash, D., Tiwari, M., Aggarwal, V.
Antifungal Role of Common Indian Spices & Herbs: A Narrative Review
(2022) *Current Nutrition and Food Science*, 18 (8), pp. 715-727.

Abstract
A large variety of spices can be found in kitchens worldwide. The usage varies from region to region as per the cuisine. They hold nutritional values and are being exploited for their anticancer, antifungal, antibacterial, antiulcer, anti-inflammatory properties. This study highlights some of the commonly used Indian spices for their antifungal properties and summarizes their potential antifungal activity. Fungal diseases are deep-rooted and cause acute/chronic infections in humans, mainly Aspergillus and Candida species. As the tropical climate provides a breeding ground for fungal infections, such regions share a huge load of mycoses. Various spices have been shown to be effective in treating fungal diseases. The current study focuses on the potential anti-fungal role of the spices and reviews the current literature on the possible mechanism of

action of the active compounds of these spices relative to commonly used antifungal drugs. The spices consist of essential oils that inhibit mycotoxin biosynthesis or disrupt and inhibit cell wall formation and efflux pumps and are comparable to the currently available antifungal drugs. © 2022 Bentham Science Publishers.

33) Piwowarczyk, L., Stawny, M., Piwowarczyk, K., Mlynarczyk, D.T., Muszalska-Kolos, I., Wierzbicka, M., Goslinski, T., Jelinska, A.
Role of curcumin in selected head and neck lesions. Limitations on the use of the Hep-2 cell line: A critical review
(2022) *Biomedicine and Pharmacotherapy*, 154, art. no. 113560, .

Abstract
Neoplastic diseases of the upper respiratory airways, as well as head and neck cancers, are a frequent cause of death and significantly affect the quality of life of both patients and survivors. As the frequency increases, new and improved treatment techniques are sought. Promising properties in this respect are expressed by a natural compound – curcumin. Along with its derivatives, it was found useful in the treatment of a series of cancers. Curcumin was found to be effective in clinical trials and in vitro, in vivo anticancer experiments. Nanoformulations (e.g., poly(lactide-co-glycolic acid)-based nanoparticles, nanoemulsions), and modifications of curcumin, as well as its combinations with other substances (e.g., catechins, cisplatin) or treatments (e.g., radiotherapy or local use in inhalation), were found to enhance the antitumor effect. This review aims to summarize the recent findings for the treatment of head and neck diseases, especially squamous cell carcinomas (HNSCCs), including drawing attention to the constant use of the misidentified Hep-2 cell line and proposing databases purposed at eliminating this problem. Moreover, this manuscript focuses on pointing out the molecular mechanisms of therapy that have been reached and emphasizing the shortcomings that still need to be addressed. © 2022 The Authors

34) Rahman, M.M., Sarker, M.T., Alam Tumpa, M.A., Yamin, M., Islam, T., Park, M.N., Islam, M.R., Rauf, A., Sharma, R., Cavalu, S., Kim, B.
Exploring the recent trends in perturbing the cellular signaling pathways in cancer by natural products
(2022) *Frontiers in Pharmacology*, 13, art. no. 950109, .

Abstract
Cancer is commonly thought to be the product of irregular cell division. According to the World Health Organization (WHO), cancer is the major cause of death globally. Nature offers an abundant supply of bioactive compounds with high therapeutic efficacy. Anticancer effects have been studied in a variety of phytochemicals found in nature. When Food and Drug Administration (FDA)-approved anticancer drugs are combined with natural compounds, the effectiveness improves. Several agents have already progressed to clinical trials based on these promising results of natural compounds against various cancer forms. Natural compounds prevent cancer cell proliferation, development, and metastasis by inducing cell cycle arrest, activating intrinsic and extrinsic apoptosis pathways, generating reactive oxygen species (ROS), and down-regulating activated signaling pathways. These natural chemicals are known to affect numerous important cellular signaling pathways, such as NF-B, MAPK, Wnt, Notch, Akt, p53, AR, ER, and many others, to cause cell death signals and induce apoptosis in pre-cancerous or cancer cells without harming normal cells. As a result, non-toxic “natural drugs” taken from nature’s bounty could be effective for the prevention of tumor progression and/or therapy of human malignancies, either alone or in combination with conventional treatments. Natural compounds have also been shown in preclinical studies to improve the sensitivity of resistant cancers to currently available chemotherapy agents. To summarize, preclinical and clinical findings against cancer indicate that natural-sourced compounds have promising anticancer efficacy. The vital purpose of these studies is to target cellular signaling pathways in cancer by natural compounds. Copyright © 2022 Rahman, Sarker, Alam Tumpa, Yamin, Islam, Park, Islam, Rauf, Sharma, Cavalu and Kim.

35) Sharma, P., Kumar, D., Shri, R., Kumar, S.
Mechanistic Insights and Docking Studies of Phytomolecules as Potential Candidates in the Management of Cancer
(2022) *Current Pharmaceutical Design*, 28 (33), pp. 2704-2724.

Abstract
Background: Cancer is a leading risk of death globally. According to the World Health Organization, it is presently the second most important disease that causes death in both developing and developed countries. Remarkable progress has been made in the war against cancer with the development of numerous novel chemotherapy agents. However, it remains an immense challenge to discover new efficient therapeutic potential candidates to combat cancer. Objectives: The majority of the currently used anticancer drugs are of natural origins, such as curcumin, colchicine, vinca alkaloid, paclitaxel, bergenin, taxols, and combretastatin. Concerning this, this review article presents the structure of the most potent molecules along with IC50 values, structure-activity relationships, mechanistic studies, docking studies, in silico studies of phytomolecules, and important key findings on human cancer cell lines. Methods: A viewpoint of drug design and development of antiproliferative agents from natural phytomolecules has been established by searching peer-reviewed literature from Google Scholar, PubMed, Scopus, Springer, Science Direct, and Web of Science over the past few years. Results: Our analysis revealed that this article would assist chemical biologists and medicinal chemists in industry and academia in gaining insights into the anticancer potential of phytomolecules. Conclusion: In vitro and in silico studies present phytomolecules, such as curcumin, colchicine, vinca alkaloids, colchicine, bergenin, combretastatin, and taxol encompassing anticancer agents, offerings abundant sanguinity and capacity in the arena of drug discovery to inspire the investigators towards the continual investigations on these phytomolecules. It is extremely expected that efforts in this track

will strengthen and grant some budding cancer therapeutics candidates in the near future. © 2022 Bentham Science Publishers.

36) Tamiji, Z., Habibi, Z., Pourjabbar, Z., Khoshayand, M.R., Sadeghi, N., Hajimahmoodi, M.
Detection and quantification of adulteration in turmeric by spectroscopy coupled with chemometrics
(2022) *Journal fur Verbraucherschutz und Lebensmittelsicherheit*, 17 (3), pp. 221-230.

Abstract
One of the main food safety concerns is the extensive fraud in food production that necessitates the development of rapid and accurate diagnostic detection methods. Recently, the near-infrared spectroscopy has been used as a non-destructive method in combination with multivariate analysis methods to evaluate the quality of foods. Spices are very useful in our daily lives. They improve the flavor, color and nutritional value of the foods. Turmeric is a member of the ginger family and its main ingredient is a polyphenol, which is called curcumin and is widely used in the pharmaceutical industry. For commercial profit, this spice can be mixed with a variety of cheap and harmful additives. In this research, the ability of near-infrared spectroscopy as a cost effective, fast and non-destructive method in combination with chemometrics was investigated to monitor and control the adulteration of turmeric with wheat flour, pistachio hull waste and dry bread. For this purpose, the near-infrared spectrum from 54 adulterated mixtures and 102 samples purchased from Tehran supermarkets was measured in the range of 12,000–4000 cm−1. The spectra were pre-processed and principal component analysis (PCA) and partial least squares regression (PLSR) were used for qualitative and quantitative analysis, respectively. PCA in the first dataset, including all three sets of turmeric spectrum, explains 99% of the variance of spectral data. These results showed a very good discrimination in all three types of fraud based on different concentrations. According to the PCA model, most of the samples in the second dataset were either turmeric samples adulterated with dry bread powder or pure turmeric samples. Therefore, the PLSR model was used to quantify the turmeric samples adulterated with dry bread powder. In PLSR, the root mean square error and determination coefficient (R2) of calibration for validation and prediction were 0.265–0.306 and 97.9–98.6%, respectively. Therefore, this method is highly useful to detect adulteration in turmeric. © 2022, Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL).

37) Kaur, B., Kaur, N., Sharma, T., Kaur, G., Chaudhary, G.R.
Metallosurfactant based synthetic liposomes as a substitute for phospholipids to safely store curcumin
(2022) *Colloids and Surfaces B: Biointerfaces*, 217, art. no. 112621, .

Abstract
Curcumin has shown remarkable therapeutic utilization for various medical conditions. Still, its limited chemical stability and rapid hydrolysis capped its applications to a certain extent. Approaches have been made in the past to surpass these shortcomings by encapsulating the drug in surfactant-based micelles or liposomes and so far, natural surfactants have been used to do this bidding. Through this report, we are presenting curcumin entrapped inside synthetic metal-based liposomal assembly (metallosomes) based on hybrid-surfactants known as metallosurfactants (MS). Three metallosomes i.e. metallosomes (a), (b), and (c) were synthesized with increasing cholesterol (Chl) ratio w.r.t MS (MS:Chl 1:0, 1:0.5, and 1:1). Firstly, the membrane properties of the metallosomes were studied in the absence of the drug. The studies confirmed the direct influence of Chl concentration on the membrane properties and the metallosomes were found to be more hydrophobic, rigid, homogenous, stable, and less fluid with Chl incorporation. These studies were proven beneficial when drug-loaded metallosomes were studied and metallosomes (c), with the highest Chl content, emerged as the maximum drug loader due to their most hydrophobic nature. However, the drug was released at the slowest rate for this metallosomal system due to its less fluid and more rigid nature. On the other hand, these metallosomes were more efficient for shielding entrapped drug from acidic and alkaline environs as lesser drug degradation was observed in the experiments compared to the free curcumin. These metallosomes also exhibited efficient interactional behavior with bacterial (MRSA) DNA. © 2022 Elsevier B.V.

38) Allal, N., Didi, W., Hassaine, H., Oudghiri, F., Bouziane, D.
Study of the Antimicrobial Activity of Curcuma longa on Streptococcus mutans Isolated from Dental Caries [Étude de l'activité antimicrobienne du Curcuma longa sur le Streptococcus mutans isolé de lésions carieuses]
(2022) *Phytotherapie*, 20 (4-5), pp. 248-253.

Abstract
Introduction: Streptococcus mutans is a bacterium mainly responsible for carious disease. From a socioeconomic point of view, a simple and inexpensive solution is necessary. This study aims to evaluate the antibacterial effect and determine the determination of the minimum inhibitory concentration of synthetic and natural curcumin on strains of Streptococcus mutans in biofilm mode. Materials and methods: The Streptococcus mutans strain was isolated from saliva samples using a special kit (CRT Bacteria® Ivoclar) at the department of conservative endodontics of CHU Tlemcen. The determination of the minimum inhibitory concentration was made by the dilution technique in 96-well microplates with double serial dilutions of synthetic curcumin (Sigma-Aldrich, Saint-Quentin-Fallavier, France) and natural curcumin (99% pure curcumin from India), prepared in Brain Heart Broth (BHIB) (Conda Pronadisa, Madrid, Spain) up to a final volume of 100 µl per well. Then an observation by an environmental scanning electron microscope was made on glass slides immersed in a suspension of Streptococcus mutans incubated for 48 hours at 37 °C and immersed for 30 minutes in a curcumin solution at its minimum inhibitory concentration. Results: The minimum inhibitory concentration of curcumin is 64 µg/ml and scanning electron microscopy has shown a significant reduction in the number of Streptococcus mutans strains adhered. Conclusion: Curcumin is a promising antibacterial agent for the prevention of carious disease. © Lavoisier SAS 2022.

39) Adnane, F., El-Zayat, E., Fahmy, H.M.
The combinational application of photodynamic therapy and nanotechnology in skin cancer treatment: A review
(2022) *Tissue and Cell*, 77, art. no. 101856, .

Abstract
Skin cancer is considered a risky worldwide disease. Traditional treatments have several weaknesses, necessitating the creation of more effective treatments. In this case, photodynamic therapy and nanotechnology were used to demonstrate their therapeutic efficacy as combinational approaches in treating different types of skin cancer. In this review, we will discuss the photoexcitation mechanism of PDT, its cell destruction capability, and give a comprehensive outlook of the different photosensitizer types. Also, light sources and their properties will be addressed. Further, we will present some of the nanoparticles used as delivery systems in the skin and show their ideal characteristics for the effective delivery of drugs for skin cancer therapy. Finally, the review aims to cover topics from the most recent reported preclinical studies and clinical trials about nanoparticles loaded with different drugs and triggered with PDT to treat different types of skin cancer. The review will demonstrate that photodynamic therapy and nanoparticles have contributed to the great evolution of skin cancer treatment by having an effective therapeutic efficiency in treating different types of skin cancer such as melanoma, squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and actinic keratosis (AK) which shows the need of using them instead of traditional technologies. © 2022 Elsevier Ltd

40) Antony, B., Benny, M., Kuruvilla, B.T., Gupta, N.K., Jacob, S.
Acute and sub chronic toxicity studies with herbal pain relieving formula (Rhuleave-K™) in rats
(2022) *Regulatory Toxicology and Pharmacology*, 133, art. no. 105214, .

Abstract
Rhuleave-K™ is a proprietary combination of Curcuma longa extract, Boswellia serrata extract and black sesame seed oil. Acute toxicity was evaluated as per OECD guidelines 423. Rhuleave-K™ was fed at 2000 mg/kg to overnight fasted female rats. Clinical signs of abnormality and mortality was observed daily for 14 days. Sub-chronic toxicity was studied by feeding Rhuleave-K™ at 100, 500 and 1000 mg/kg/day to rats as per OECD guidelines 408. After 90 days feeding, hematological and biochemical parameters were analyzed. Histopathology of all the major organs was also studied. In the acute toxicity study, there was no clinical sign of toxicity in any of the rats at maximum dose of 2000 mg/kg. The LD50 was computed as >2000 mg/kg in rats. The repeated dosing of Rhuleave-K™ at the maximum dose level of 1000 mg/kg for 90 days did not induce any observable toxic effects in rats, when compared to its corresponding control. The hematology and biochemistry profiles of treated rats were similar to control animals and difference was non-significant ($p > 0.05$). The histopathology of major organs of all the control and treated animals was normal. In this study the NOAEL for Rhuleave-K™ was calculated as 1000 mg/kg daily in rats. © 2022 Elsevier Inc.

41) Vesco, G., Brambati, M., Scapinello, L., Penoni, A., Mella, M., Masson, M., Gaware, V., Maspero, A., Nardo, L.
Asymmetric Phenyl Substitution: An Effective Strategy to Enhance the Photosensitizing Potential of Curcuminoids
(2022) *Pharmaceuticals*, 15 (7), art. no. 843, .

Abstract
Curcumin has been demonstrated to exhibit photosensitized bactericidal activity. However, the full exploitation of curcumin as a photo-pharmaceutical active principle is hindered by fast deactivation of the excited state through the transfer of the enol proton to the keto oxygen. Introducing an asymmetry in the molecular structure through acting on the phenyl substituents is expected to be a valuable strategy to impair this undesired de-excitation mechanism competing with the therapeutically relevant ones. In this study, two asymmetric curcumin analogs were synthesized and characterized as to their electronic-state transition spectroscopic properties. Fluorescence decay distributions were also reconstructed. Their analysis confirmed the substantial stabilization of the fluorescent state with respect to the parent compound. Nuclear magnetic resonance experiments were performed with the aim of determining the structural features of the keto–enol ring and the strength of the keto–enol hydrogen bond. Electronic structure calculations were also undertaken to elucidate the effects of substitution on the features of the keto–enol semi-aromatic system and the proneness to proton transfer. Finally, their singlet oxygen-generation efficiency was compared to that of curcumin through the 9,10-dimethylanthracene fluorescent assay. © 2022 by the authors.

42) Dezhenkova, L.G., Druzina, A.A., Volodina, Y.L., Dudarova, N.V., Nekrasova, N.A., Zhidkova, O.B., Grin, M.A., Bregadze, V.I.
Synthesis of Cobalt Bis(Dicarbollide)—Curcumin Conjugates for Potential Use in Boron Neutron Capture Therapy
(2022) *Molecules*, 27 (14), art. no. 4658, .

Abstract
A series of novel cobalt bis(dicarbollide)—curcumin conjugates were synthesized. Two conjugates were obtained through the nucleophilic ring-opening reaction of the 1,4-dioxane and tetrahydropyran derivatives of cobalt bis(dicarbollide) with the OH group of curcumin, and using two equiv. of the oxonium derivatives, two other conjugates containing two cobalt bis(dicarbollide) units per molecule were obtained. In contrast to curcumin, the conjugates obtained were found to be non-

cytotoxic against both tumor and normal cell lines. The analysis of the intracellular accumulation of the conjugates by flow cytometry showed that all cobalt bis(dicarbollide)—curcumin conjugates entered HCT116 colorectal carcinoma cells in a time-dependent manner. New non-cytotoxic conjugates contain a large amount of boron atoms in the biomolecule and can potentially be used for further biological research into boron neutron capture therapy (BNCT). © 2022 by the authors.

43) Nguyen, N.Y., Luong, H.V.T., Pham, D.T., Tran, T.B.Q., Dang, H.G.
Chitosan-functionalized Fe3O4@SiO2 nanoparticles as a potential drug delivery system
(2022) *Chemical Papers*, 76 (7), pp. 4561-4570.

Abstract
This study developed and characterized the chitosan-functionalized Fe3O4@SiO2 nanoparticles (Fe3O4@SiO2@CS NP) as a drug delivery system. Fe3O4 NP were first synthesized by co-precipitation method, followed by coating with SiO2, and functionalized with chitosan via glutaraldehyde crosslinking bridges. The newly synthesized Fe3O4@SiO2@CS NP possessed an octagonal shape with a diameter of ~ 20 nm. In the FT-IR spectrum, the Fe3O4@SiO2@CS NP demonstrated the appearances of C–O, N–H, and C–H peaks, indicating the presence of chitosan in their structures. The Fe3O4@SiO2@CS NP could preserve the Fe3O4 magnetic property with a magnetization value of 52.43 emu/g, a magnetization remanence of almost 0 emu/g, and minimal residual coercivity. Utilizing curcumin as a drug model, the Fe3O4@SiO2@CS NP could adsorb the drug rapidly, to more than 71% within 20 min, with an adsorption capacity of 6.54 mg/g and an adsorption energy of 0.2029 kJ/mol (following the Dubinin–Radushkevich model). The curcumin adsorption process was in good agreement with the pseudo-second-order kinetics (R2 = 0.9975). Interestingly, in the simulated body fluid, the curcumin-loaded Fe3O4@SiO2@CS NP could retain the curcumin release, with no detectable drug release, in the first hour, followed by a burst release within the next hour. This confirms the contribution of CS in the system. Conclusively, the Fe3O4@SiO2@CS NP could be further developed to potentially become a controlled-release drug delivery system. © 2022, Institute of Chemistry, Slovak Academy of Sciences.

44) Tahay, P., Parsa, Z., Zamani, P., Safari, N.
A structural and optical study of curcumin and curcumin analogs
(2022) *Journal of the Iranian Chemical Society*, 19 (7), pp. 3177-3188.

Abstract
Curcumin dye was extracted from turmeric and purified. Also, some curcumin analogous which have similar structures with different functional groups, and π electrons length extension were synthesized. The chemical structure of these molecules was investigated and characterized by UV–Vis, 1H NMR, and IR spectroscopies. The obtained UV–Vis spectra indicated that the strong electron-donating groups on aryl rings of these molecules enhance the intensity of λmax and shift it toward the lower absorption energy. The conformation and structure of these molecules were investigated in solution and on the TiO2 anatase surfaces. Accordingly, three conformations could be existed in the solution including Cis-Enol, Keto, and twisted (in nanoparticles). Also, these molecules anchor on the TiO2 surface in a monodentate and bidentate chelating mode, depending on the TiO2 surface sites. Furthermore, the application of these molecules as dye in the dye-sensitized solar cell was studied. The observed data indicated that the best efficiency belongs to the 1,7-bis(4-dimethylaminophenyl)-1,6-heptadiene-3,5-dione dye (A3) which has strong electron-donating group (dimethylamine) on the para phenyl ring of the compound. Also, the appropriate IPCE of the A3 dye in the 460 nm (90%electron injection efficiency), demonstrate that the β-dicarbonyl group is suitable anchoring group for DSSC application. © 2022, Iranian Chemical Society.

45) Bhattacharjee, A., Bose, S.
Zinc curcumin complex on fluoride doped hydroxyapatite with enhanced biological properties for dental and orthopedic applications
(2022) *Journal of Materials Research*, 37 (12), pp. 2009-2020.

Abstract
Since antiquity, curcumin, from turmeric is utilized in traditional Indian medicine (Ayurveda) to treat bone disorders. However, the hydrophobic nature and poor absorption of curcumin limit its clinical applications. There is a need to develop a novel strategy that can significantly enhance curcumin's biological properties. The current work reports the utilization of Zn2+–curcumin complex from a fluoride doped hydroxyapatite matrix for osteosarcoma inhibition, osteoblast growth, and anti-bacterial properties. The interaction between Zn2+ and curcumin increases curcumin release by ~ 2.5 folds. The fabricated drug delivery system shows up to ~ 1.6 times enhancement in osteoblast cell viability. The presence of curcumin results in ~ 4 times more osteosarcoma inhibition compared to control. The antibacterial efficacy of this system is confirmed against Staphylococcus aureus, due to the presence of antibacterial fluoride, zinc, and curcumin. This multifunctional drug delivery system can be utilized for various bone-tissue engineering and dental applications. Graphical abstract: Graphical abstract representing the summary of the current work from sample preparation to assessment of biological properties [Figure not available: see fulltext.]. © 2022, The Author(s), under exclusive licence to The Materials Research Society.

46) Lim, D.-J.
3-O-Ethyl-L-Ascorbic Acid Doped Enteric-Coated Gelatin Capsules towards the Advanced Oral Curcumin Delivery

for Cancers
(2022) *Polymers*, 14 (11), art. no. 2207, .

Abstract
Among plant-derived polyphenols, curcumin has been recognized as a therapeutically potent nutrient presenting pleiotropic pharmacological effects on various cancers. However, the poor absorption and bioavailability of curcumin limit the use of this excellent naturally occurring polyphenol. 3-O-ethyl-L-ascorbic acid (EA) doped enteric-coated gelatin capsules were studied in the search for advanced oral curcumin delivery. The EA doped enteric-coated gelatin capsules were successfully created based on a developed inner dual enteric coating technique. When placed in four buffer solutions with different pHs (pH 2.0, 5.0, 6.0, and 7.3), the coated gelatin capsules showed delayed-release profiles of curcumin below pH 6.0. In contrast, both pristine and fabricated gelatin capsules showed similar curcumin release profiles at pH 7.3, which is a common pH observed in the lower gastrointestinal tract, especially intestinal regions. In conclusion, these results demonstrated the potential of the EA doped enteric-coated gelatin capsules in developing advanced oral delivery of curcumin targeting intestinal-specific regions. © 2022 by the author. Licensee MDPI, Basel, Switzerland.

47) Ferreira, L.L.C., Abreu, M.P., Costa, C.B., Leda, P.O., Behrens, M.D., dos Santos, E.P.
Curcumin and Its Analogs as a Therapeutic Strategy in Infections Caused by RNA Genome Viruses
(2022) *Food and Environmental Virology*, 14 (2), pp. 120-137.

Abstract
The use of natural resources for the prevention and treatment of diseases considered fatal to humanity has evolved. Several medicinal plants have nutritional and pharmacological potential in the prevention and treatment of viral infections, among them, turmeric, which is recognized for its biological properties associated with curcuminoids, mainly represented by curcumin, and found mostly in rhizomes. The purpose of this review was to compile the pharmacological activities of curcumin and its analogs, aiming at stimulating their use as a therapeutic strategy to treat infections caused by RNA genome viruses. We revisited its historical application as an anti-inflammatory, antioxidant, and antiviral agent that combined with low toxicity, motivated research against viruses affecting the population for decades. Most findings concentrate particularly on arboviruses, HIV, and the recent SARS-CoV-2. As one of the main conclusions, associating curcuminoids with nanomaterials increases solubility, bioavailability, and antiviral effects, characterized by blocking the entry of the virus into the cell or by inhibiting key enzymes in viral replication and transcription. © 2022, The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

48) Ju, D.-T., Tsai, B.C.-K., Sitorus, M.A., Kuo, W.-W., Kuo, C.-H., Chen, T.-S., Hsieh, D.J.-Y., Ho, T.-J., Huang, C.-Y., Wang, C.-H.
Curcumin-Pretreated Adipose-Derived Stem Cells Enhance the Neuroprotective Ability to Repair Rheumatoid Arthritis-Induced Damage in the Rat Brain
(2022) *American Journal of Chinese Medicine*, 50 (5), pp. 1299-1314.

Abstract
Neurodegenerative diseases have become increasingly prevalent in the aged population. Rheumatoid arthritis (RA) is an autoimmune disease that causes systemic inflammation, damaging the neurons. However, only a few treatment options can reduce RA-induced neurodegeneration. This study aimed to evaluate whether adipose-derived stem cells (ADSCs) pretreated with curcumin could ameliorate RA-induced neurodegenerative illness in an RA rat model. Wistar rats were randomly classified into the following four groups: control, RA, RA + ADSC (1 × 106 cells per rat), and RA + curcumin-pretreated ADSC (1 × 106 cells per rat). After treatment for two months, the effects were specifically evaluated in the brains collected from the rats. Our results demonstrated that the transplantation of curcumin-pretreated ADSCs substantially reduced inflammation and apoptosis in the cortices of RA rats compared to those of other groups. Thus, the combination of ADSCs and curcumin exerts a synergistic effect in enhancing neuronal protection in RA rats. In the future, this combination therapeutic strategy can potentially be used as a novel treatment method to reduce RA-induced neurodegenerative disorders. © 2022 World Scientific Publishing Company.

49) Ning, S., Zang, J., Zhang, B., Feng, X., Qiu, F.
Botanical Drugs in Traditional Chinese Medicine With Wound Healing Properties
(2022) *Frontiers in Pharmacology*, 13, art. no. 885484, .

Abstract
Chronic and unhealed wound is a serious public problem, which brings severe economic burdens and psychological pressure to patients. Various botanical drugs in traditional Chinese medicine have been used for the treatment of wounds since ancient time. Nowadays, multiple wound healing therapeutics derived from botanical drugs are commercially available worldwide. An increasing number of investigations have been conducted to elucidate the wound healing activities and the potential mechanisms of botanical drugs in recent years. The aim of this review is to summarize the botanical drugs in traditional Chinese medicine with wound healing properties and the underlying mechanisms of them, which can contribute to the research of wound healing and drug development. Taken together, five botanical drugs that have been developed into commercially available products, and 24 botanical drugs with excellent wound healing activities and several multiherbal preparations are reviewed in this article. Copyright © 2022 Ning, Zang, Zhang, Feng and Qiu.

50) Wünsche, S., Seidel-Morgenstern, A., Lorenz, H.
Cocrystallization of Curcuminoids with Hydroxybenzenes Pyrogallol and Hydroxyquinol: Investigations of Binary Thermal Phase Behaviors
(2022) *Crystal Growth and Design*, 22 (5), pp. 3303-3310.

Abstract
The binary thermal phase behaviors of the curcuminoids (CURDs) curcumin (CUR), demethoxycurcumin (DMC), and bis(demethoxy)curcumin (BDMC) with either pyrogallol (PYR) and hydroxyquinol (HYQ) as potential cocrystal formers were investigated. Earlier, it was reported that CUR and BDMC form cocrystals in a 1:1 stoichiometric ratio with the aforementioned coformers. Here, we report for the first time cocrystallization experiments of DMC. Two different cocrystallization techniques, namely, liquid-assisted grinding and cocrystallization from the melt phase, were applied. Analyses of the cocrystallization outcomes were performed using powder X-ray diffraction and differential scanning calorimetry (DSC). A cocrystal phase of DMC with one of the two trihydroxybenzenes could not be found, but a simple eutectic behavior was proven. Binary phase diagrams of all six systems were constructed from DSC measurements revealing distinct thermal behaviors: The CUR cocrystals both melt congruently, while the BDMC cocrystals show an incongruent melting behavior. Together with the eutectic DMC systems, we found three different types of binary phase behaviors for the CURD systems, which can serve as a basis for future crystallization-based purification of structurally similar CURDs.

51) Tomaras, S., Keyßer, G., Feist, E.
Curcumin: Useful add-on for Rheumatic Diseases?
(2022) *Journal of Clinical Medicine*, 11 (10), art. no. 2908, .

Abstract
Plant-derived nutraceuticals are proposed as new key instruments to represent a profound “back to basics” shift in medical treatment. Data accumulated over the past ten years suggest that curcumin, the major active compound of the turmeric plant, has anti-inflammatory properties. It has yet to be determined whether the anti-inflammatory profile of curcumin is potent enough to justify the application of this substance as a nutritional supplement for patients with rheumatic diseases. To address this question, the most relevant in vitro studies that investigate the mechanism of action of curcumin were reviewed in this article. In addition, a total of 18 animal and human trials were evaluated. The pleiotropic, anti-inflammatory and immunomodulatory effects of curcumin were observed in animal studies. In addition, human trials demonstrated promising findings. In these studies, curcumin was able to reduce the expression of proinflammatory cytokines, lower the level of the C-reactive protein and improve clinical parameters. A limiting factor of the application of curcumin is the inconsistent bioavailability of the substance. Therefore, new formulations have been developed to improve the pharmacodynamic profile of curcumin. The future acceptance of the substance is dependent on new controlled clinical trials with a standardised formulation of curcumin administered as well as standard of care.

52) Druzina, A.A., Grammatikova, N., Zhidkova, O., Nekrasova, N., Dudarova, N., Kosenko, I., Grin, M., Bregadze, V.I.
Synthesis and Antibacterial Activity Studies of the Conjugates of Curcumin with closo-Dodecaborate and Cobalt Bis (Dicarbollide) Boron Clusters
(2022) *Molecules*, 27 (9), art. no. 2920, .

Abstract
A series of novel conjugates of cobalt bis(dicarbollide) and closo-dodecaborate with curcumin were synthesized by copper(I)-catalyzed azide-alkyne cycloaddition. These conjugates were tested for antibacterial activity. It was shown that all derivatives are active when exposed to Bacillus cereus ATCC 10702 and are not active against Gram-negative microorganisms and Candida albicans at the maximum studied concentration of 1000 mg/L. The conjugate of alkynyl-curcumin with azide synthesized from the tetrahydropyran derivative of cobalt bis(dicarbollide) exhibited activity against Gram-positive microorganisms: Staphylococcus aureus ATCC 29213, Enterococcus faecalis ATCC 29212 and the clinical isolate MRSA 17, that surpassed curcumin by 2–4 times.

53) Mohammadi, A., Khanbabaei, H., Zandi, F., Ahmadi, A., Haftcheshmeh, S.M., Johnston, T.P., Sahebkar, A.
Curcumin: A therapeutic strategy for targeting the Helicobacter pylori-related diseases
(2022) *Microbial Pathogenesis*, 166, art. no. 105552, .

Abstract
Helicobacter pylori is a significant human pathogen of the stomach's epithelial lining. This type of carcinogen is associated with gastric cancer, indigestion, peptic ulcers, and upper digestive diseases. Therefore, successful treatment and eradication of this bacterium are required to reduce the prevalence of these diseases, especially in high-risk individuals. Moreover, some concerns exist regarding the extensive use of elimination therapy, such as anti-microbial resistance and rising H. pylori-associated diseases. Since there is still no effective vaccine, finding alternative therapies would appear to be a worthwhile pursuit. In this regard, curcumin exhibits anti-inflammatory, anti-carcinogenic, anti-oxidant properties and is widely used as a natural product-derived medicine or nutraceutical. Furthermore, curcumin has been reported to have anti-bacterial activity. Therefore, curcumin might be an effective herbal-based medicine for preventing, managing, or treating H.

pylori infection. This review discusses the anti-inflammatory, anti-cancer, and anti-bacterial properties of curcumin as it pertains to gastric cancer and H. pylori-associated diseases. © 2022 Elsevier Ltd

54) He, H.-J., Xiong, X., Zhou, S., Zhang, X.-R., Zhao, X., Chen, L., Xie, C.-L.
Neuroprotective effects of curcumin via autophagy induction in 6-hydroxydopamine Parkinson's models
(2022) *Neurochemistry International*, 155, art. no. 105297, .

Abstract
Curcumin, a polyphenolic compound extracted from curcuma longa, acts as a nontoxic matter with anti-oxidant and anti-inflammatory effects as well as antiproliferative activities. Here, our research aimed to explore the neuroprotective effects of curcumin both in the 6-hydroxydopamine (6-OHDA)-lesioned rat model of Parkinson's disease (PD) in vivo and 6-OHDA-lesioned PC12 cells in vitro. In vitro, 6-OHDA caused a distinct decrease in cell viability of PC12 cells (150 μM). With the incubation of curcumin (1 μM), 6-OHDA-induced apoptosis was suppressed, increasing the autophagy markers (LC3-II/LC3-I, Beclin-1) and inhibiting phosphor-AKT/AKT, phosphor-mTOR/mTOR. In vivo, curcumin (50 mg/kg) reduced the accumulation of a-synuclein and led to higher parkinsonian disability scores in 6-OHDA-lesioned PD rats, contributing to induction of autophagy through inhibiting AKT/mTOR signal pathway. Moreover, treatment with autophagy inhibitors, such as 3-MA and chloroquine, abolished the neuroprotective effects of curcumin as evidence by compromised autophagy and declined motor behavior in PD rats. In conclusion, the present study demonstrated that curcumin repressed PC12 cell death in vitro and improved parkinsonian disability scores in vivo by inhibiting AKT/mTOR signaling pathway which mediated by autophagy, indicating a potential value of curcumin in the therapeutic intervention of Parkinson's disease. © 2022 Elsevier Ltd

55) Weinzierl, A., Ampofo, E., Menger, M.D., Laschke, M.W.
Tissue-Protective Mechanisms of Bioactive Phytochemicals in Flap Surgery
(2022) *Frontiers in Pharmacology*, 13, art. no. 864351, .

Abstract
Despite careful preoperative planning, surgical flaps are prone to ischemic tissue damage and ischemia–reperfusion injury. The resulting wound breakdown and flap necrosis increase both treatment costs and patient morbidity. Hence, there is a need for strategies to promote flap survival and prevent ischemia-induced tissue damage. Phytochemicals, defined as non-essential, bioactive, and plant-derived molecules, are attractive candidates for perioperative treatment as they have little to no side effects and are well tolerated by most patients. Furthermore, they have been shown to exert beneficial combinations of pro-angiogenic, anti-inflammatory, anti-oxidant, and anti-apoptotic effects. This review provides an overview of bioactive phytochemicals that have been used to increase flap survival in preclinical animal models and discusses the underlying molecular and cellular mechanisms. Copyright © 2022 Weinzierl, Ampofo, Menger and Laschke.

56) Purbadi, S., Yusuf, M., Arozal, W., Naroeni, A., Winarto, H., Putra, A.D., Sotarduga, G.E.
Antiproliferation and Apoptosis Effect of Cisplatin and Nanocurcumin on Ovarian Cancer SKOV3 Cell
(2022) *Bali Medical Journal*, 11 (1), pp. 377-381.

Abstract
Background: Ovarian cancer is one of the leading cancers in women. Seventy percent were founded in the advanced stage, with a 5-year survival rate of only 46%. The current treatment modality is cytoreduction with platinum-based adjuvant chemotherapy as the first line. The effectiveness of chemotherapy is only 60% in the advanced stage, later developing into recurrent. Therefore, additional types of therapy are required based on agents that work specifically in cancer cells and synergize with current standard treatments. This study aimed to know the anti-proliferation effect and apoptosis effect of combination cisplatin with nanocurcumin on SKOV3 cells. Methods: This experimental study was conducted in vitro using the biological cell line SKOV3 to determine the anti-proliferation effect (expression Ki67) and the apoptosis effect (caspase 3 and 8) of combination cisplatin with combination with cisplatin nanocurcumin on the cell. The data were analyzed with unpaired T when regular distribution/Mann Whitney test when the distribution is abnormal and using Graph Pad Prism. Results: Based on this result, 50cc of nanocurcumin is 67 μm, and 50cc of cisplatin is 54 μm, using the MTT Assay method. The viability of the cells in this study decreased according to the dose-dependent, whereas the combined dose of 134 μm nanocurcumin with 108 μm cisplatin found the lowest life cell, 24.3% ($p < 0.001$). Ki67 expression was low in the SKOV3 cells post-exposure to cisplatin, but increased post-exposure to nanocurcumin, suspected nanocurcumin at certain doses of pro-oxidant properties that triggered proliferation. Caspase 3 and 8 cannot be detected in this cell by the ELISA method. Conclusions: Nanocurcumin has a potential effect on chemosensitive cells. However, our study shows no healing effect in chemoresistance cells, particularly SKOV3. © 2022, Sanglah General Hospital. All rights reserved.

57) Mehta, S.P., Balaraman, R.
A Review on Herbal Remedies for Alzheimer’s Disease
(2022) *Journal of Natural Remedies*, 22 (2), pp. 123-135.

Abstract
Among the neurodegenerative disorders, Alzheimer’s disease is the most common type where the individual suffers from

dementia. It usually affects citizens aged 65 and above. Its high prevalence and debilitating effects call for the need of effective therapeutic interventions to deal with this grave disease. The inefficiency of currently available therapeutic options pushes our attention towards finding effective alternative therapeutic options to either successfully prevent or treat AD. Herbal remedies are a potential gold mine that offer hope against this crippling disease. The aim of this review is to throw a light on the potential of a few potential and promising herbal which can provide an alternative therapeutic intervention for the prevention and management of AD amongst a plethora of herbal drugs. © 2022, Informatics Publishing Limited.

58) Mohammad, C.A., Ali, K.M., Al-rawi, R.A., Gul, S.S.
Effects of Curcumin and Tetracycline Gel on Experimental Induced Periodontitis as an Anti-Inflammatory, Osteogenesis Promoter and Enhanced Bone Density through Altered Iron Levels: Histopathological Study
(2022) *Antibiotics*, 11 (4), art. no. 521, .

Abstract
Adjunctive use of antimicrobials with scaling and root planing (SRP) is necessary to better eradicate dental biofilm. Tetracycline (T) is the most commonly used antimicrobial; however, it has limitations. This study evaluates the effect of curcumin (CU) as adjunct to SRP on inflammatory markers, collagen fiber deposition, and altered iron level. A total of 32 Wistar rats were divided into five groups: no experimental periodontitis (healthy control), experimental periodontitis (EPD), EPD treated with SRP alone (SRP), EPD treated with SRP+T (SRP+T), and EPD treated with SRP+CU (SRP+CU). After 2 and 4 weeks of treatment, tissue samples were assessed by hematoxylin and eo-sin, and special stains (Perls' stain and Masson's Trichrome) for counting of inflammatory cells, angiogenesis, collagen fibers, and iron deposition. Significant reductions in inflammatory cells in-filtration and alveolar bone resorption with angiogenesis and collagen fibers deposition were de-tected after 2 and 4 weeks in both SRP+T and SRP+CU groups. SRP+CU resulted in a significant reduction in osteoclast numbers (week 2) and iron deposition (week 4) in bone trabeculae as compared to SRP and SRP+T groups. The adjunctive use of CU showed comparable results to T in the reduction in inflammation and bone resorption. Furthermore, CU has potential osteogenesis and healing effects. © 2022 by the authors. Licensee MDPI, Basel, Switzerland.

59) Caruso, G., Torrisi, S.A., Mogavero, M.P., Currenti, W., Castellano, S., Godos, J., Ferri, R., Galvano, F., Leggio, G.M., Grosso, G., Caraci, F.
Polyphenols and neuroprotection: Therapeutic implications for cognitive decline
(2022) *Pharmacology and Therapeutics*, 232, art. no. 108013, .

Abstract
Dietary polyphenols have been the focus of major interest for their potential benefits on human health. Several preclinical studies have been conducted to provide a rationale for their potential use as therapeutic agents in preventing or ameliorating cognitive decline. However, results from human studies are scarce and poorly documented. The aim of this review was to discuss the potential mechanisms involved in age-related cognitive decline or early stage cognitive impairment and current evidence from clinical human studies conducted on polyphenols and the aforementioned outcomes. The evidence published so far is encouraging but contrasting findings are to be taken into account. Most studies on anthocyanins showed a consistent positive effect on various cognitive aspects related to aging or early stages of cognitive impairment. Studies on cocoa flavanols, resveratrol, and isoflavones provided substantial contrasting results and further research is needed to clarify the therapeutic potential of these compounds. Results from other studies on quercetin, green tea flavanols, hydroxycinnamic acids (such as chlorogenic acid), curcumin, and olive oil tyrosol and derivatives are rather promising but still too few to provide any real conclusions. Future translational studies are needed to address issues related to dosage, optimal formulations to improve bioavailability, as well as better control for the overall diet, and correct target population. © 2021 Elsevier Inc.

60) Bakhouche, K., Dhaouadi, Z., Hammoutène, D.
Thermodynamic, reactivity and spectroscopic properties of curcumin: solvent effect
(2022) *Journal of the Iranian Chemical Society*, 19 (4), pp. 1159-1165.

Abstract
The M06/6-31+G(d) method has been used to study the reactivity of the two forms of curcumin (enol and keto). The energies needed for the three thermodynamic mechanisms: HAT, SET-PT and SPLET, have been calculated, in different solvents, to determine the most probable hydrogen atom transfer mechanism. The solvent effect is evaluated using an implicit solvation model (IEF-PCM). The results show the existence of an intramolecular hydrogen bond strength, in the enol form, which prevents the dissociation of hydrogen atom. In nonpolar solvent, the value of BDFE is lower than PA and IP; this means that HAT is the most favorable mechanism of the two forms of curcumin, while the SPLET mechanism is thermodynamically preferred in polar solvent. The UV/Vis spectra have been determined by the time-dependent density functional theory (TD-DFT) to show the maximum absorption wavelength value of curcumin and the nature of the excited states. © 2021, Iranian Chemical Society.

61) Santosa, D., Suharti, C., Riwanto, I., Dharmana, E., Pangarsa, E.A., Setiawan, B., Suyono, S., Tobing, M.L., Suhartono, S., Hadisapurto, S.

Curcumin as adjuvant therapy to improve remission in myeloma patients: A pilot randomized clinical trial
(2022) *Caspian Journal of Internal Medicine*, 13 (2), pp. 375-384.

Abstract
Background: The treatment for ineligible transplant multiple myeloma is melphalan prednisone. Curcumin has an anti-inflammatory and antiangiogenesis in cancer-directed to nuclear factor-kappa B (NF-kB) pathway. Interleukin 6 (IL-6), vascular endothelial growth factor (VEGF), tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), and lactate dehydrogenase (LDH) were also involved in the pathogenesis of myeloma. No clinical study has evaluated the efficacy of curcumin in myeloma patients. To evaluate the efficacy of curcumin as adjuvant into melphalan prednisone in myeloma patients Methods: 33 myeloma patients at Dr. Kariadi General Hospital, Semarang, Indonesia during 2016-2017 were randomly assigned single-blindedly into MPC (n=17) and control group (n=16). The MPC group was treated with melphalan 4 mg/m2, prednisone 40 mg/m2 for 7 days, and curcumin 8 gram daily for 28 days. The MP control group was treated with melphalan, prednisone, and placebo. The primary endpoint was the overall remission. Pre- and post-treatment was examined for NF-κB, VEGF, TNF-α, IL-6, LDH, and CRP levels All data analyses were per protocol. Results: There was a significant difference in overall remission between the MPC and MP control groups [75%vs 33.3%, x2=6.89, P=0.009]. A significant decrease of NF-κB, VEGF, TNF-α levels were shown in the MPC group compared with the MP control group. There was a significant decrease in IL-6 levels in a subgroup analysis of the MPC group. TNF-α levels had a significant correlation with remission [OR=1.35; (95%CI=1.03-1.76); P=0.03]. Conclusion: Curcumin has an efficacy in improving overall remission and decreasing NF-κB, VEGF, TNF-α, and IL-6 levels in myeloma patients. © The Author(s).

62) El-Shamarka, M.E.-S., Abdel-Salam, O.M.E., Shafee, N., Zeidan, H.M.
Curcumin modulation of L-dopa and rasagiline-induced neuroprotection in rotenone model of Parkinson's disease
(2022) *Iranian Journal of Basic Medical Sciences*, 26 (2), pp. 139-147.

Abstract
Objective(s): Parkinson's disease (PD) is one of the most incurable, chronic, and progressive neurodegenerative disorders Worldwide. Curcumin, a natural polyphenolic anti-oxidant compound, has a long history in traditional medicine. We investigate the effect of curcumin on brain oxidative stress, DNA fragmentation, and motor changes in rotenone-induced PD in mice. The possible modulation of the anti-parkinsonian action of drugs L-dopa and rasagiline by curcumin was also studied. Materials and Methods: Mice received rotenone 1.5 mg/kg and were treated with curcumin (150 mg/kg), L-dopa (25 mg/kg), rasagiline (1 mg/kg), L-dopa+curcumin, or rasagiline+curcumin. Striatal malondialdehyde, reduced glutathione, nitric oxide, tyrosine hydroxylase, and brain DNA fragmentations were measured. Histopathological examination of brain tissues was done. Motor coordination and behavioral tests such as wire-hanging, stair, and wood-waking tests were included. Results: Rotenone caused elevation in brain malondialdehyde and nitric oxide contents, depletion of reduced glutathione accompanied by a reduction in rearing behavior, and impairment of motor activity in wire-hanging, stair, and wood-waking tests. Also, severe DNA fragmentation in the striatum, marked decrease of substantia nigra pigmented neurons, neuronal degeneration in the cerebral cortex and hippocampus, decreased glial fibrillary acidic protein reaction (GFAP) and glial cell size in the cerebral cortex were caused by rotenone. In rotenone-treated mice, brain oxidative stress was decreased by curcumin, L-dopa, rasagiline, curcumin+L-dopa, and curcumin+rasagiline. These treatments also prevented DNA fragmentation and markedly improved the motor and behavioral impairment caused by rotenone. Rotenone-induced histopathological changes were ameliorated by curcumin which had an additive effect to that of l-dopa or rasagiline. Conclusion: These data indicate that curcumin showed additive neuroprotective effects to L-dopa or rasagiline and ameliorated neurodegeneration, DNA fragmentation, and motor defects caused by rotenone in mice. © 2022 Mashhad University of Medical Sciences. All rights reserved.

63) Shahbaz, S.K., Koushki, K., Sathyapalan, T., Majeed, M., Sahebkar, A.
PLGA-Based Curcumin Delivery System: An Interesting Therapeutic Approach in the Treatment of Alzheimer's Disease
(2022) *Current Neuropharmacology*, 20 (2), pp. 309-323.

Abstract
Progressive degeneration and dysfunction of the nervous system because of oxidative stress, aggregations of misfolded proteins, and neuroinflammation are the key pathological features of neurodegenerative diseases. Alzheimer's disease is a chronic neurodegenerative disorder driven by uncontrolled extracellular deposition of β-amyloid (Aβ) in the amyloid plaques and intracellular accumulation of hyperphosphorylated tau protein. Curcumin is a hydrophobic polyphenol with noticeable neuroprotective and anti-inflammatory effects that can cross the blood-brain barrier. Therefore, it is widely studied for the alleviation of inflammatory and neurological disorders. However, the clinical application of curcumin is limited due to its low aqueous solubility and bioavailability. Recently, nano-based curcumin delivery systems are developed to overcome these limitations effectively. This review article discusses the effects and potential mechanisms of curcumin-loaded PLGA nanoparticles in Alzheimer's disease. © 2022 Bentham Science Publishers.

64) Singh, B., Singh, H., Singh, B., Kumar, N., Rajput, A., Sidhu, D., Kaur, A., Arora, S., Kaur, S.
A Comprehensive Review on Medicinal Herbs and Novel Formulations for the Prevention of Alzheimer's Disease
(2022) *Current Drug Delivery*, 19 (2), pp. 212-228.

Abstract
Alzheimer's disease (AD) is one of the most prevalent neurodegenerative diseases reported in the aging population across

the globe. About 46.8 million people are reported to have dementia, and AD is mainly responsible for dementia in aged people. Alzheimer's disease (AD) is thought to occur due to the accumulation of β-amyloid (Aβ) in the neocortex portion of the brain, nitric oxide mediated dysfunctioning of blood-brain barrier, reduced activity of serine racemase enzyme, cell cycle disturbances, damage of N-methyl-D-aspartate (NMDA) receptors and glutamatergic neurotransmission. Modern treatment methods target the pathways responsible for the disease. To date, solely symptomatic treatments exist for this disease, all making an attempt to counterbalance the neurotransmitter disturbance. Treatments able to prevent or at least effectively modifying the course of AD, referred to as 'disease-modifying' drugs, are still under extensive research. Effective treatments entail a better indulgence of the herbal bioactives by novel drug delivery systems. The herbal bioactive administered by novel drug delivery systems have proved beneficial in treating this disease. This review provides detailed information about the role of medicinal plants and their formulations in treating Alzheimer's disease which will be highly beneficial for the researchers working in this area.

65) Saifi, B., Haftcheshmeh, S.M., Feligioni, M., Izadpanah, E., Rahimi, K., Hassanzadeh, K., Mohammadi, A., Sahebkar, A.
An overview of the therapeutic effects of curcumin in reproductive disorders with a focus on the antiinflammatory and immunomodulatory activities
(2022) *Phytotherapy Research*, 36 (2), pp. 808-823.

Abstract
Curcumin, the polyphenolic compound obtained from turmeric, has several pharmacological properties. These properties include antioxidant, antimicrobial, anti-angiogenic, anticarcinogenic, antiinflammatory, and immunomodulatory activities. Therefore, the clinical efficacy of this substance has been largely investigated for curing numerous disorders. Based on a growing body of literature, this review aimed to investigate curcumin's molecular and clinical effects on reproduction and related disorders. Curcumin in the female reproductive system attenuates folliculogenesis, promotes apoptosis of oocytes and blastocyst, and decreases embryo implantation and survival. Curcumin at <100 mg concentration shows protective effects against testicular injury. The concentration of >250 mg of curcumin exhibits immobilizing action on sperms, and at 500 mg concentration completely blocks pregnancy. Curcumin inhibits vaginal infections, attenuates the severity of the premenstrual syndrome, ameliorates inflammatory conditions in polycystic ovary syndrome, improves preeclampsia, and prevents ectopic endometrial lesions. Taken together, curcumin, because of the numerous biological activities, low level of toxicity, and lower adverse effects compared to the synthetic drugs, could be considered as a protective agent for preserving the semen quality parameters, a contraceptive, and chemotherapeutic or chemopreventive agent, as well as an appropriate agent for the treatment of female reproductive disorders. © 2022 John Wiley & Sons, Ltd.

66) Gupta, S., Kumar, A., Mahajan, A., Sharma, P., Sachan, V., Aggrawal, J., Yadav, S., Saxena, A., Kumar Swain, D.
Curcumin in a tris-based semen extender improves cryosurvival of Hariana bull spermatozoa
(2022) *Andrologia*, 54 (1), art. no. e14255, .

Abstract
In this study, the cryoprotective potential of natural antioxidant curcumin in Hariana bull semen was evaluated as an additive in a tris-based extender with the assessment of motility and motion parameters of spermatozoa, membrane intactness, progesterone-receptor binding, protein carbonyl content, cervical mucus penetration, cryocapacitation-associated and apoptotic-like changes. The collected ejaculates were divided into five groups in the tris-based extender (control without curcumin-I, 10 μM-II, 25 μM-III, 50 μM-IV and 75μM-V) and were cryopreserved. Groups II and III containing 10 and 25 μM curcumin substantially ($p < .05$) improved the post-thaw sperm parameters like viability, motility, and velocity parameters; intact acrosome and membrane; lowered protein carbonyl content; DNA fragmentation and cryocapacitation-associated changes in comparison to control. It was interesting to note that early apoptotic-like changes in sperm cells were significantly ($p < .05$) decreased in Group II along with an increase in a higher population of sperm cells having high mitochondrial transmembrane potential. Higher progesterone-receptor binding, Vanguard distance and in vitro capacitation response were observed only in Group II (10μM) compared to other groups. In conclusion, curcumin in a semen extender manifests cryoprotective effects and may be incorporated at 10 μM concentration in a Hariana bull semen extender for better post-thaw sperm quality. © 2021 Wiley-VCH GmbH

67) Attia, M.M., Abou-Okada, M., Shamseldean, M.S.M., El-Gameel, S.M.
Insecticidal effects of Curcumin (Curcuma longa) against the horse stomach bot fly, Gasterophilus intestinalis (Diptera: Oestridae)
(2022) *International Journal of Tropical Insect Science*, 42 (1), pp. 917-926.

Abstract
Stomach horse bots (Gasterophilus intestinalis larvae; Diptera: Oestridae) are obligatory parasites inhabit the stomach of domestic Equidae. Colonization of Gasterophilus intestinalis larvae cause funnel-shaped stomach ulcers, sub-serosal abscess, and peritonitis. In the current research work, 3rd instar larvae of G. intestinalis were exposed to different concentrations (5, 10, 20, 40, 80 and 100 ppm) of curcumin from turmeric plant root (Curcuma longa). Survival of insect larvae, their morphological characterization, growth regulation, enzymatic assay and comet assay were assessed. Curcumin exhibited time and concentration dependent insecticidal effect on survival of 3rd instar larvae of G. intestinalis (bot flies). The aqueous extract of curcumin was highly toxic to G. intestinalis larvae with LC50 value of 16.92 ppm after 24 h. The mean comet tail length (μm) and tail moment (μm) at the highest curcumin concentration of 100 ppm were 16.03 ± 0.15 and 3.03 ± 0.09 μm, whereas DNA damage percent was 14.77 ± 0.12%. Further, remarkable inhibition of Glutathione S-transferases (GST) and Acetylcholinesterase (AChE) enzymatic activity were detected. Aqueous extract of curcumin exhibited potent

lethal effects to the 3rd instar larvae of G. intestinalis, therefore, it could be used as an active and harmless natural insecticidal to control bot flies' larvae in donkeys. © 2021, African Association of Insect Scientists.

68) Monika, P., Chandraprabha, M.N., Rangarajan, A., Waiker, P.V., Chidambara Murthy, K.N.
Challenges in Healing Wound: Role of Complementary and Alternative Medicine
(2022) *Frontiers in Nutrition*, 8, art. no. 791899, .

Abstract
Although the word wound sounds like a simple injury to tissue, individual's health status and other inherent factors may make it very complicated. Hence, wound healing has gained major attention in the healthcare. The biology wound healing is precise and highly programmed, through phases of hemostasis, inflammation, proliferation and remodeling. Current options for wound healing which includes, use of anti-microbial agents, healing promoters along with application of herbal and natural products. However, there is no efficient evidence-based therapy available for specific chronic wounds that can result in definitive clinical outcomes. Under co-morbid conditions, chronic would poses numerous challenges. Use of Complementary and Alternative Medicines (CAMs) in health care sector is increasing and its applications in wound management remains like to "separate the diamonds from ore." Attempts have been made to understand the wound at the molecular level, mainly through the analysis of signature genes and the influence of several synthetic and natural molecules on these. We have outlined a review of challenges in chronic wound healing and the role of CAMs in chronic wound management. The main focus is on the applications and limitations of currently available treatment options for a non-healing wound and the best possible alternates to consider. This information generates broader knowledge on challenges in chronic wound healing, which can be further addressed using multidisciplinary approach and combination therapies. Copyright © 2022 Monika, Chandraprabha, Rangarajan, Waiker and Chidambara Murthy.

69) Mortazavian, A.M., Yari, Z., Khorshidian, N.
Effects of Healthful Bioactive Compounds on the Gastrointestinal Tract
(2022) *Effects of Healthful Bioactive Compounds on the Gastrointestinal Tract*, pp. 1-178.

Abstract
Optimal performance of the liver and gastrointestinal tract is vital for general human health. The gastrointestinal system is the main site of nutrient digestion and absorption, and therefore has substantial effects on providing energy and growth for the body. All nutrient and non-nutrient components have an impact on the gastrointestinal system, either locally or systemically. Undeniably, gastrointestinal disorders, with increasing lifetime prevalence, have a profound effect on human health and reduce the quality of life. Nowadays, therapeutic options are limited to medical therapy, including pharmacologic approaches and surgical intervention or lifestyle changes aimed at dietary modifications and increased physical activity. Certainly, dietary modifications can be effective in preventing, treating, and alleviating associated symptoms and complications. In addition to improving whole dietary patterns, the components of foods, collectively or independently, also have a substantial role in their therapeutic features. These components, particularly bioactive compounds, confer unique health benefits and aid in management of various diseases. Recently, investigators have paid much attention to chemopreventive activity of bioactive dietary compounds in the treatment and prevention of gastrointestinal diseases. Fruits, vegetables and edible plants are the main source of biologically active compounds with anti-inflammatory, antioxidant, and protective properties. Most importantly, no major side effects have been reported for these compounds until now. Therefore, this book offers novel targets for prevention, treatment and management of liver and gastrointestinal diseases by providing evidence of effectiveness of bioactive compounds of functional foods. Furthermore, intracellular and molecular pharmacological mechanisms of action of bioactive compounds will also be discussed. It seems that bioactive compounds bring new hope for patients with gastrointestinal disorders through their anti-inflammatory and anti-oxidative potential. © 2022 by Nova Science Publishers, Inc. All rights reserved.

70) Vaghari-Tabari, M., Alemi, F., Zokaei, M., Moein, S., Qujeq, D., Yousefi, B., Farzami, P., Hosseininasab, S.S.
Polyphenols and inflammatory bowel disease: Natural products with therapeutic effects?
(2022) *Critical Reviews in Food Science and Nutrition*, .

Abstract
Inflammatory bowel disease (IBD) is a long-life disease with periods of recurrence and relief. Oxidative stress plays an important role in the pathogenesis of this disease. Recent years' studies in the field of IBD treatment mostly have focused on targeting cytokines and immune cell trafficking using antibodies and inhibitors, altering the composition of intestinal bacteria in the line of attenuation of inflammation using probiotics and prebiotics, and attenuating oxidative stress through antioxidant supplementation. Studies in animal models of IBD have shown that some polyphenolic compounds including curcumin, quercetin, resveratrol, naringenin, and epigallocatechin-3-gallate can affect almost all of the above aspects and are useful compounds in the treatment of IBD. Clinical studies performed on IBD patients have also confirmed the findings of animal model studies and have shown that supplementation with some of the above-mentioned polyphenolic compounds has positive effects in reducing disease clinical and endoscopic activity, inducing and maintaining remission, and improving quality of life. In this review article, in addition to a detailed reviewing the effects of the above-mentioned polyphenolic compounds on the events involved in the pathogenesis of IBD, the results of these clinical studies will also be reviewed. © 2022 Taylor & Francis Group, LLC.

71) Zhang, Y., Yan, J., Liu, Y., Song, L., Zhu, Y., Xu, P., Mao, S., Hu, B., Wu, J., Wang, B.
Comparison study of antibacterial properties of curcumin from Curcuma longa and enrofloxacin against Aeromonas hydrophila
(2022) *Israeli Journal of Aquaculture - Bamidgeh*, 74, art. no. IJA.74.2022.1766053, .

Abstract
Antibacterial properties of curcumin from turmeric (Curcuma longa) and enrofloxacin against Aeromonas hydrophila were assayed. The minimum inhibitory concentration (MIC) values of curcumin and enrofloxacin against A. hydrophila were found to be 100ug/ml and 9.375ug/ml, respectively. To realize the mechanisms of action of curcumin against A. hydrophila, we researched the antibacterial activity and bacterial membrane permeability of A. hydrophila cells treated with curcumin or enrofloxacin. All results elucidated that curcumin increased membrane permeabilization and caused leakage of intracellular contents, while its role was not as good as enrofloxacin. Moreover, a synergistic effect was shown between curcumin and enrofloxacin. The present study suggests that curcumin extracted from turmeric has the potential to be used as an antimicrobial for the control of A. hydrophila.

72) Şen, A.
Complementary medicines used in ulcerative colitis and unintended interactions with cytochrome P450-dependent drug-metabolizing enzymes
(2022) *Turkish Journal of Medical Sciences*, 52 (5), art. no. 2, pp. 1425-1447.

Abstract
Ulcerative colitis (UC) is an idiopathic, chronic inflammatory disease with multiple genetic and a variety of environmental risk factors. Although current drugs significantly aid in controlling the disease, many people have led to the application of complementary therapies due to the common belief that they are natural and safe, as well as due to the consideration of the side effect of current drugs. Curcumin, cannabinoids, wheatgrass, Boswellia, wormwood and Aloe vera are among the most commonly used complementary medicines in UC. However, these treatments may have adverse and toxic effects due to unintended interactions with drugs or drug-metabolizing enzymes such as cytochrome P450s; thus, being ignorant of these interactions might cause deleterious effects with severe consequences. In addition, the lack of complete and controlled long-term studies with the use of these complementary medicines regarding drug metabolism pose additional risk and unsafety. Thus, this review aims to give an overview of the potential interactions of drug-metabolizing enzymes with the complementary botanical medicines used in UC, drawing attention to possible adverse effects.

73) Pandey, M.K., Von Suskil, M., Chitren, R., Al-Odat, O., Jonnalagadda, S.C., Aggarwal, B.B.
Cancer on fire: role of inflammation in prevention and treatment
(2022) *Current Advances for Development of Functional Foods Modulating Inflammation and Oxidative Stress*, pp. 605-626.

Abstract
It has been established that chronic inflammation plays a critical role in chronic diseases including cancers. Inflammation regulates various steps of neoplasia and is crucial in the tumor microenvironment. In the tumor microenvironment, proinflammatory gene products mediate various undesirable pathological processes including apoptosis suppression, survival, proliferation, invasion, metastasis, and angiogenesis. Among these gene products are members of the tumor necrosis factor (TNF) superfamily, interleukins, chemokines, matrix metalloproteinases, vascular epithelial growth factor, cyclooxygenases. The nuclear factor-B (NF-B) regulates the expression of these gene products and is often overexpressed in the majority of cancers. Because various factors contribute in tumorigenesis, it is logical to consider “magic bullets” for cancer prevention and treatment. The nutraceuticals derived from dietary agents including fruits, vegetables, spices, and cereals, possess immense potential. The mammoth research suggests that antiinflammatory nutraceuticals that suppress a variety of gene products important in the tumor microenvironment should have potential in both the prevention and treatment of cancer. Importantly, these nutraceuticals are safe and affordable. The present chapter discusses the molecular targets of common nutraceuticals and their role in cancer prevention and treatment.

74) Upmanyu, V., Sapra, L., Srivastava, R.K.
Employment of selective pharmacologically active natural compounds in treatment and management of osteoporosis
(2022) *Studies in Natural Products Chemistry*, 75, pp. 161-241.

Abstract
Osteoporosis is often known as a silent disease and is estimated to affect approximately 200 million people across the globe. It is projected that by 2050, the economic burden of osteoporosis will be more than 130 USD on the world's economy. Bone remodeling is a dynamic process that maintains the balance between bone degradation by osteoclasts and bone synthesis by osteoblasts. Any imbalance in the bone remodeling process results in the development of osteoporosis. Most of the currently available drugs being employed for the treatment of osteoporosis result in various side effects in the long run, viz. cardiovascular diseases, skin allergy, and gastrointestinal tract disorders. Thus, there is an imperative need to identify natural compounds that exhibit antiosteoporotic potential with the least side effects. In the present review, we summarize the antiosteoporotic abilities of selective herbal plants and their bioactive compounds as potential future therapeutics for the management and treatment of osteoporosis.

75) Banerjee, S., Tudu, C.K., Nandy, S., Pandey, D.K., Ghorai, M., Shekhawat, M.S., Ghosh, A., Nongdam, P., Al-Tawaha, A.R., Bursal, E., Batiha, G.E.-S., Ghosh, S., Kumar, V., Dey, A.
Herbal remedies against Huntington's disease: Preclinical evidences and future directions
(2022) *Herbal Medicines: A Boon for Healthy Human Life*, pp. 37-69.

Abstract
Herbal medicines, or phytochemicals can treat various neurological disorders, and is actually preferred over synthetic drugs due to their lower cost, negligible side effects, easy availability and therapeutic efficiency. This article lists a total of 13 plant extracts, 27 plant derived natural compounds and 3 herbal formulations that were found to therapeutically cure Huntington's Disease, mainly by eliminating the toxic mHtt proteins(the product of the mutant gene responsible for HD). The various plant compounds, fractions, extracts and herbal formulations were summarized from popular scientific search engines and then analyzed on the basis of their source and bioactivity. To understand the behavioral, biochemical and morphological changes caused by HD, experimental models like 3-NP and transgenic animal models like rats, mice, Drosophila and Caenorhaditis elegans were used. Plants such as Bacopa monnieri, Celastrus paniculatus, Centella asiatica, Gastrodia elata, Panax ginseng, and Withania somnifera are some examples that possess anti-HD properties. Some examples of promising plant compounds possessing similar properties are fisetin, curcumin, hesperidin, trehalose, onjisaponin B, sesamol, resveratrol, kaempferol and melatonin. Herbal formulations discussed here are B307, CLMT and YGS. These are proved to be more beneficial than single herbs because they can regulate more targets. However, detailed study and further research should be conducted to determine the therapeutic efficacy of herbal extracts and compounds in HD models. © 2022 Elsevier Inc. All rights reserved.

76) Obulesu, M.
Plant Extracts in Neurodegenerative Diseases
(2022) *Plant Extracts in Neurodegenerative Diseases*, pp. 1-134.

Abstract
Plant Extracts in Neurodegenerative Disease examines the therapeutic efficacy of plant extracts and the lead compounds contained therein that can significantly improve symptoms of diseases of the brain. Providing insights into the protective mechanisms of these bioactive plant compounds to treat Alzheimer’s Disease, Parkinson’s Disease, motor neuron disease, and other neurodegenerative diseases, the book also discusses the pros and cons of using these types of treatments, along with perspectives to overcome current challenges. With chapters looking at individual diseases, readers will learn about studies unique to each condition, including Huntington’s Disease, spinocerebellar ataxia, SMA, ALS and prion disease. © 2022 Elsevier Inc. All rights reserved.

77) Calderon-Rivera, A., Loya-Lopez, S., Gomez, K., Khanna, R.
Plant and fungi derived analgesic natural products targeting voltage-gated sodium and calcium channels
(2022) *Channels*, 16 (1), pp. 198-215.

Abstract
Voltage-gated sodium and calcium channels (VGSCs and VGCCs) play an important role in the modulation of physiologically relevant processes in excitable cells that range from action potential generation to neurotransmission. Once their expression and/or function is altered in disease, specific pharmacological approaches become necessary to mitigate the negative consequences of such dysregulation. Several classes of small molecules have been developed with demonstrated effectiveness on VGSCs and VGCCs; however, off-target effects have also been described, limiting their use and spurring efforts to find more specific and safer molecules to target these channels. There are a great number of plants and herbal preparations that have been empirically used for the treatment of diseases in which VGSCs and VGCCs are involved. Some of these natural products have progressed to clinical trials, while others are under investigation for their action mechanisms on signaling pathways, including channels. In this review, we synthesize information from ~30 compounds derived from natural sources like plants and fungi and delineate their effects on VGSCs and VGCCs in human disease, particularly pain. (Figure presented.). © 2022 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

78) Jenifer, J., Upputuri, R.T.P.
In vitro release mechanism and cytotoxic behavior of curcumin loaded casein nanoparticles
(2022) *Brazilian Journal of Pharmaceutical Sciences*, 58, art. no. e19801, .

Abstract
In the recent past, drug delivery through nanoparticles is considered an effective tool to treat various diseases. Biopolymeric nanoparticles such as protein based nanoparticles have vital role as drug carrier as it is non-antigenic, and easily biodegradable. Curcumin, plant polyphenolic anticancerous compound was loaded into the casein nanoparticles by coacervation method. Particle size and surface charge of spherical casein nanoparticles as observed to be 201.4 nm and-86.9 mV. The loading efficiency of curcumin loaded casein nanoparticles was found to 85.05 %. In vitro drug release was performed at different pH (7.4 and 3.0), and the cumulative release was observed to be 24.8 and 20.13% and at different

temperatures (25°C and 37°C), the cumulative release was observed to be 24.8 and 28.60 % respectively in 48 h. Curcumin release from casein nanoparticles was shown to be in a steady, and prolonged rate. The nanoparticles were observed to have an effective antimocrobial activity than curcumin in free form. The drug loaded casein nanoparticles were found to be potent particles to protect cells from hydrogen peroxide and UV light damage. The cytotoxic activity of nanoparticles on MCF7 and A549 cells were assayed and was observed to have an IC50 value of 609 and 825.2µg/ml. Cell death was observed to be through apoptosis, accompanied by DNA fragmentation.

79) Alanyali, F.S., Alkan, M.
The antiproliferative and cytotoxic effects of curcumin on human cervical cancer Hep2C cell line [Kurkuminin insan servikal kanseri Hep2C hücre hattı üzerindeki antiproliferatif ve sitotoksik etkileri]
(2022) *Turk Hijyen ve Deneysel Biyoloji Dergisi*, 79 (2), pp. 293-300.

Abstract
cytotoxic effects of different concentrations of curcumin on cervical cancer Hep2C cells were investigated with microscopic methods and MTT assay. Methods: Hep2C (human carcinoma cancer cell line, ATCC:CCL-23) cells were cultured. For cytotoxicity evaluation Hep2C cells exposed to curcumin at different concentrations of 30 µg/ml, 15 µg/ml, 7.5 µg/ml, 3.7 µg/ml, 1.9 µg/ml, 0.9 µg/ml, 0.45 µg/ml for 24 hours These Hep2C cells are evaluated with MTT assay. The IC50 value of the agent for 24 h of exposure was detected. The graph of the absorbance data obtained by the Spectramax I3 device. Viability values of Hep2C cells calculated from the absorbances obtained from MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay are gained. The preparations were observed based on changes in nuclei and structures using an inverted microscope (Leica Microsystems). Nontreated cells were used as negative control and for positive control Hep2C cells were exposed to ammonium molibdate (1mg/ml) for the above given incubation period. Results: High doses of curcumin (30 µg/ml, 15 µg/ml, 7.5 µg/ml) showed high antiproliferative and cytotoxic effects on Hep2C cells. The antiproliferative and cytotoxic effects were not observed on cervical cancer Hep2C cells treated with lower concentrations of curcumin. Conclusion: Curcumin has been shown that it is non-toxic, can be used as a highly antioxidant and antiinflammatory agent and has multifaced therapeuticpharmacological effects. However, researches on the antiproliferative, anti-cancer effects of curcumin in cervical cancer cells is not sufficient. The present study evaluates the antiproliferative and cytotoxic effects of curcumin on human cervical cancer Hep2C cells as the first time. The results of our study support these effects of curcumin on Hep2C cells in a concentrationdependent manner. © 2022. Turk Hijyen ve Deneysel Biyoloji Dergisi. All Rights Reserved.

80) Vargas-Mendoza, N., Sandoval-Gallegos, E.M., Madrigal-Santillán, E.O., Morales-Martínez, M., Soriano-Ursúa, M.A., Angeles-Valencia, M., Morales-González, Á., Portillo-Reyes, J., Morales-González, J.A.
The Cytoprotective Activity of Nrf2 Is Regulated by Phytochemicals (Sulforaphane, Curcumin, and Silymarin)
(2022) *Reference Series in Phytochemistry*, pp. 455-505.

Abstract
The evolution of species has encouraged organisms to adapt to their environment; in this process, an aerobic metabolism was the product of exposure to certain atmospheric conditions. Oxygen consumption in most cellular systems results in the production of reactive oxygen species (ROS) that may be capable of causing cellular damage at a certain level; however, these molecules are crucial to trigger cell signaling pathways for the maintenance of homeostasis. The high production of ROS increases oxidative stress (OS) which may affect some cellular structures. Thus, cells have to develop effective cytoprotective systems to defend themselves against damage. Nuclear factor erythroid 2-related factor 2 (Nrf2) is the master regulator of protection; its activation induces the Nrf2/Keap1/ARE pathway for the expression of a wide range of genes involved in detoxification and the antioxidant response. Researchers have paid special attention to the mechanism that favors this pathway and have found that some phytochemicals are potent Nrf2 activators. Therefore, in this work, we provide an overview of three of the most efficient bioactivators and the evidence supporting them as potential therapeutic elements under different medical conditions. © 2022, Springer Nature Switzerland AG.

81) Bhatt, V., Tiwari, A.K.
Sirtuins, a key regulator of ageing and age-related neurodegenerative diseases
(2022) *International Journal of Neuroscience*, .

Abstract
Sirtuins are Nicotinamide Adenine Dinucleotide (NAD+) dependent class III histone deacetylases enzymes (HDACs) present from lower to higher organisms such as bacteria (Sulfolobus solfataricus L. major), yeasts (Saccharomyces cerevisiae), nematodes (Caenorhabditis elegans), fruit flies (Drosophila melanogaster), humans (Homo sapiens sapiens), even in plants such as rice (Oryza sativa), thale cress (Arabidopsis thaliana), vine (Vitis vinifera L.) tomato (Solanum lycopersicum). Sirtuins play an important role in the regulation of various vital cellular functions during metabolism and ageing. It also plays a neuroprotective role by modulating several biological pathways such as apoptosis, DNA repair, protein aggregation, and inflammatory processes associated with ageing and neurodegenerative diseases. In this review, we have presented an updated Sirtuins and its role in ageing and age-related neurodegenerative diseases (NDDs). Further, this review also describes the therapeutic potential of Sirtuins and the use of Sirtuins inhibitor/activator for altering the NDDs disease pathology. © 2022 Informa UK Limited, trading as Taylor & Francis Group.

82) Arican, C.D., Gokdemir, G.S., Gokdemir, M.T., Yokus, B., Tasdemir, E., Sermet, A.
Curcumin reduced diabetic nephropathy in a rat model
(2022) *Genetics and Molecular Research*, 21 (2), art. no. gmr19026, .

Abstract
This study aimed to examine the effects of curcumin, a phytochemical antioxidant, on the treatment and care of diabetic nephropathy and to contribute to alternative treatment strategies for diabetes. Male Wistar albino rats (8–10 weeks old) were divided into five groups of seven. Experimental diabetes was induced in all rats except for those in Group 1 (placebo group) by administration of 110 mg/kg nicotinamide, followed by intraperitoneal administration (after 15 min) of 55 mg/kg streptozotocin. Groups 1, 3, 4, and 5 were treated with 0.1 ml normal saline (0.9% NaCl), 150mg/kg/day metformin, 10 mg/kg/day glycazide (diamicron), and 200 mg/kg/day curcumin, respectively. Group 2 did not receive any treatment. Kidney tissues of rats were collected for histopathological examination. There were no significant differences in the kidney dimensions of the rats. In the histopathological evaluation of kidney tissues with diabetic nephropathy, glomerular congestion and destruction were observed. Rats treated with curcumin had significantly less kidney damage, based on histopathological analysis, than those treated with the diabetes drugs. We conclude that curcumin has protective effects in kidneys due to its antioxidant properties. It has potential for use, in addition to antidiabetic drugs, for diabetes treatment. © FUNPEC-RP.

83) Jie, Z., Jinna, Z., Jingjun, Z., Pengcheng, L., Fang, Y., Qinyang, C., Taiyu, C., Hequn, J., Tao, R.
Antitumor Effects of 10058-F4 and Curcumin in Combination Therapy for Pancreatic Cancer in Vitro and in Vivo
(2022) *Journal of Healthcare Engineering*, 2022, art. no. 1620802, .

Abstract
Objectives of the Study. In vitro and in vivo evaluation of the antipancreatic cancer effects and benefits of the 10058-F4 and curcumin combination therapy. Background. Pancreatic cancer (PC) stands out as one of the most lethal cancers. Due to late diagnosis, only a fraction of patients can be resected. Although it still has significant adverse effects and poor results, the treatment is connected with better overall survival than the prior treatment. Thus, new alternative therapy for advanced PC is needed. Materials/Methods. The impact of 10058-F4 and curcumin combination therapy on apoptosis and cell growth in SW1990 pancreatic cancer cells were determined in vitro using the CCK-8 assay and flow cytometry of Annexin V-FITC/PI, and the in vivo antitumor effect was determined utilizing SW1990-bearing pancreatic tumor mouse models induced by subcutaneous implantation. Results. At concentrations of (10 mol/L+2 mol/L), 10058-F4+curcumin obtained the highest rate of SW1990 cell death, and they had a beneficial effect on SW1990 pancreatic tumor-bearing animals. Furthermore, c-Myc, Akt phosphorylation, and the expression of apoptosis-related molecular were reduced, and the combination therapy modified the expression of apoptosis-related molecular. Conclusions. In vitro and in vivo, the combination of 10058-F4 plus curcumin has antipancreatic cancer actions that are substantially effective. © 2022 Zhang Jie et al.

84) Xia, S., Weng, T., Jin, R., Yang, M., Yu, M., Zhang, W., Wang, X., Han, C.
Curcumin-incorporated 3D bioprinting gelatin methacryloyl hydrogel reduces reactive oxygen species-induced adipose-derived stem cell apoptosis and improves implanting survival in diabetic wounds
(2022) *Burns and Trauma*, 10, art. no. tkac001, .

Abstract
Background: Gelatin methacryloyl (GelMA) hydrogels loaded with stem cells have proved to be an effective clinical treatment for wound healing. Advanced glycation end product (AGE), interacting with its particular receptor (AGER), gives rise to reactive oxygen species (ROS) and apoptosis. Curcumin (Cur) has excellent antioxidant activity and regulates intracellular ROS production and apoptosis. In this study, we developed a Cur-incorporated 3D-printed GelMA to insert into adipose-derived stem cells (ADSCs) and applied it to diabetic wounds. Methods: GelMA hydrogels with Cur were fabricated and their in vitro effects on ADSCs were investigated. We used structural characterization, western blot, ROS and apoptosis assay to evaluate the antioxidant and anti-apoptotic activity, and assessed the wound healing effects to investigate the mechanism underlying regulation of apoptosis by Cur via the AGE/AGER/nuclear factor-κB (NF-κB) p65 pathway. Results: A 10% GelMA scaffold exhibited appropriate mechanical properties and biocompatibility for ADSCs. The circular mesh structure demonstrated printability of 10% GelMA and Cur-GelMA bioinks. The incorporation of Cur into the 10% GelMA hydrogel showed an inhibitory effect on AGEs/AGER/NF-κB p65-induced ROS generation and ADSC apoptosis. Furthermore, Cur-GelMA scaffold promoted cell survival and expedited in vivo diabetic wound healing. Conclusions: The incorporation of Cur improved the antioxidant activity of 3D-printed GelMA hydrogel and mitigated AGE/AGER/p65 axis-induced ROS and apoptosis in ADSCs. The effects of scaffolds on wound healing suggested that Cur/GelMA-ADSC hydrogel could be an effective biological material for accelerating wound healing. © 2022 The Author(s) 2022.

85) Pluta, R., Furmaga-Jabłońska, W., Januszewski, S., Czuczwar, S.J.
Post-Ischemic Brain Neurodegeneration in the Form of Alzheimer's Disease Proteinopathy: Possible Therapeutic Role of Curcumin
(2022) *Nutrients*, 14 (2), art. no. 248, .

Abstract
For thousands of years, mankind has been using plant extracts or plants themselves as medicinal herbs. Currently, there is

a great deal of public interest in naturally occurring medicinal substances that are virtually non-toxic, readily available, and have an impact on well-being and health. It has been noted that dietary curcumin is one of the regulators that may positively influence changes in the brain after ischemia. Curcumin is a natural polyphenolic compound with pleiotropic biological properties. The observed death of pyramidal neurons in the CA1 region of the hippocam-pus and its atrophy are considered to be typical changes for post-ischemic brain neurodegeneration and for Alzheimer's disease. Additionally, it has been shown that one of the potential mechanisms of severe neuronal death is the accumulation of neurotoxic amyloid and dysfunctional tau protein after cerebral ischemia. Post-ischemic studies of human and animal brains have shown the presence of amyloid plaques and neurofibrillary tangles. The significant therapeutic feature of curcumin is that it can affect the aging-related cellular proteins, i.e., amyloid and tau protein, preventing their aggregation and insolubility after ischemia. Curcumin also decreases the neurotoxicity of amyloid and tau protein by affecting their structure. Studies in animal models of cerebral ischemia have shown that curcumin reduces infarct volume, brain edema, blood-brain barrier permeability, apoptosis, neuroinflammation, glutamate neurotoxicity, inhibits autophagy and oxidative stress, and improves neurological and behavioral deficits. The available data suggest that curcumin may be a new therapeutic substance in both regenerative medicine and the treatment of neurodegenerative disor-ders such as post-ischemic neurodegeneration.

86) Vahedian-Azimi, A., Abbasifard, M., Rahimi-Bashar, F., Guest, P.C., Majeed, M., Mohammadi, A., Banach, M., Jamialahmadi, T., Sahebkar, A.
Effectiveness of Curcumin on Outcomes of Hospitalized COVID-19 Patients: A Systematic Review of Clinical Trials
(2022) *Nutrients*, 14 (2), art. no. 256, .

Abstract
Despite the ongoing vaccination efforts, there is still an urgent need for safe and effective treatments to help curb the debilitating effects of COVID-19 disease. This systematic review aimed to investigate the efficacy of supplemental curcumin treatment on clinical outcomes and inflammation-related biomarker profiles in COVID-19 patients. We searched PubMed, Scopus, Web of Science, EMBASE, ProQuest, and Ovid databases up to 30 June 2021 to find studies that assessed the effects of curcumin-related compounds in mild to severe COVID-19 patients. Six studies were identified which showed that curcumin supplementation led to a significant decrease in common symptoms, duration of hospitalization and deaths. In addition, all of these studies showed that the intervention led to amelioration of cytokine storm effects thought to be a driving force in severe COVID-19 cases. This was seen as a significant ($p < 0.05$) decrease in proinflammatory cytokines such as IL1β and IL6, with a concomitant significant ($p < 0.05$) increase in anti-inflammatory cytokines, including IL-10, IL-35 and TGF-α. Taken together, these findings suggested that curcumin exerts its beneficial effects through at least partial restoration of pro-inflammatory/anti-inflammatory balance. In conclusion, curcumin supplementation may offer an efficacious and safe option for improving COVID-19 disease outcomes. We highlight the point that future clinical studies of COVID-19 disease should employ larger cohorts of patients in different clinical settings with standardized preparations of curcumin-related compounds.

87) Adami, R., Bottai, D.
Curcumin and neurological diseases
(2022) *Nutritional Neuroscience*, 25 (3), pp. 441-461.

Abstract
Objectives: The beneficial effects of many substances have been discovered because of regular dietary consumption. This is also the case with curcumin, whose effects have been known for more than 4,000 years in Eastern countries such as China and India. A curcumin-rich diet has been known to counteract many human diseases, including cancer and diabetes, and has been shown to reduce inflammation. The effect of a curcumin treatment for neurological diseases, such as spinal muscular atrophy; Alzheimer's disease; Parkinson's disease; amyotrophic lateral sclerosis; multiple sclerosis; and others, has only recently been brought to the attention of researchers and the wider population. Methods: In this paper, we summarise the studies on this natural product, from its isolation two centuries ago to its characterisation a century later. Results: We describe its role in the treatment of neurological diseases, including its cellular and common molecular mechanisms, and we report on the clinical trials of curcumin with healthy people and patients. Discussion: Commenting on the different approaches adopted by the efforts made to increase its bioavailability.

88) Sharma, M., Kumari, M., Rani, S., Yadav, A.K., Solanki, P.R., Mozumdar, S.
Influence of pH, β-Cyclodextrin, and Metal Ions on the Solubility and Stability of the Medicinally Competent Isoxazole Derivative of Curcumin: A Photophysical Study
(2021) *ACS Applied Bio Materials*, 4 (12), pp. 8407-8423.

Abstract
The β-diketo-modified isoxazole derivative of curcumin (IOC) is well renowned for its anticancer, antioxidant, antimalarial, antiproliferative, and many other biological activities. With the aim of obtaining fundamental knowledge on the photophysics of IOC, the present work was directed toward delineating those at different pH environments and studying the degradation profiles of IOC at five different pH values. Because one of the primary drawbacks of curcumin is its rapid degradation at physiological conditions, the studies showed that the problem could be resolved, as the IOC molecule was extremely stable even in a highly alkaline medium. Further, in order to encounter the problems associated with the low solubility of IOC in aqueous media, β-CD (β-cyclodextrin) was used and calculations of the thermodynamic parameters revealed that the

process of development of the host-guest inclusion complex was highly spontaneous in nature. The synthesis of the IOC:β-CD inclusion complex has also been accomplished in the solid state, and the solid formed has been characterized using various physicochemical techniques. Finally, while variations in the pH as well as addition of foreign metal ions in +1 and +2 oxidation states showed minimal effect on the photophysics of the IOC:β-CD inclusion complex, antiproliferative studies performed with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assays revealed their nontoxic nature on fibroblast L929 normal cell lines and extremely toxic activity on human lung cancer A549 cell lines. © 2021 American Chemical Society.

89) Xu, T., Tian, Y., Zhang, R., Yu, B., Cong, H., Shen, Y.
Hydrogel vectors based on peptide and peptide-like substances: For treating bacterial infections and promoting wound healing
(2021) *Applied Materials Today*, 25, art. no. 101224, .

Abstract
Open wounds have the risk of infections with bacteria, but the direct use of antibiotics and other antibacterial drugs may cause bacteria to develop resistance and invade the human immune system. Liposomes, micelles and hydrogels are common drug vectors, and currently the most widely used dressing for open wounds is hydrogel. As a highly cross-linked three-dimensional network material, hydrogel is considered to be a material that has the ability to efficiently load and release drugs. Wound dressings usually require materials with high biological activity, but some synthetic materials will inevitably face the problem of unsatisfactory biocompatibility. Hydrogel vectors prepared with peptide and peptide-like substances avoid this problem. At present, hydrogel vectors based on peptide and peptide-like substances have been widely used in medical fields such as drug delivery, sterilization, tissue engineering, and promotion of wound healing. In this review, we first roughly classified antibacterial hydrogels based on peptide and peptide-like substances as hydrogel vectors, introduced the applications of various types of hydrogels, and then briefly summarized the research progress of these hydrogels in medical fields such as treating wound infections and promoting wound healing. Finally, we predicted the application prospects of hydrogel vectors based on peptide and peptide-like substances in clinical medicine, and made a simple outlook. © 2021 Elsevier Ltd

90) Shin, G.H., Kim, J.T.
Comparative study of Chitosan and Oligochitosan coatings on mucoadhesion of curcumin nanosuspensions
(2021) *Pharmaceutics*, 13 (12), art. no. 2154, .

Abstract
Curcumin nanosuspensions (Cur-NSs), chitosan-coated Cur-NSs (CS-Cur-NSs), and oligoch itosan-coated Cur-NSs (OCS-Cur-NSs) were prepared by using an ultrasonic homogenization technique. The mean particle size of Cur-NSs was 210.9 nm and significantly ($p < 0.05$) increased to 368.8 nm by CS coating and decreased to 172.8 nm by OCS coating. Encapsulation efficiencies of Cur-NSs, CS-Cur-NSs, and OCS-Cur-NSs were 80.6%, 91.4%, and 88.5%, respectively. The mucin adsorption of Cur-NSs was steeply increased about 3–4 times by CS and OCS coating. Morphological changes of these NSs were studied using circular dichroism spectroscopy, Fourier-transform infrared (FT-IR) spectroscopy, and transmission electron microscopy (TEM). Thus, CS-Cur-NSs and OCS-Cur-NSs showed great potential as mucoadhesive nano-carriers for the efficient delivery of water insoluble compounds like curcumin to the gastrointestinal system. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

91) Sohn, S.-I., Priya, A., Balasubramaniam, B., Muthuramalingam, P., Sivasankar, C., Selvaraj, A., Valliammai, A., Jothi, R., Pandian, S.
Biomedical applications and bioavailability of curcumin—an updated overview
(2021) *Pharmaceutics*, 13 (12), art. no. 2102, .

Abstract
Curcumin, a yellow-colored molecule derived from the rhizome of Curcuma longa, has been identified as the bioactive compound responsible for numerous pharmacological activities of turmeric, including anticancer, antimicrobial, anti-inflammatory, antioxidant, antidiabetic, etc. Nevertheless, the clinical application of curcumin is inadequate due to its low solubility, poor absorption, rapid metabolism and elimination. Advancements in recent research have shown several components and techniques to increase the bioavailability of curcumin. Combining with adjuvants, encapsulating in carriers and formulating in nanoforms, in combination with other bioactive agents, synthetic derivatives and structural analogs of curcumin, have shown increased efficiency and bioavailability, thereby augmenting the range of applications of curcumin. The scope for incorporating biotechnology and nanotechnology in amending the current drawbacks would help in expanding the biomedical applications and clinical efficacy of curcumin. Therefore, in this review, we provide a comprehensive overview of the plethora of therapeutic potentials of curcumin, their drawbacks in efficient clinical applications and the recent advancements in improving curcumin's bioavailability for effective use in various biomedical applications. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

92) Satyavert, Gupta, S., Choudhury, H., Jacob, S., Nair, A.B., Dhanawat, M., Munjal, K.
Pharmacokinetics and tissue distribution of hydrazinocurcumin in rats

(2021) *Pharmacological Reports*, 73 (6), pp. 1734-1743.

Abstract
Background: Curcumin, a natural polyphenol from Curcuma longa, is known to possess diversified pharmacological roles including anti-inflammatory, antioxidant, antiproliferative and antiangiogenic properties; however, its bioavailability is severely limited due to its poor solubility, poor absorption, rapid metabolism, and significant elimination. Hydrazinocurcumin (HZC), a novel analogue of curcumin has been reported to overcome the limitations of curcumin and also possesses multiple pharmacological activities. The present study aimed to evaluate the unexplored pharmacokinetic profile of this agent in experimental rats. Methods: Drug formulations were administered to the experimental animals via oral, intravenous and intraperitoneal routes. Blood samples were collected at different pre-determined time intervals to determine the pharmacokinetic parameters. To understand the biodistribution profile of HCZ, tissue samples were isolated from different groups of Sprague–Dawley rats at different time points. The pharmacokinetic parameters of HZC were evaluated after administration through oral (100 mg/kg), intraperitoneal (100 mg/kg) and intravenous (10 mg/kg) routes. Results: Significantly ($p < 0.05$) higher total AUC along with maximum concentration were evident with intraperitoneal administration when compared to the results of oral administration at a similar dose. In addition, shorter time to peak was observed with intraperitoneal administration. These results revealed a faster rate and longer duration of absorption with intraperitoneal administration, which further resulted in enhanced absolute bioavailability of HZC (29.17%) when compared to 5.1% upon oral dosing. The obtained data from the pharmacokinetic study indicated that HZC was instantaneously distributed and moderately eliminated from body fluids. Conclusion: Based on the findings, it could be concluded that absorption of HZC is much higher via intraperitoneal route of administration compared to the oral administration. Graphic abstract: [Figure not available: see fulltext.]. © 2021, Maj Institute of Pharmacology Polish Academy of Sciences.

93) Prasad, R., Shivay, Y.S.
Scientific and Medical Research Support can Increase Export Earnings from Turmeric (Curcuma longa)
(2021) *National Academy Science Letters*, 44 (6), pp. 481-483.

Abstract
India, the world's largest producer and exporter of turmeric accounts for about 80% of global production. With the exports recorded at US 236 million dollars in 2018, turmeric has rightly been called as Indian Gold. It is cultivated in many states including Tamil Nadu, Andhra Pradesh, Odisha, West Bengal and Assam. However, the yields are low and can be increased by agricultural research. Also, to maintain a consistent position on top in international market scientific research is needed to quantify its main ingredient, the Curcumin, and any other ingredient of importance. Medical research is needed to prove its importance in curing several diseases for which claims have been made. Marketing pure ingredients as medicines can fetch more foreign exchange than marketing crude turmeric. However, turmeric-based research and development certainly needs utmost attention to earn the foreign money. © 2021, The National Academy of Sciences, India.

94) Bernardo, A., Plumitallo, C., De Nuccio, C., Visentin, S., Minghetti, L.
Curcumin promotes oligodendrocyte differentiation and their protection against TNF-α through the activation of the nuclear receptor PPAR-γ
(2021) *Scientific Reports*, 11 (1), art. no. 4952, .

Abstract
Curcumin is a compound found in the rhizome of Curcuma longa (turmeric) with a large repertoire of pharmacological properties, including anti-inflammatory and neuroprotective activities. The current study aims to assess the effects of this natural compound on oligodendrocyte progenitor (OP) differentiation, particularly in inflammatory conditions. We found that curcumin can promote the differentiation of OPs and to counteract the maturation arrest of OPs induced by TNF-α by a mechanism involving PPAR-γ (peroxisome proliferator activated receptor), a ligand-activated transcription factor with neuroprotective and anti-inflammatory capabilities. Furthermore, curcumin induces the phosphorylation of the protein kinase ERK1/2 known to regulate the transition from OPs to immature oligodendrocytes (OLs), by a mechanism only partially dependent on PPAR-γ. Curcumin is also able to raise the levels of the co-factor PGC1-α and of the cytochrome c oxidase core protein COX1, even when OPs are exposed to TNF-α, through a PPAR-γ-mediated mechanism, in line with the known ability of PPAR-γ to promote mitochondrial integrity and functions, which are crucial for OL differentiation to occur. Altogether, this study provides evidence for a further mechanism of action of curcumin besides its well-known anti-inflammatory properties and supports the suggested therapeutic potential of this nutraceutical in demyelinating diseases. © 2021, The Author(s).

95) Rinkunaite, I., Simoliunas, E., Alksne, M., Dapkute, D., Bukelskiene, V.
Anti-inflammatory effect of different curcumin preparations on adjuvant-induced arthritis in rats
(2021) *BMC Complementary Medicine and Therapies*, 21 (1), art. no. 39, .

Abstract
Background: Curcumin, a natural polyphenolic substance, has been known for more than two millennia as having strong anti-inflammatory activity towards multiple ailments, including arthritis. The main drawback of curcumin is its poor solubility in water, which leads to low intestinal absorption and minimal bioavailability. In this study, we aimed to compare the anti-arthritic in vivo effect of different curcumin preparations – basic curcumin extract, micellar curcumin, curcumin mixture with piperine, and microencapsulated curcumin. Methods: Arthritis was induced in Wistar rats by complete Freund's adjuvant, and the severity of arthritis was evaluated daily using the arthritis score system. Curcumin preparations were given to

animals per os daily for 20 consecutive days, starting at 6th day after arthritis induction. To determine the inflammatory background, pro-inflammatory cytokines were determined using the ELISA test. In addition, hematologic test, weight change, and limb swelling were tracked. Results: Our results indicate that curcumin had a rather weak effect on arthritis progression in the Wistar rat model, microencapsulated curcumin effectively prevented the progression of arthritis – the disease stabilized after 10 days of supplementation. It also reduced the levels of immune cells (neutrophils and leukocytes), as well as pro-inflammatory cytokines – TNFα, IL-1, and IL-6, which levels were close to arthritis-free control. Other formulations of curcumin had lower or no effect on arthritis progression. Conclusion: Our study shows that the same concentrations of curcumin had a distinctly expressed positive anti-inflammatory effect depending on the form of its delivery. Specifically, we found that microencapsulated curcumin had the most promising effect for treatment. Graphical abstract: [Figure not available: see fulltext.] © 2021, The Author(s).

96) Li, W., Jiang, L., Lu, X., Liu, X., Ling, M.
Curcumin protects radiation-induced liver damage in rats through the NF-κB signaling pathway
(2021) *BMC Complementary Medicine and Therapies*, 21 (1), art. no. 10, .

Abstract
Background: Curcumin has been demonstrated to exert anti-oxidant, anti-fibrotic, anti-inflammatory, and anti-cancer activities. This study was conducted to observe the effect and inner mechanism of curcumin in rats with radiation-induced liver damage (RILD). Methods: Thirty SD rats were classified into Control, Radiation group and Curcumin (Cur) + Radiation group (n = 10 in each group). The changes in body weight of the rats were observed on the 3rd, 7th and 14th days after the treatment with curcumin. On the 14th day post treatment, the heart blood of the rats was drawn for measurement of liver function indices including total protein (TP), alanine aminotransfetase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) as well as aspartate aminotransfetase (AST). Subsequently, the rats were euthanized and liver tissues were taken to observe liver morphological changes using hematoxylin-eosin (HE), and to analyze apoptosis condition using transferase-mediated deoxyuridine triphosphate-biotin nick end labeling (TUNEL) assays. Meanwhile, the oxidative stress level in liver tissue homogenate was determined by biochemical analysis. The expression of nuclear factor kappa B (NF-κB) pathway-associated and apoptosis-associated proteins was detected using Western blot analysis, and the expression levels of inflammatory factors were measured by Enzyme-linked immunosorbent assay (ELISA). Results: The reduced body weight was observed in rats of the Radiation group compared to the Control and Cur + Radiation groups on day 14. In the Radiation group, hepatic cell edema and inflammatory cell infiltration could be visible under the light microscope, and the hepatocytes presented with vacuolar degeneration. In the Cur + Radiation group, the hepatocytes swelled under the microscope, but the pathological changes were alleviated in comparison with the Radiation group. RILD rats with curcumin treatment presented with decreased ALT, AST, ALP, LDH, and maleicdialdehyde (MDA) levels, and elevated TP, superoxide dismutase (SOD), caspase activated DNase (CAD) and glutathione (GSH) levels. Apoptosis and inflammation in rats with RILD were up-regulated, and the NF-κB pathway was activated, but they were reversed after continuously intragastric administration of curcumin for 14 days. Conclusion: Our study highlights that curcumin treatment reduces the liver damage caused by radiation through the inhibition of the NF-κB pathway. © 2020, The Author(s).

97) van Riel Neto, F., Foschini, M., Tozoni, J.R., Piovesan, E., Cristovan, F.H., Marletta, A.
Optical spectroscopy study of the interaction between curcumin and acrylic polymers
(2021) *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, 260, art. no. 119954, .

Abstract
This paper presents the results of a study conducted on the interaction between curcumin, a compound with several biomedical applications in traditional and modern medicine, and the acrylic polymers poly(methyl methacrylate), poly(ethyl methacrylate), and poly(n-butyl methacrylate), through photophysical experiments in curcumin/acrylic polymers casting films. Optical absorption intensity at ~340 nm increases relatively to its maximum at ~417 nm when the amount of curcumin in the polymeric film decreases, due to a significant change in the concentration of the isomers cis- or trans-form of curcumin, regardless of the acrylic polymer. Fluorescence (FL) spectra of the films depend on the curcumin concentration in the matrix with well-resolved line shape. They show two distinct bands, one at ~525 nm, for higher curcumin concentration (5.00 mmol.L-1), related to the aggregated curcumin species, and another at ~465 nm, for lower concentration of curcumin (0.10 mmol.L-1), related to the effects of the solvent on the conformational structure of the curcumin molecule and the presence of the trans-form of curcumin. The parameter Kagg, related to the contribution of the aggregated curcumin, shows the influence of the polymeric lateral chain length of the matrix in the de-aggregation of the curcumin. The Huang-Rhys factor indicates that curcumin aggregated species are conformationally more stable, and that the isolate species depends on the chemical environment and the matrix/curcumin interaction, decreasing its conformational degrees of freedom. Arrhenius plots, obtained via FL experiment in function of the sample temperature, show that, for higher curcumin concentration, the value for the relaxation energy process is not well defined, due the decrease in the interaction between the matrix and the curcumin molecules. With these results, it is possible to infer that the interaction matrix/curcumin must occur via lateral chemical alkyl groups. © 2021 Elsevier B.V.

98) Elanthendral, G., Shobana, N., Meena, R., P, P., Samrot, A.V.
Utilizing pharmacological properties of polyphenolic curcumin in nanotechnology
(2021) *Biocatalysis and Agricultural Biotechnology*, 38, art. no. 102212, .

Abstract
Turmeric is a natural nutraceutical and a bioactive polyphenol molecule. It is universally considered to be one of the

"Wonder drug of Life". Curcumin is nourishing and restorative in nature with numerous therapeutic effects such as antimicrobial, anticancer, and anti-nflammatory. Despite all the benefits, its poor pharmacological characteristics such as limited solubility, instability, and substantial metabolic conversion, its applicability in medicine is limited. Curcumin's pharmacological properties can be improved through a variety of approaches. Curcumin incorporated into nanoformulations have become a better therapeutic option for its superior therapeutic effects. This review shows how nanotechnological formulations have aided curcumin in improving its drug-likeness, as seen by several research completed previously. © 2021 Elsevier Ltd

99) Jayasuriya, R., Dhamodharan, U., Ali, D., Ganesan, K., Xu, B., Ramkumar, K.M.
Targeting Nrf2/Keap1 signaling pathway by bioactive natural agents: Possible therapeutic strategy to combat liver disease
(2021) *Phytomedicine*, 92, art. no. 153755, .

Abstract
Background: Nuclear factor erythroid 2-related factor (Nrf2), a stress-activated transcription factor, has been documented to induce a defense mechanism against oxidative stress damage, and growing evidence considers this signaling pathway a key pharmacological target for the treatment of liver diseases. Purpose: The present review highlights the role of phytochemical compounds in activating Nrf2 and mitigate toxicant-induced stress on liver injury. Methods: A comprehensive search of published articles was carried out to focus on original publications related to Nrf2 activators against liver disease using various literature databases, including the scientific Databases of Science Direct, Web of Science, Pubmed, Google, EMBASE, and Scientific Information (SID). Results: Nrf2 activators exhibited promising effects in resisting a variety of liver diseases induced by different toxicants in preclinical experiments and in vitro studies by regulating cell proliferation and apoptosis as well as an antioxidant defense mechanism. We found that the phytochemical compounds, such as curcumin, naringenin, sulforaphane, diallyl disulfide, mangiferin, oleanolic acid, umbelliferone, daphnetin, quercetin, isorhamnetin-3-O-galactoside, hesperidin, diammonium glycyrrhizinate, corilagin, shikonin, farrerol, and chenpi, had the potential to improve the Nrf2-ARE signaling thereby combat hepatotoxicity. Conclusion: Nrf2 activators may offer a novel potential strategy for the prevention and treatment of liver diseases. More extensive studies are essential to identify the underlying mechanisms and establish future therapeutic potentials of these signaling modulators. Further clinical trials are warranted to determine the safety and effectiveness of Nrf2 activators for hepatopathy. © 2021 Elsevier GmbH

100) Yuan, D., Zhou, F., Shen, P., Zhang, Y., Lin, L., Zhao, M.
Self-assembled soy protein nanoparticles by partial enzymatic hydrolysis for pH-Driven Encapsulation and Delivery of Hydrophobic Cargo Curcumin
(2021) *Food Hydrocolloids*, 120, art. no. 106759, .

Abstract
Controlled partial enzymatic hydrolysis has been shown to be an efficacious strategy for devising and construction of multifunctional soy protein nanoparticles (SPNPs). In this work, we reported a successful fabrication of novel SPNPs obtained from self-assembly of the amphiphilic hydrolysate after partial hydrolysis of soy protein isolate (DH, 4%), and explored their potential as a nanocarrier for active cargo delivery. Curcumin was effectively loaded into the hydrophobic core of SPNPs by utilizing the pH-driven method, and the resultant curcumin-loaded SPNPs were spherical with a small particle size (80 nm in diameter), homogeneous size distribution and relatively high encapsulation efficiency (78%). The solubility and stability of curcumin against different NaCl concentrations (0–300 mM) and temperatures (75–95 °C) were remarkably enhanced by encapsulation into SPNPs. Additionally, SPNPs were able to effectively protect curcumin from degradation or precipitation during simulated gastric-intestinal digestion, showing a significantly enhanced bioaccessibility. Encapsulated curcumin was valid in alleviating cell oxidative damage induced by H2O2, mainly by scavenging intracellular free radicals, inhibiting lipid oxidation, and elevating endogenous antioxidant enzymes levels. Interestingly, the vehicle SPNPs showed synergistic antioxidant effect, creatively evidencing their bifunctionality in cellular antioxidant activity. © 2021

101) Molinari, C., Ruga, S., Farghali, M., Galla, R., Bassiouny, A., Uberti, F.
Preventing c2c12 muscular cells damage combining magnesium and potassium with vitamin D3 and curcumin
(2021) *Journal of Traditional and Complementary Medicine*, 11 (6), pp. 532-544.

Abstract
Background and aim: Physical activity is defined as any bodily movement produced by skeletal muscles which causes energy consumption; moderate and constant physical activity is known to be beneficial and to slow the muscle loss process associated with aging. The aim of the present study was to test, in an in vitro exercise model, the biological effects of a new formulation composed of magnesium and potassium combined with vitamin D and curcumin created to support muscle activity and to prevent hypercontraction damage. Experimental procedure: C2C12 cells were treated with vitamin D, buffered magnesium bisglycinate, curcumin, and potassium citrate. Cell viability, morpho-functional changes, calcium and magnesium movements, and the main kinases involved in glucose uptake were analyzed. The glycogen level and lactate were also evaluated. Results and conclusion: Important results about a positive effect on mitochondrial activity, ATP production, oxygen consumption and in the physiological differentiation of C2C12 cells were obtained. Further experiments were performed under conditions that mimic the biological aspects of strenuous exercise. The combination of magnesium, vitamin D3, curcumin, and potassium citrate revealed beneficial effects on skeletal muscle cells under physiological conditions as well as while mimicking intense activity. In particular, in an in vitro model, they were able to control the hypercontraction, restoring ion fluxes, reducing inflammation signaling and supporting the main mechanism involved on

aerobic activity. Our results have indicated for the first time that this new combination could be considered as a new nutraceutical formulation to improve physical performance and muscle recovery. © 2021 Center for Food and Biomolecules, National Taiwan University

102) Wang, P., Li, H., Lin, Z., Luo, H., Luo, W.
Comparing the Effect of Piperine and Ilepcimide on the Pharmacokinetics of Curcumin in SD Rats
(2021) *Frontiers in Pharmacology*, 12, art. no. 725362, .

Abstract
The poor bioavailability and rapid metabolism of curcumin (CUR) restrict its clinical application. Piperine (PIP), which was extracted from natural compounds, can increase the plasma concentration of curcumin in humanidad. As an artificial synthetic piperine analog, silepcimide (ILE) has significant advantages because of the low price and simple synthesis process. In this study, a simple and rapid HPLC-UV method was developed for determination of the plasma concentration of CUR, PIP,ILE and dihydrocurcumin (DHC, a metabolite of CUR) simultaneously. Meanwhile, the effects of PIP and ILE on the plasma concentration and pharmacokinetics of DHC in SD rats was studied to explore whether ILE could serve as a CUR bioavailability enhancer. The metabolic pathway of CUR was studied by comparing the differences of CUR plasma concentration between intravenous injection and oral administration over the same time period, and reacting with small intestine homogenate without microbes of SD rats. The results of drug-time curve showed that combined administration of ILE and CUR had significant effect on plasma concentrations of DHC. Repeated administration of PIP or ILE could significantly increase the plasma concentration of DHC. Plasma CUR could be detected in the samples of from intravenous injection of CUR rats, whereas, it couldn't be detected in the plasma sample form oral administration rats. CUR incubated with intestinal homogenate without intestinal bacteria could not be transformed into DHC. In conclusion, our results show that ILE can improve the bioavailability of CUR. Additionally, it was inferred that most of the CUR was reduced to DHC by NADPH when it was absorbed from gastrointestinal tract, and our results demonstrated that this pathway might be mediated by gastrointestinal microorganisms. Copyright © 2021 Wang, Li, Lin, Luo and Luo.

103) Tabanelli, R., Brogi, S., Calderone, V.
Improving curcumin bioavailability: Current strategies and future perspectives
(2021) *Pharmaceutics*, 13 (10), art. no. 1715, .

Abstract
Curcumin possesses a plethora of interesting pharmacological effects. Unfortunately, it is also characterized by problematic drug delivery and scarce bioavailability, representing the main problem related to the use of this compound. Poor absorption, fast metabolism, and rapid systemic clearance are the most important factors contributing to low curcumin levels in plasma and tissues. Accordingly, to overcome these issues, numerous strategies have been proposed and are investigated in this article. Due to advances in the drug delivery field, we describe here the most promising strategies for increasing curcumin bioavailability, including the use of adjuvant, complexed/encapsulated curcumin, specific curcumin formulations, and curcumin nanoparticles. We analyze current strategies, already available in the market, and the most advanced technologies that can offer a future perspective for effective curcumin formulations. We focus the attention on the effectiveness of curcumin-based formulations in clinical trials, providing a comprehensive summary. Clinical trial results, employing various delivery methods for curcumin, showed that improved bioavailability corresponds to increased therapeutic efficacy. Furthermore, advances in the field of nanoparticles hold great promise for developing curcumin-based complexes as effective therapeutic agents. Summarizing, suitable delivery methods for this polyphenol will ensure the possibility of using curcumin-derived formulations in clinical practice as preventive and disease-modifying therapeutics. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

104) Rodrigues, S.O., da Cunha, C.M.C., Soares, G.M.V., Silva, P.L., Silva, A.R., Gonçalves-De-albuquerque, C.F.
Mechanisms, pathophysiology and currently proposed treatments of chronic obstructive pulmonary disease
(2021) *Pharmaceuticals*, 14 (10), art. no. 979, .

Abstract
Chronic obstructive pulmonary disease (COPD) is one of the leading global causes of morbidity and mortality. A hallmark of COPD is progressive airflow obstruction primarily caused by cigarette smoke (CS). CS exposure causes an imbalance favoring pro-over antioxidants (oxidative stress), leading to transcription factor activation and increased expression of inflammatory mediators and proteases. Different cell types, including macrophages, epithelial cells, neutrophils, and T lymphocytes, contribute to COPD pathophysiology. Alteration in cell functions results in the generation of an oxidative and inflammatory microenvironment, which contributes to disease progression. Current treatments include inhaled corticosteroids and bronchodilator therapy. However, these therapies do not effectively halt disease progression. Due to the complexity of its pathophysiology, and the risk of exacerbating symptoms with existing therapies, other specific and effective treatment options are required. Therapies directly or indirectly targeting the oxidative imbalance may be promising alternatives. This review briefly discusses COPD pathophysiology, and provides an update on the development and clinical testing of novel COPD treatments. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

105)

Zhang, H.A., Kitts, D.D.
Turmeric and its bioactive constituents trigger cell signaling mechanisms that protect against diabetes and cardiovascular diseases
(2021) *Molecular and Cellular Biochemistry*, 476 (10), pp. 3785-3814.

Abstract
Turmeric, the rhizome of Curcuma longa plant belonging to the ginger family Zingiberaceae, has a history in Ayurvedic and traditional Chinese medicine for treatment of chronic diseases, including metabolic and cardiovascular diseases (CVD). This parallels a prevalence of age- and lifestyle-related diseases, especially CVD and type 2 diabetes (T2D), and associated mortality which has occurred in recent decades. While the chemical composition of turmeric is complex, curcuminoids and essential oils are known as two major groups that display bioactive properties. Curcumin, the most predominant curcuminoid, can modulate several cell signaling pathways involved in the etiology and pathogenesis of CVD, T2D, and related morbidities. Lesser bioactivities have been reported from other curcuminoids and essential oils. This review examines the chemical compositions of turmeric, and related bioactive constituents. A focus was placed on the cellular and molecular mechanisms that underlie the protective effects of turmeric and turmeric-derived compounds against diabetes and CVD, compiled from the findings obtained with cell-based and animal models. Evidence from clinical trials is also presented to identify potential preventative and therapeutic efficacies. Clinical studies with longer intervention durations and specific endpoints for assessing health outcomes are warranted in order to fully evaluate the long-term protective efficacy of turmeric. © 2021, The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature.

106) Shetty, N.P., Prabhakaran, M., Srivastava, A.K.
Pleiotropic nature of curcumin in targeting multiple apoptotic-mediated factors and related strategies to treat gastric cancer: A review
(2021) *Phytotherapy Research*, 35 (10), pp. 5397-5416.

Abstract
Gastric cancer (GC) is one of the major reasons for cancer-associated death and exhibits the second-highest mortality rate worldwide. Several advanced approaches have been designed to treat GC; however, these strategies possess many innate complications. In view of this, the upcoming research relying on natural products could result in designing potential anticancer agents with fewer side effects. Curcumin, isolated from the rhizomes of Curcuma longa L. has several medicinal properties like antiinflammatory, antioxidant, antiapoptotic, antitumor, and antimetastatic. Such pleiotropic nature of curcumin impedes the invasion and proliferation of GC by targeting several oncogenic factors like p23, human epidermal factor receptor2 including Helicobacter pylori. The side effect of chemotherapy, that is, chemotherapeutic resistance and radiotherapy could be reduced combination therapy of curcumin. Moreover, the photodynamic therapy of curcumin destroys the cancer cells without affecting normal cells. However, further more potential studies are required to establish the potent efficacy of curcumin in the treatment of GC. The current review details the anticancer activities of curcumin and related strategies which could be employed to treat GC with additional focus on its inhibitory properties against viability, proliferation, and migration of GC cells through cell cycle arrest and stimulation by apoptosis-mediated factors. © 2021 John Wiley & Sons Ltd.

107) Majumder, K.K., Kumar, M., Pahwa, R., Lamba, A.K., Shankar, R., Tiwari, A., Tiwari, V., Rishabh
Formulation and characterization of floating tablet dosage form of dual delivery of drug curcumin and berberine hydrochloride using simultaneous estimation by uv spectroscopy
(2021) *International Journal of Applied Pharmaceutics*, 13 (5), pp. 306-310.

Abstract
Objective: The present study was aimed to develop a combinational floating tablet of curcumin and berberine HCl utilizing synthetic polymers synthetic HPMC K-15M and evaluate its various characteristics. Methods: The formulations were developed by the process of wet granulation and evaluated for drug content, content uniformity, floating lag time, total floating time, in vitro buoyancy studies, and in vitro drug release profile. A simultaneous estimation method for curcumin and berberine was developed using U. V spectroscopy. Results: The results clearly indicated that the tablets produced were having acceptable physical parameters. The absence of any drug/polymer/excipient interactions was confirmed using infrared spectroscopy. It was found that the drug content of was in between 96.22 to 99.45 % in all the formulations. Because of their low densities, in vitro floatability tests showed that most of the tablets floated for more than 8 h. The in vitro release studies confirmed the sustained release of more than 80 percent of drug contained within a period of 8 h. In vitro buoyancy was good in all three batches (F1-F3). The overall floating time for the F2 formulation was 24 h. After one month of storage at 40 °C and 75 percent RH, the F2 formulation showed no noticeable change in physical as well as pharmaceutical performance characteristics. Conclusion: Floating tablets of curcumin and berberine was successfully developed and had passed on various pharmaceutical parameters. © 2021 The Authors. Published by Innovare Academic Sciences Pvt Ltd.

108) Sandoval-gallegos, E.M., Ramírez-moreno, E., Vargas-mendoza, N., Arias-rico, J., Estrada-luna, D., Cuevas-cancino, J.J., Jiménez-sánchez, R.C., Flores-chávez, O.R., Baltazar-téllez, R.M., Morales-gonzález, J.A.
Phytochemicals and their possible mechanisms in managing covid-19 and diabetes
(2021) *Applied Sciences (Switzerland)*, 11 (17), art. no. 8163, .

Abstract

For the writing of this manuscript, we searched information published from 2000 to 2021, through PubMed, Web of Science, Springer, and Science Direct. Focusing on the effects related to respiratory diseases, in addition to possible direct effects towards SARS-CoV-2, coupled with dia-betes. Diabetes is a metabolic disease that is characterized by affecting the function of glucose, in addition to insulin insufficiency. This leads to patients with such pathologies as being at greater risk for developing multiple complications and increase exposure to viruses infections. This is the case of severe acute respiratory disease coronavirus 19 (SARS-CoV-2), which gave rise to coronavirus disease 2019 (COVID-19), declared an international public health emergency in March of 2020 Cur-rently, several strategies have been applied in order to prevent the majority of the consequences of COVID-19, especially in patients with chronic diseases such as diabetes. Among the possible treatment options, we found that the use of phytochemical compounds has exhibited beneficial effects for the prevention and inhibition of infection by SARS-CoV-2, as well as for the improvement of the manifestations of diabetes.

109) Akbari, A., Sedaghat, M., Heshmati, J., Tabaeian, S.P., Dehghani, S., Pizarro, A.B., Rostami, Z., Agah, S.
Molecular mechanisms underlying curcumin-mediated microRNA regulation in carcinogenesis; Focused on gastrointestinal cancers
(2021) *Biomedicine and Pharmacotherapy*, 141, art. no. 111849, .

Abstract
Curcumin is a bioactive ingredient found in the Rhizomes of Curcuma longa. Curcumin is well known for its chemopreventive and anti-cancer properties. Recent findings have demonstrated several pharmacological and biological impacts of curcumin, related to the control and the management of gastrointestinal cancers. Mechanistically, curcumin exerts its biological impacts via antioxidant and anti-inflammatory effects through the interaction with various transcription factors and signaling molecules. Moreover, epigenetic modulators such as microRNAs (miRNAs) have been revealed as novel targets of curcumin. Curcumin was discovered to regulate the expression of numerous pathogenic miRNAs in gastric, colorectal, esophageal and liver cancers. The present systematic review was performed to identify miRNAs that are modulated by curcumin in gastrointestinal cancers. © 2021

110) Kumar, P., Saha, T., Behera, S., Gupta, S., Das, S., Mukhopadhyay, K.
Enhanced efficacy of a Cu2+ complex of curcumin against Gram-positive and Gram-negative bacteria: Attributes of complex formation
(2021) *Journal of Inorganic Biochemistry*, 222, art. no. 111494, .

Abstract
Curcumin is a tantalizing molecule with multifaceted therapeutic potentials. However, its therapeutic applications are severely hampered because of poor bioavailability, attributed to its instability and aqueous insolubility. In an attempt to overcome this inherent limitation and develop curcumin-based antibacterials, we had earlier synthesized and characterized a metal complex of Cu(II) with curcumin, having the formula [Cu(Curcumin)(OCOCH3)(H2O)], hereafter referred to as Cu(Cur). In this study, the complex, i.e., Cu(Cur), was investigated for its stability and antibacterial activity along with its possible mechanism of action in comparison to the parent molecule, curcumin. Complex formation resulted in improved stability as Cu(Cur) was found to be highly stable under different physiological conditions. Such improved stability was verified with the help of UV–Vis spectroscopy and HPLC. With improved stability, Cu(Cur) exhibited potent and significantly enhanced activity over curcumin against both E. coli and S. aureus. Calcein leakage assay revealed that the complex triggered immediate membrane permeabilization in S. aureus. This membrane disruptive mode of action was further corroborated by microscopic visualization. The excellent potency of the complex was augmented by its safe toxicological profile as it was non-hemolytic and non-cytotoxic towards mammalian cells, making it a suitable candidate for in vivo investigations. Altogether, this investigation is a critical appraisal that advocates the antibacterial potential of this stable, membrane-targeting and non-toxic complex, thereby presenting new perspectives for its therapeutic application against bacterial infections. © 2021

111) Mohanty, B.P., Mitra, T., Ganguly, S., Sarkar, S.D., Mahanty, A.
Curcumin Has Protective Effect on the Eye Lens Against Arsenic Toxicity
(2021) *Biological Trace Element Research*, 199 (9), pp. 3354-3359.

Abstract
Arsenic is a highly carcinogenic environmental contaminant. Curcumin, the bioactive component of turmeric, exhibits therapeutic efficacy against several chronic inflammatory and infectious diseases. The present study was carried out to investigate the impact of arsenic on eye lens and evaluate the ameliorative potential of curcumin against arsenic toxicity. Gene expression analysis of α, β, and γ-crystallins and fatty acid profile of lens tissues of arsenic-exposed Labeo rohita was examined and the protective effect of curcumin as diet supplement was evaluated. Curcumin-supplemented diet was prepared at 1.5% and 3% and fed to four groups of fish for 7 days prior to arsenic exposure (at 5 ppm and 15 ppm) for 15 days. Gene expression analysis showed downregulation of α and β-crystallins in the eye lens of arsenic-exposed groups (fed basal diet), whereas the groups fed a curcumin-supplemented diet showed insignificant alterations. Similarly, fatty acid fingerprint of lens lipids arsenic-exposed group exhibited reduction in saturated fatty acid and docosahexaenoic acid (DHA) content. However, in 3% curcumin-supplemented diet–fed and arsenic exposed group group, fatty acid profile remained unchanged. Interestingly, concentration of one non-fatty acid, an antioxidant compound (phenol 2,4-bis 1,1 dimethyl; PD) that was identified in the GC-MS fingerprinting through NIST library (version 2.2, 2014), decreased in response to arsenic exposure which was restored to normal level in curcumin-supplemented groups proving the therapeutic potential of

curcumin. The findings of the study suggest that curcumin has a protective effect on eye lens against arsenic toxicity. © 2020, Springer Science+Business Media, LLC, part of Springer Nature.

112) Astudillo-Sánchez, P.D., Enrique J. Soriano-Castillo, M.S., Manzanilla, B., Rocha-Ortiz, G., Trujano-Ortiz, L.G., Matus, M.H., Domínguez, Z., Salas-Reyes, M.
Electrochemical Oxidation of Symmetrical Antioxidant Chicoric Acid in DMSO: Is this a Sequential or a Simultaneous 2ECE Mechanism?
(2021) *ChemistrySelect*, 6 (31), pp. 8158-8164.

Abstract
Chicoric acid (ChA) is present in various plants, and it is known to have interesting biological properties, e. g., antioxidant activity. In this work, a detailed analysis of the electrochemical oxidation mechanism of L-(ChA) in DMSO on glassy carbon is reported, for the first time. Since geometry optimization of ChA using Density Functional Theory, confirms a C2 symmetry, three mechanistic routes involving electron transfers (E) and deprotonation reactions (C) were proposed for the simulation work: 1) EECCEECC, 2) ECECECEC, and 3) two simultaneous 2(ECE) steps. Thermodynamic and kinetic parameters of the electrochemical and chemical steps were estimated by fitting the voltammetric simulation with the experimental voltammograms at different scan rates. Results showed that only the ECECECEC mechanism presented an adequate fitting with respect to experimental voltammograms. Homogeneous kinetic constants were close to a diffusion-limited process (ca. 1×1010 M−1 s−1, for bimolecular reactions) and equilibrium constants, within the range of 1.5–12.0. © 2021 Wiley-VCH GmbH

113) Lika, E., Kostić, M., Vještica, S., Milojević, I., Puvača, N.
Honeybee and plant products as natural antimicrobials in enhancement of poultry health and production
(2021) *Sustainability (Switzerland)*, 13 (15), art. no. 8467, .

Abstract
The quality and safety attributes of poultry products have attracted increasing widespread attention and interest from scholarly groups and the general population. As natural and safe alternatives to synthetic and artificial chemical drugs (e.g., antibiotics), botanical products are recently being used in poultry farms more than 60% of the time for producing organic products. Medicinal plants, and honeybee products, are natural substances, and they were added to poultry diets in a small amount (between 1% and 3%) as a source of nutrition and to provide health benefits for poultry. In addition, they have several biological functions in the poultry body and may help to enhance their welfare. These supplements can increase the bodyweight of broilers and the egg production of laying hens by approximately 7% and 10% and enhance meat and egg quality by more than 25%. Moreover, they can improve rooster semen quality by an average of 20%. Previous research on the main biological activities performed by biotics has shown that most research only concentrated on the notion of using botanical products as growth promoters, anti-inflammatory, and antibacterial agents. In the current review, the critical effects and functions of bee products and botanicals are explored as natural and safe alternative feed additives in poultry production, such as antioxidants, sexual-stimulants, immuno-stimulants, and for producing healthy products. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

114) Mohankumar, K., Francis, A.P., Pajaniradje, S., Rajagopalan, R.
Synthetic curcumin analog: inhibiting the invasion, angiogenesis, and metastasis in human laryngeal carcinoma cells via NF-kB pathway
(2021) *Molecular Biology Reports*, 48 (8), pp. 6065-6074.

Abstract
Background: Laryngeal carcinoma, the most common among head and neck squamous cell carcinoma (HNSCC), induces 1% of all cancer deaths. Curcumin the active constituent of turmeric, is shown to be effective in the treatment of various cancers. In the present study, we explored the mechanistic role of bis-demethoxy curcumin analog (BDMC-A) as a chemotherapeutic agent. We investigated its inhibitory effect on invasion, angiogenesis, and metastasis in human laryngeal carcinoma (Hep-2) cells in comparison with curcumin. Methods: The effect of curcumin and BDMC-A on transcription factors (NF-κB, p65, c-Jun, c-Fos, STAT3, 5, PPAR-γ, β-catenin, COX-2, MMP-9, VEGF, TIMP-2) involved in signal transduction cascade, invasion, and angiogenesis in Hep-2 cells were quantified using Western blotting and RT-PCR technique. ELISA was used to measure the pro-inflammatory markers in Hep-2 cells treated with curcumin and BDMC-A. Results: The results showed that BDMC-A inhibits the transcription factors NF-κB, p65, c-Jun, c-Fos, STAT3, STAT5, PPAR-γ and β-catenin, which are responsible for tumor progression and malignancy. Moreover, BDMC-A treatment downregulated MMP-9, VEGF, TGF- β, IL-6 and IL-8 and upregulated TIMP-2 levels. The effects were more significant compared to curcumin. Conclusion: Our overall results revealed that BDMC-A more effectively inhibited the markers of invasion, angiogenesis and metastasis in comparison with curcumin. © 2021, The Author(s), under exclusive licence to Springer Nature B.V.

115) Pierre, M.B.R.
Nanocarriers for Photodynamic Therapy Intended to Cutaneous Tumors
(2021) *Current Drug Targets*, 22 (10), pp. 1090-1107.

Abstract
Photodynamic Therapy (PDT) is a therapeutic modality used for several malignant and premalignant skin disorders, including Bowen's disease skin cancers and Superficial Basal Cell Carcinoma (BCC). Several photosensitizers (PSs) have been explored for tumor destruction of skin cancers, after their activation by a light source of appropriate wavelength. Topical release of PSs avoids prolonged photosensitization reactions associated with systemic administration; however, its clinical usefulness is influenced by its poor tissue penetration and the stability of the active agent. Nanotechnology-based drug delivery systems are promising tool to enhance the efficiency for PDT of cancer. This review focuses on PSs encapsulated in nanocarriers explored for PDT of skin tumors. © 2021 Bentham Science Publishers.

116) Bazzolo, B., Mittal, L., Sieni, E., Piovan, A., Filippini, R., Conconi, M.T., Camarillo, I.G., Sundararajan, R.
The electrical pulse application enhances intra-cellular localization and potentiates cytotoxicity of curcumin in breast cancer cells
(2021) *Bioelectrochemistry*, 140, art. no. 107817, .

Abstract
Breast cancer is the most common cancer of women, and fifth leading cause of mortality worldwide. Existing breast cancer regimens are costly and produce severe side effects. This highlights a need for the development of efficient novel therapies, which are cost effective and limit side effects. An electrical pulse (EP)-based chemo therapy, known as electrochemotherapy (ECT) using the natural compound curcumin could be an effective alternative. ECT is a non-surgical modality, which produces excellent anti-tumor efficacy at small drug concentrations due to increased uptake of drugs. In clinics, ECT is shown to be effective in treating advanced, recurrent, and metastatic breast cancers, which are refractory to multiple modalities. ECT with curcumin triggers apoptotic cell death in breast cancer cells and could be an effective alternative, due to curcumin's low cost and reduced side-effects. However, there is a lack of studies quantifying the uptake of curcumin in response to EP application. Towards this, we determined the uptake of different curcuminoids (curcumin, desmethoxycurcumin, and bisdemethoxycurcumin) upon EP application and their impact on cell cytotoxicity. Additionally, we studied the combined effect of calcium chloride (CaCl2) and a curcuminoids (Cur) mixture, based on initial studies suggesting calcium electroporation as a potential inexpensive anti-cancer treatment. Our results indicate EP with Cur increases cellular uptake, cell shrinkage, and cytotoxicity. The EP + Cur resulted in the highest uptake of the bisdemethoxycurcumin. Further, EP also potentiated the cytotoxicity of CaCl2 and of the Cur and CaCl2 combination against breast cancer cells and caused apoptosis. Our preliminary data pave the way to further studies on Cur and CaCl2 combination treating breast cancer. © 2021 Elsevier B.V.

117) Miranda, P.H.S., Santos, A.C.D., Freitas, B.C.B.D., Martins, G.A.D.S., Vilas Boas, E.V.D.B., Damiani, C.
A scientific approach to extraction methods and stability of pigments from Amazonian fruits
(2021) *Trends in Food Science and Technology*, 113, pp. 335-345.

Abstract
Background: Pigments are substances that give color to different types of products from the food, pharmaceutical, and cosmetic industry, which are naturally found in different kinds of fruits and are classified as natural dyes. For the study of extraction method, it is not enough to consider only the extraction medium; it is necessary to have in-depth knowledge of how to maintain its stability and how a specific pigment will behave with the temperature variation, exposure to light, pH, and storage. Scope and approach: This review highlights the profile of the main groups of pigments such as carotenoids, anthocyanins, betalains, and chlorophyll, also citing the main theoretical aspects of the most used methods for the extraction and stability of these compounds. Besides, a wide range of fruits from the Amazon region with high levels of pigments is explored by this review. Key Findings and Conclusions: Due to the restrictions imposed by conventional extraction processes, it is necessary to study techniques to maximize the extraction efficiency and pigment stability. There are several techniques and methods of extraction that can be used to obtain good yields and preserve the natural characteristics of the pigments. The methods commonly used for pigment extraction are solvent, microwave, ultrasound, pressurized liquid, pulsed electric field, supercritical fluid, enzymes, and extraction methods using green chemistry. © 2021 Elsevier Ltd

118) Periyathambi, P., Hemalatha, T.
Development of water-soluble curcumin grafted magnetic nanoparticles for enhancing bioavailability, fluorescence, and magnetic resonance imaging activity
(2021) *Materials Letters*, 294, art. no. 129763, .

Abstract
The chemo-fluorescent drug curcumin (CUR) is a safe and effective anticancer agent. The primary limitation of CUR is its poor solubility in water, which limits its bioavailability. We have developed an efficient chemotherapeutic and amorphous magneto-fluorescent CUR grafted magnetic nanoparticles (CUR-MAG NPs) using wet chemical process. The CUR grafting of MAG NPs improved the solubility, bioavailability, and internalization activities of CUR. CUR-MAG NPs can be used as a novel platform for in vivo biomedical applications. © 2021 Elsevier B.V.

119) Kulyal, P., Acharya, S., Ankari, A.B., Kokkiripati, P.K., Tetali, S.D., Raghavendra, A.S.
Variable Secondary Metabolite Profiles Across Cultivars of Curcuma longa L. and C. aromatica Salisb.
(2021) *Frontiers in Pharmacology*, 12, art. no. 659546, .

Abstract
Background: Curcuma spp. (Zingiberaceae) are used as a spice and coloring agent. Their rhizomes and essential oils are known for medicinal properties, besides their use in the flavoring and cosmetic industry. Most of these biological activities were attributed to volatile and nonvolatile secondary metabolites present in the rhizomes of Curcuma spp. The metabolite variations among the species and even cultivars need to be established for optimized use of Curcuma spp. Objectives: We compared the phytochemical profiles of rhizomes and their essential oils to establish the variability among seven cultivars: five of Curcuma longa L. (Alleppey Supreme, Duggirala Red, Prathibha, Salem, Suguna) and two of C. aromatica Salisb. (Kasturi Araku, Kasturi Avidi). The GC-MS and LC-MS-based analyses were employed to profile secondary metabolites of these selected cultivars. Methods: Rhizomes of Curcuma spp. were subjected to hydro-distillation to collect essential oil and analyzed by GC-MS. The methanol extracts of fresh rhizomes were subjected to LC-MS analyses. The compounds were identified by using the relevant MS library databases as many compounds as possible. Results: The essential oil content of the cultivars was in the range of 0.74–1.62%. Several compounds were detected from the essential oils and rhizome extracts by GC-MS and LC-MS, respectively. Of these, 28 compounds (13 from GCMS and 15 from LCMS) were common in all seven cultivars, e.g., α-thujene, and diarylheptanoids like curcumin. Furthermore, a total of 39 new compounds were identified from C. longa L. and/or C. aromatica Salisb., most of them being cultivar-specific. Of these compounds, 35 were detected by GC-MS analyses of essential oils, 1,2-cyclohexanediol, 1-methyl-4-(1-methylethyl)-, and santolina alcohol, to name a few. The other four compounds were detected by LC-MS of the methanolic extracts of the rhizomes, e.g., kaempferol-3,7-O-dimethyl ether and 5,7,8-trihydroxy-2′,5′-dimethoxy-3′,4′-methylene dioxyisoflavanone. Conclusions: We identified and recorded the variability in the metabolite profiles of essential oils and whole rhizome extracts from the seven cultivars of Curcuma longa L. and C. aromatica Salisb. As many as 39 new metabolites were detected in these seven Indian cultivars of Curcuma spp. Many of these compounds have health benefits. © Copyright © 2021 Kulyal, Acharya, Ankari, Kokkiripati, Tetali and Raghavendra.

120) Li, B., Ouchi, T., Cao, Y., Zhao, Z., Men, Y.
Dental-Derived Mesenchymal Stem Cells: State of the Art
(2021) *Frontiers in Cell and Developmental Biology*, 9, art. no. 654559, .

Abstract
Mesenchymal stem cells (MSCs) could be identified in mammalian teeth. Currently, dental-derived MSCs (DMSCs) has become a collective term for all the MSCs isolated from dental pulp, periodontal ligament, dental follicle, apical papilla, and even gingiva. These DMSCs possess similar multipotent potential as bone marrow-derived MSCs, including differentiation into cells that have the characteristics of odontoblasts, cementoblasts, osteoblasts, chondrocytes, myocytes, epithelial cells, neural cells, hepatocytes, and adipocytes. Besides, DMSCs also have powerful immunomodulatory functions, which enable them to orchestrate the surrounding immune microenvironment. These properties enable DMSCs to have a promising approach in injury repair, tissue regeneration, and treatment of various diseases. This review outlines the most recent advances in DMSCs' functions and applications and enlightens how these advances are paving the path for DMSC-based therapies. © Copyright © 2021 Li, Ouchi, Cao, Zhao and Men.

121) Wang, L.-H., Xiao, J.-X., Li, X.-D., Huang, G.-Q.
Carboxymethyl konjac glucomannan coating on multilayered emulsions for improved bioavailability and targeted delivery of curcumin
(2021) *Food and Function*, 12 (12), pp. 5429-5439.

Abstract
Curcumin was entrapped in multilayered emulsions to increase its stability and bioavailability. Curcumin emulsion stabilized by whey protein isolate (WPI) was coated with chitosan (CHI) or carboxymethyl konjac glucomannan (CMKGM) alone to form secondary emulsions and their combination in sequence to form the tertiary emulsion, in which, the polyelectrolyte concentrations were 1.0% WPI for the primary emulsion, 0.4% CMKGM for the secondary emulsion -CMKGM, 0.2% CHI for the secondary emulsion -CHI, and 0.1% CMKGM for the tertiary emulsion. The characteristics of the emulsions, including their particle size, ? potential, microstructure, creaming stability, and biopolymer distribution, were investigated and their colon-targeted delivery potential was evaluated through both in vitro and in vivo studies as well. The curcumin-loaded secondary and tertiary emulsions were stable with a narrow size distribution and were generated by layer-by-layer assembly according to confocal laser scanning microscope observation. When CMKGM was located at the outermost layer, the corresponding secondary and tertiary emulsions showed a greatly reduced release of curcumin in the simulated gastric fluid, but exhibited increased release in the ß-mannanase-containing simulated colonic fluid. In vivo evaluation in mice demonstrated that the bioavailability of curcumin in the CMKGM-coated secondary and tertiary emulsions was increased by about 4 folds compared with that of free curcumin and curcumin could be released in a sustainable manner. These results demonstrated that multilayered emulsions coated with CMKGM could promote curcumin absorption in the gastrointestinal tract and hence is a promising colon-targeted delivery system for curcumin. © The Royal Society of Chemistry.

122) Wang, H., Xu, Y., Sun, J., Sui, Z.
The Novel Curcumin Derivative 1g Induces Mitochondrial and ER-Stress-Dependent Apoptosis in Colon Cancer

Cells by Induction of ROS Production
(2021) *Frontiers in Oncology*, 11, art. no. 644197, .

Abstract
Reactive oxygen species (ROS) play an important role in cellular metabolism. Many chemotherapeutic drugs are known to promote apoptosis through the production of ROS. In the present study, the novel curcumin derivative, 1g, was found to inhibit tumor growth in colon cancer cells both in vitro and in vivo. Bioinformatics was used to analyze the differentially expressed mRNAs. The mechanism of this effect was a change in mitochondrial membrane potential caused by 1g that increased its pro-apoptotic activity. In addition, 1g produced ROS, induced G1 checkpoint blockade, and enhanced endoplasmic reticulum (ER)-stress in colon cancer cells. Conversely, pretreatment with the ROS scavenging agent N-acetyl-l-cysteine (NAC) inhibited the mitochondrial dysfunction caused by 1g and reversed ER-stress, cell cycle stagnation, and apoptosis. Additionally, pretreatment with the p-PERK inhibitor GSK2606414 significantly reduced ER-stress and reversed the apoptosis induced by colon cancer cells. In summary, the production of ROS plays an important role in the destruction of colon cancer cells by 1g and demonstrates that targeted strategies based on ROS represent a promising approach to inhibit colon cancer proliferation. These findings reveal that the novel curcumin derivative 1g represents a potential candidate therapeutics for the treatment of colon cancer cells, via apoptosis caused by mitochondrial dysfunction and endoplasmic reticulum stress. © Copyright © 2021 Wang, Xu, Sun and Sui.

123) Tripathy, S., Verma, D.K., Thakur, M., Patel, A.R., Srivastav, P.P., Singh, S., Chávez-González, M.L., Aguilar, C.N.
Encapsulated Food Products as a Strategy to Strengthen Immunity Against COVID-19
(2021) *Frontiers in Nutrition*, 8, art. no. 673174, .

Abstract
In December 2019, the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2)—a novel coronavirus was identified which was quickly distributed to more than 100 countries around the world. There are currently no approved treatments available but only a few preventive measures are available. Among them, maintaining strong immunity through the intake of functional foods is a sustainable solution to resist the virus attack. For this, bioactive compounds (BACs) are delivered safely inside the body through encapsulated food items. Encapsulated food products have benefits such as high stability and bioavailability, sustained release of functional compounds; inhibit the undesired interaction, and high antimicrobial and antioxidant activity. Several BACs such as ω-3 fatty acid, curcumin, vitamins, essential oils, antimicrobials, and probiotic bacteria can be encapsulated which exhibit immunological activity through different mechanisms. These encapsulated compounds can be recommended for use by various researchers, scientists, and industrial peoples to develop functional foods that can improve immunity to withstand the coronavirus disease 2019 (COVID-19) outbreak in the future. Encapsulated BACs, upon incorporation into food, offer increased functionality and facilitate their potential use as an immunity booster. This review paper aims to target various encapsulated food products and their role in improving the immunity system. The bioactive components like antioxidants, minerals, vitamins, polyphenols, omega (ω)-3 fatty acids, lycopene, probiotics, etc. which boost the immunity and may be a potential measure to prevent COVID-19 outbreak were comprehensively discussed. This article also highlights the potential mechanisms; a BAC undergoes, to improve the immune system. © Copyright © 2021 Tripathy, Verma, Thakur, Patel, Srivastav, Singh, Chávez-González and Aguilar.

124) Lilie, C., Morris, P., Tippett, J.C.
Herbal substances that affect hemostasis
(2021) *Essentials of Blood Product Management in Anesthesia Practice*, pp. 89-100.

Abstract
The use of naturally occurring plants, which have been used for thousands of years by humans for their medicinal properties, is steadily growing in popularity. Their pharmacologically active constituents which confer medicinal benefit also pose risks, including the potential for causing or contributing to bleeding. This is especially problematic in patients undergoing surgery or procedures as the unrecognized bleeding potential of many natural substances could lead to perioperative hemorrhage and related complications. Perioperative practitioners should understand the importance of completing a full medication review preoperatively which includes disclosure of natural substances. An understanding of the bleeding risks of these substances should also be appreciated. © Springer Nature Switzerland AG 2021. All rights reserved.

125) Hu, Q., Luo, Y.
Chitosan-based nanocarriers for encapsulation and delivery of curcumin: A review
(2021) *International Journal of Biological Macromolecules*, 179, pp. 125-135.

Abstract
To overcome the poor aqueous solubility and bioavailability of curcumin, emphasize its functional features, and broaden its applications in the food and pharmaceutical industries, many nanoscale systems have been widely applied for its encapsulation and delivery. Over many decades, chitosan as a natural biopolymer has been extensively studied due to its polycationic nature, biodegradability, biocompatibility, non-toxicity, and non-allergenic. Various chitosan-based nanocarriers with unique properties for curcumin delivery, including but not limited to, self-assembled nanoparticles, nanocomposites, nanoemulsions, nanotubes, and nanofibers, have been designed. This review focuses on the most-recently reported fabrication techniques of different types of chitosan-based nanocarriers. The functionalities of chitosan in each formulation which determine the physicochemical properties such as surface charge, morphology, encapsulation driving force, and release profile, were discussed in detail. Moreover, the current pharmaceutical applications of curcumin-loaded chitosan

nanoparticles were elaborated. The role of chitosan in facilitating the delivery of curcumin and improving the therapeutic effects on many chronic diseases, including cancer, bacterial infection, wound healing, Alzheimer's diseases, inflammatory bowel disease, and hepatitis C virus, were illustrated. Particularly, the recently discovered mechanisms of action of curcumin-loaded chitosan nanoparticles against the abovementioned diseases were highlighted. © 2021 Elsevier B.V.

126) Gunnam, A., Nangia, A.K.
Solubility improvement of curcumin with amino acids
(2021) *CrystEngComm*, 23 (18), pp. 3398-3410.

Abstract
Curcumin (CUR) is used as a dietary and food supplement with medicinal properties. It has a wide range of therapeutic activities such as antioxidant, anti-inflammatory, anti-arthritis, anti-tumor, anti-hyperglycemic, anti-malarial, anti-bacterial, and antiviral properties. The low solubility of curcumin in aqueous medium (7.8 μg mL-1) and low bioavailability leads to its lack of use as an oral medicine. In this work, the use of basic amino acids and their biological derivatives to improve the physicochemical properties of curcumin is described. Binary adducts of CUR with tyramine, tryptamine, arginine, asparagine, glutamine, lysine, histidine, and citrulline were characterized by spectroscopic, thermal, X-ray and microscopic techniques. The solubility and dissolution of curcumin in 40% ethanol-water solution exhibited a considerable improvement for these binary products. The use of amino acids as additives to improve the solubility of CUR in medical supplements is described. © The Royal Society of Chemistry.

127) Sethi, S., Choudhary, S., Sharma, D., Jyothi, V.G.S.S., Baldi, A., Madan, N.K.M.J.
Armamentarium of anticancer analogues of curcumin: Portray of structural insight, bioavailability, drug-target interaction and therapeutic efficacy
(2021) *Journal of Molecular Structure*, 1231, art. no. 129691, .

Abstract
Cancer represents one of the leading health-care issues around the globe. The overall life expectancy of cancer patients remains dismal regardless of enduring investigations and advances in the management of a disease. Thus the focus is always on the discovery of potential and less toxic alternatives of anticancer agents. Natural compounds from plant and animal kingdoms are grabbing eyeballs around the world owing to their relatively safer and huge unexplored therapeutic potential. One such natural compound is curcumin, which is a yellow polyphenolic compound procured from the plant “Curcuma longa Linn” and used widely as a spice in Indian households. Curcumin has proved its worth in various pathological conditions at preclinical stages. Despite the enormous therapeutic potential, low bioavailability and rapid metabolism are the roadblocks in the journey of curcumin to be a successful clinical candidate. This review is an earnest attempt to provide a summarized account of all the strategies to overcome obstacles of limited bioavailability and improving the therapeutic efficacy of curcumin.Special emphasis is laid on the structural insights into the development of novel curcumin based synthetic analogues endowed with anticancer potential and their docking analysis. Important aspects related to a possible mechanism of action and future prospects in designing of novel curcumin based anticancer analogues are also roofed in this article. © 2020

128) Goenka, S., Johnson, F., Simon, S.R.
Novel chemically modified curcumin (Cmc) derivatives inhibit tyrosinase activity and melanin synthesis in b16f10 mouse melanoma cells
(2021) *Biomolecules*, 11 (5), art. no. 674, .

Abstract
Skin hyperpigmentation disorders arise due to excessive production of the macromolecu-lar pigment melanin catalyzed by the enzyme tyrosinase. Recently, the therapeutic use of curcumin for inhibiting tyrosinase activity and production of melanin have been recognized, but poor stability and solubility have limited its use, which has inspired synthesis of curcumin analogs. Here, we investigated four novel chemically modified curcumin (CMC) derivatives (CMC2.14, CMC2.5, CMC2.23 and CMC2.24) and compared them to the parent compound curcumin (PC) for inhibition of in vitro tyrosinase activity using two substrates for monophenolase and diphenolase activities of the enzyme and for diminution of cellular melanogenesis. Enzyme kinetics were analyzed using Lineweaver-Burk and Dixon plots and nonlinear curve-fitting to determine the mechanism for ty-rosinase inhibition. Copper chelating activity, using pyrocatechol violet dye indicator assay, and antioxidant activity, using a DPPH radical scavenging assay, were also conducted. Next, the capac-ity of these derivatives to inhibit tyrosinase-catalyzed melanogenesis was studied in B16F10 mouse melanoma cells and the mechanisms of inhibition were elucidated. Inhibition mechanisms were studied by measuring intracellular tyrosinase activity, cell-free and intracellular α-glucosidase enzyme activity, and effects on MITF protein level and cAMP maturation factor. Our results showed that CMC2.24 showed the greatest efficacy as a tyrosinase inhibitor of all the CMCs and was better than PC as well as a popular tyrosinase inhibitor-kojic acid. Both CMC2.24 and CMC2.23 inhibited tyrosinase enzyme activity by a mixed mode of inhibition with a predominant competitive mode. In addition, CMC2.24 as well as CMC2.23 showed a comparable robust efficacy in inhibiting mel-anogenesis in cultured melanocytes. Furthermore, after removal of CMC2.24 or CMC2.23 from the medium, we could demonstrate a partial recovery of the suppressed intracellular tyrosinase activity in the melanocytes. Our results provide a proof-of-principle for the novel use of the CMCs that shows them to be far superior to the parent compound, curcumin, for skin depigmentation. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

129) Pettinari, R., Marchetti, F., Tombesi, A., Duan, F., Zhou, L., Messori, L., Giacomelli, C., Marchetti, L., Trincavelli, M.L., Marzo, T., La Mendola, D., Balducci, G., Alessio, E.
Ruthenium(II) 1,4,7-trithiacyclononane complexes of curcumin and bisdemethoxycurcumin: Synthesis, characterization, and biological activity
(2021) *Journal of Inorganic Biochemistry*, 218, art. no. 111387, .

Abstract
Two cationic ruthenium(II) 1,4,7-trithiacyclononane ([9]aneS3) complexes of curcumin (curcH) and bisdemethoxycurcumin (bdcurcH), namely [Ru(curc)(dmso-S)([9]aneS3)]Cl (1) and [Ru(bdcurc)(dmso-S)([9]aneS3)]Cl (2) were prepared from the [RuCl2(dmso-S)([9]-aneS3)] precursor and structurally characterized, both in solution and in the solid state by X-ray crystallography. The corresponding PTA complexes [Ru(curc)(PTA)([9]aneS3)]Cl (3) and [Ru(bdcurc)(PTA)([9]aneS3)]Cl (4) have been also synthesized and characterized (PTA = 1,3,5-triaza-7-phosphaadamantane). Bioinorganic studies relying on mass spectrometry were performed on complexes 1–4 to assess their interactions with the model protein lysozyme. Overall, a rather limited reactivity with lysozyme was highlighted accompanied by a modest cytotoxic potency against three representative cancer cell lines. The moderate pharmacological activity is likely connected to the relatively high stability of these complexes. © 2021 Elsevier Inc.

130) Wang, W., Yao, Q., Teng, F., Cui, J., Dong, J., Wei, Y.
Active ingredients from Chinese medicine plants as therapeutic strategies for asthma: Overview and challenges
(2021) *Biomedicine and Pharmacotherapy*, 137, art. no. 111383, .

Abstract
Although considerable advance has been made in diagnosing and treating, asthma is still a serious public health challenge. Traditional Chinese medicine (TCM) is an effective therapy of complementary and alternative medicine. More and more scientific evidences support the use of TCM for asthma treatment, and active ingredients from Chinese medicine plants are becoming a hot issue. Purpose of review: To summarize the frontier knowledge on the function and underlying mechanisms of the active ingredients in asthma treatments and provide a fully integrated, reliable reference for exploring innovative treatments for asthma. Methods: The cited literature was obtained from the PubMed and CNIK databases (up to September 2020). Experimental studies on the active ingredients of Chinese medicine and their therapeutic mechanisms were identified. The key words used in the literature retrieval were “asthma” and “traditional Chinese medicine” or “Chinese herbal medicine”. The literature on the active ingredients was then screened manually. Results: We summarized the effect of these active ingredients on asthma, primarily including the effect through which these ingredients can regulate the immunologic equilibrium mechanism by acting on a number of signalling pathways, such as Notch, JAK-STAT-MAPK, adiponectin-iNOS-NF-κB, PGD2-CRTH2, PI3K/AKT, Keap1-Nrf2/HO-1, T-bet/Gata-3 and Foxp3-RORγt, thereby regulating the progression of asthma. Conclusion: The active ingredients from Chinese medicine have multilevel effects on asthma by regulating the immunologic equilibrium mechanism or signalling pathways, giving them great clinical value. However, the safety and functional mechanism of these ingredients still must be further determined. © 2021 The Authors

131) Tang, W., Du, M., Zhang, S., Jiang, H.
Therapeutic effect of curcumin on oral diseases: A literature review
(2021) *Phytotherapy Research*, 35 (5), pp. 2287-2295.

Abstract
Curcumin (diferuloylmethane) is a polyphenol compound extracted from the rhizome of the plant Curcuma longa. It has the feature of being a yellow or orange pigment with a variety of biological properties, including anti-inflammation, antioxidation, anti-tumor, anti-bacteria, anti-fungus, and wound healing. Previous studies have reported the role of curcumin in treating different inflammatory diseases and tumors in vitro and in vivo. Recently, it has been demonstrated that curcumin has therapeutic benefits in oral mucosal diseases, periodontal diseases, and mouth neoplasms. In this review, we will focus on the therapeutic effects of curcumin on oral diseases. © 2020 John Wiley & Sons, Ltd.

132) Neves, A.R., van der Putten, L., Queiroz, J.F., Pinheiro, M., Reis, S.
Transferrin-functionalized lipid nanoparticles for curcumin brain delivery
(2021) *Journal of Biotechnology*, 331, pp. 108-117.

Abstract
Curcumin is an anti-inflammatory and antioxidant compound with potent neuroprotective activity. Due to its poor water solubility, low bioavailability, rapid elimination and the challenges for crossing and transposing the blood-brain barrier (BBB), solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) loaded with curcumin were successfully produced and functionalized with transferrin, in order to mediate the transport of these particles through the BBB endothelium to the brain. The nanosystems revealed Z-averages under 200 nm, polydispersity index below 0.2 and zeta potential around -30 mV. Curcumin encapsulation around 65 % for SLNs and 80 % for NLCs was accomplished, while the functionalized nanoparticles presented a value around 70–75 %. A stability study revealed these characteristics remained unchanged for at least 3 months. hCMEC/D3 cells viability was firstly analysed by MTT and LDH assays, respectively, and a concentration of 10 μM of curcumin-loaded nanoparticles were then selected for the subsequent permeability assay. The permeability study was conducted using transwell devices with hCMEC/D3 cells monolayers and a 1.5-fold higher permeation of curcumin

through the BBB was verified. Both SLNs and NLCs are promising for curcumin brain delivery, protecting the incorporated curcumin and targeting to the brain by the addition of transferrin to the nanoparticles surface. © 2021 Elsevier B.V.

133) Seibel, R., Schneider, R.H., Gottlieb, M.G.V.
Effects of spices (Saffron, rosemary, cinnamon, turmeric and ginger) in alzheimer's disease
(2021) *Current Alzheimer Research*, 18 (4), pp. 347-357.

Abstract
Alzheimer's disease (AD) is the most prevalent dementia in the elderly, causing disabili-ty, physical, psychological, social, and economic damage to the individual, their families, and care-givers. Studies have shown some spices, such as saffron, rosemary, cinnamon, turmeric, and gin-ger, have antioxidant and anti-inflammatory properties that act in inhibiting the aggregation of acetylcholinesterase and amyloid in AD. For this reason, spices have been studied as beneficial sources against neurodegenerative diseases, including AD. In this sense, this study aims to present a review of some spices (Saffron, Rosemary, Cinnamon, Turmeric and Ginger) and their bioactive compounds, most consumed and investigated in the world regarding AD. In this article, scientific evidence is compiled in clinical trials in adults, the elderly, animals, and in vitro, on properties con-sidered neuroprotective, having no or negative effects on neuroprotection of these spices and their bioactive compounds. The importance of this issue is based on the pharmacological treatment for AD that is still not very effective. In addition, the recommendations and prescriptions of these spices are still permeated by questioning and lack of robust evidence of their effects on neurodegen-eration. The literature search suggests all spices included in this article have bioactive compounds with anti-inflammatory and antioxidant actions associated with neuroprotection. To date, the amounts of spice ingestion in humans are not uniform, and there is no consensus on its indication and chronic consumption guarantees safety and efficacy in neuroprotection. Therefore, clinical evidence on this topic is necessary to become a formal adjuvant treatment for AD. © 2021 Bentham Science Publishers.

134) Zhang, Y., Song, L., Guo, H., Wu, J., Wang, X., Yao, F.
Effects of curcumin on growth and liver-protection in common carp, cyprinus carpio
(2021) *Pakistan Journal of Zoology*, 53 (4), pp. 1211-1220.

Abstract
We evaluated the growth performance and the hepatoprotective and antioxidant effects of curcumin against carbon tetrachloride (CCl4)-induced liver injury in common carp Cyprinus carpio. A 10-week feeding trial was carried out. A basal feed was supplemented with 0 (control), 30, 60, 120 and 240 mg/kg curcumin to formulate five experimental feeds. At the end of the feeding trial, the growth performance was determined. Subsequently, CCl4 was used for the model experiment. The plasma and liver were collected for the test after 72 h. Results showed that there was a significant (P<0.05) increase in weight gain rate (WG) and a special growth rate (SGR) of fish fed feeds supplemented with 60 and 120 mg curcumin kg-1. When fish were induced by CCl4 after 72 h, fish fed the diet supplemented with 120 mg (P5) curcumin kg-1 had significantly (P<0.05) lower plasma GOT, GPT activities and MDA content and higher plasma TP content and activities of liver SOD, GSH, GSH-Px and plasma T-AOC than those of P1 group. Curcumin (120 mg kg-1 curcumin per feed) inhibited the damage of liver tissue structure caused by carbon tetrachloride and made liver tissue structure return to normal. Meanwhile, dietary curcumin supplementation could also increase the live Nrf2 mRNA level and Nrf2 protein level in the liver nucleus, and those of the P5 group were highest. Overall, the results indicated that appropriate dietary curcumin supplementation could enhance the growth (especially 60 and 120 mg kg-1 curcumin per feed) of common carp and effectively protect the liver against CCl4 induced injury (especially 120 mg kg-1 curcumin per feed) in fish. Copyright 2021 Zoological Society of Pakistan.

135) Rodrigues, F.C., Kumar, N.A., Thakur, G.
The potency of heterocyclic curcumin analogues: An evidence-based review
(2021) *Pharmacological Research*, 166, art. no. 105489, .

Abstract
Curcumin, a potent phytochemical, has been a significant lead compound and has been extensively investigated for its multiple bioactivities. Owing to its natural origin, non-toxic, safe, and pleiotropic behavior, it has been extensively explored. However, several limitations such as its poor stability, bioavailability, and fast metabolism prove to be a constraint to achieve its full therapeutic potential. Many approaches have been adopted to improve its profile, amongst which, structural modifications have indicated promising results. Its symmetric structure and simple chemistry have prompted organic and medicinal chemists to manipulate its arrangement and study its implications on the corresponding activity. One such recurring and favorable modification is at the diketo moiety with the aim to achieve isoxazole and pyrazole analogues of curcumin. A modification at this site is not only simple to achieve, but also has indicated a superior activity consistently. This review is a comprehensive and wide-ranged report of the different methods adopted to achieve several cyclized curcumin analogues along with the improvement in the efficacy of the corresponding activities observed. © 2021 Elsevier Ltd

136) Sharma, A., Panwar, V., Thomas, J., Chopra, V., Roy, H.S., Ghosh, D.
Actin-binding carbon dots selectively target glioblastoma cells while sparing normal cells
(2021) *Colloids and Surfaces B: Biointerfaces*, 200, art. no. 111572, .

Abstract
Curcumin, a pleiotropic signalling molecule from Curcuma longa, is reported to be effective against multiple cancers. Despite its promising effect, curcumin had failed in clinical trials due to its low aqueous solubility, stability and poor bioavailability. While several approaches are being attempted to overcome the limitations, the improved solubility observed with curcumin-derived carbon dots appeared to be a strategy worth exploring. To assess if the carbon dots possess bio-activity similar to curcumin, we synthesized carbon dots (CurCD) from curcumin and ethylenediamine. Unlike curcumin, the as-synthesized curcumin carbon dots exhibited excellent solubility, excitation-dependent emission and photostability. The anti-cancer activity evaluated with glioblastoma cells using the well-established in vitro models indicated its comparable/enhanced activity over curcumin. Besides, the selective affinity of CurCD to the actin filament, indicated it's prospective to serve as a marker of actin filaments. In addition, the non-toxic effects observed in normal cells and fish embryos indicated CurCD was more biocompatible than curcumin. While this work reveals the superior properties of CurCD over curcumin, it provides a new approach to explore other plant derived molecules with similar limitations like curcumin. © 2021

137) Pourbagher-Shahri, A.M., Farkhondeh, T., Ashrafizadeh, M., Talebi, M., Samargahndian, S.
Curcumin and cardiovascular diseases: Focus on cellular targets and cascades
(2021) *Biomedicine and Pharmacotherapy*, 136, art. no. 111214, .

Abstract
Cardiovascular diseases (CVDs) are one of the leading causes of the most considerable mortality globally, and it has been tried to find the molecular mechanisms and design new drugs that triggered the molecular target. Curcumin is the main ingredient of Curcuma longa (turmeric) that has been used in traditional medicine for treating several diseases for years. Numerous investigations have indicated the beneficial effect of Curcumin in modulating multiple signaling pathways involved in oxidative stress, inflammation, apoptosis, and proliferation. The cardiovascular protective effects of Curcumin against CVDs have been indicated in several studies. In the current review study, we provided novel information on Curcumin's protective effects against various CVDs and potential molecular signaling targets of Curcumin. Nonetheless, more studies should be performed to discover the exact molecular target of Curcumin against CVDs. © 2020

138) Tung, B.T.
Medicinal plants and their bioactive compounds for the management and treatment of gout
(2021) *Enhancing the Therapeutic Efficacy of Herbal Formulations*, pp. 267-287.

Abstract
Gout is a complex form of arthritis which is characterized by sudden, severe attacks of pain, swelling, redness, and tenderness in the joints. Gout is a type of inflammatory arthritis that is triggered by the crystallization of uric acid within the joints and is often associated with hyperuricemia. Natural products offer many options to reduce the progress and symptoms of diseases, including gout. Natural compound structure including lignans, flavonoids, tannins, polyphenols, triterpenes, sterols, and alkaloids have anti-inflammatory, antioxidant, and XO activities. In this chapter, the authors present medicinal plants and isolated compounds which are used to prevent and reduce the pathogenesis of gout.

139) Tanwar, A.K., Dhiman, N., Kumar, A., Jaitak, V.
Engagement of phytoestrogens in breast cancer suppression: Structural classification and mechanistic approach
(2021) *European Journal of Medicinal Chemistry*, 213, art. no. 113037, .

Abstract
Cancer is the world's devastating disease, and breast cancer is the most common reason for the death of women worldwide. Many synthetic drugs and medications are provided with their beneficial actions, but all of these have side effects and resistance problems. Natural remedies are coming forward to overcome the disadvantages of synthetic drugs. Among the natural categories, phytoestrogens having a structural similarity of mammalian oestradiol proves its benefit with various mechanisms not only in the treatment of breast cancer but even to prevent the occurrence of postmenopausal symptoms. Phytoestrogens are plant-derived compounds that were utilized in ancient medications and traditional knowledge for its sex hormone properties. Phytoestrogens exert pleiotropic effects on cellular signalling and show effects on estrogen-dependent diseases. However, because of activation/inhibition of steroid hormonal receptor ER-α or ER-β, these compounds induce or inhibit steroid hormonal (estrogen) action and, therefore, have the potential to disrupt hormone (estrogen) signalling pathway. In this review, we have discussed and summarize the effect of certain phytoestrogens and their possible mechanisms that can substantiate advantageous benefits for the treatment of post-menopausal symptoms as well as for breast cancer. © 2020 Elsevier Masson SAS

140) Mighani, H., Hajiaghaei, F.
Synthesis and semi-synthesis of curcumin as a medical precursor and its derivatives with desirable purity and qualitative and quantitative evaluation
(2021) *Journal of Medicinal and Chemical Sciences*, 4 (2), pp. 84-92.

Abstract
Spices and herbs are considered rich sources of powerful antioxidants. Since 2000 years ago, spices and herbs have been utilized as fragrances, colourants, and medicines. Both natural and synthetic antioxidants inhibit or delay oxidation. Due to multiple adverse effects of synthetic antioxidants on human health, there is currently an ever-increasing demand for the natural antioxidants. One of the useful spices, turmeric, with the folk name of Curcuma longa belongs to the ginger family. Turmeric usually grows in tropical regions in India, China, Malaysia, and the Philippines. Antioxidant and medicinal substances are derived from turmeric's rhizome. Turmeric has been used to treat many diseases due to its wide range of medicinal applications. Turmeric has been used as herbal medicine. It is traditionally used to treat a variety of diseases such as head cold, cough, sinusitis, anorexia, diabetic ulcers, cramps, and liver obstruction of gastric ulcer. Three different types of curcuminoids exist as bioactive compounds in turmeric including curcumin as the main constituent, and dimethoxy curcumin, and bis-dimethoxy curcumin. These compounds differ in the position of the methoxy group. This study aimed at synthesizing and analyzing the curcuminoid using the HPLC technique and related tests. The results obtained from the analysis of the synthetic curcumin were consistent with those for the standard curcumin. The reaction was carried out at relatively milder conditions than earlier reported methods. © 2020 by SPC (Sami Publishing Company)

141) Huang, L., Yong, K.W.L., Fernando, W.C., Carpinelli de Jesus, M., De Voss, J.J., Sultanbawa, Y., Fletcher, M.T.
The Inactivation by Curcumin-Mediated Photosensitization of Botrytis cinerea Spores Isolated from Strawberry Fruits
(2021) *Toxins*, 13 (3), art. no. 196, .

Abstract
Photosensitization is a novel environmentally friendly technology with promising applications in the food industry to extend food shelf life. In this study, the natural food dye curcumin, when combined with visible light (430 nm), was shown to be an effective photosensitizer against the common phytopathogenic fungi Botrytis cinerea (the cause of grey mould). Production of the associated phytotoxic metabolites botrydial and dihydrobotrydial was measured by our newly developed and validated HRAM UPLC-MS/MS method, and was also shown to be reduced by this treatment. With a light dose of 120 J/cm2, the reduction in spore viability was directly proportional to curcumin concentrations, and the overall concentration of both botrydial and dihydrobotrydial also decreased with increasing curcumin concentration above 200 μM. With curcumin concentrations above 600 μM, the percentage reduction in fungal spores was close to 100%. When the dye concentration was increased to 800 μM, the spores were completely inactive and neither botrydial nor dihydrobotrydial could be detected. These results suggest that curcumin-mediated photosensitization is a potentially effective method to control B. cinerea spoilage, and also to reduce the formation of these phytotoxic botryane secondary metabolites. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

142) Sudhakar Johnson, T., Narayana, D.B.A.
Role of spices in offering natural immunity to fight various diseases
(2021) *Pharmacognosy Journal*, 13 (2), pp. 600-613.

Abstract
Adequate nutrition intake is one of main factors to strengthen immunity.Traditional and cultural practices of food consumption involve use of several spices in limited quantities as part of food. Spices have offered versatile biological effects due to presence of valuable biochemicals. The aim of the present paper is to review published scientific evidence on potential role of spices in offering innate and adaptive immunity to human body. It has been demonstrated that, turmeric, one of the widely used spices, acts as an anti-viral agent through inhibition of viral entry into cells, suppression of viral replication and modulation of cytokines. A field study revealed that nations with higher consumption of spices have shown lesser COVID-19 cases and higher recovery rates. Further, spices also have shown to possess antioxidant activity superior or equivalent to ascorbic acid and are known to regulate inflammation processes. Evidence generated from the published literature is compelling to arrive at a conclusion that consumption of spices might improve immunity there by offering protection against various diseases including COVID-19. It is also noted that there are lesser number of human clinical trials in this area which warrants immediate attention to provide scientific evidence to immunity offered by spices. © 2021 Phcogj.Com.

143) Brotons-Canto, A., González-Navarro, C.J., Gil, A.G., Asin-Prieto, E., Saiz, M.J., Llabrés, J.M.
Zein nanoparticles improve the oral bioavailability of curcumin in wistar rats
(2021) *Pharmaceutics*, 13 (3), art. no. 361, .

Abstract
Curcumin is a natural compound obtained from turmeric root with high antioxidant and anti-inflammatory activities. However, clinical application of curcumin has been limited due to its low solubility and bioavailability and rapid metabolism and degradation. This study was con-ducted to evaluate the effect of curcumin incorporation in zein nanoparticles on the pharmacokinetic parameters of systemic curcumin in plasma. Wistar rats were administered a single oral dose of 250 mg/kg of standard curcumin (control) or nanocurcumin (zein-based nanoparticles, Nucaps). The proposed new formulation was also compared with two commercially available curcumin com-plexes. Blood samples were collected at different times, and plasma levels were determined using HPLC-MS/MS. Overall, nanocurcumin (Nucaps) formulation was well tolerated and showed a 9-fold increase in oral bioavailability when compared to the standard curcumin natural extract. In addition, the nanoparticles prepared in this study demonstrated a bioavailability profile superior to that of other bioavailability-enhanced

curcumin complexes currently available in the marketplace. Thus, our nanoparticle-based formulation has shown great potential as a nutraceutical for the oral administration of curcumin. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

144) Kannamangalam Vijayan, U., Shah, N.N., Muley, A.B., Singhal, R.S.
Complexation of curcumin using proteins to enhance aqueous solubility and bioaccessibility: Pea protein vis-à-vis whey protein
(2021) *Journal of Food Engineering*, 292, art. no. 110258, .

Abstract
Curcumin faces challenges such as poor aqueous solubility and limited bioaccessibility which limits its oral therapeutic applications. This work evaluated the complexation of curcumin using pea protein isolate (PPI, leguminous protein) vis-à-vis whey protein isolate (WPI, animal protein) to overcome these limitations. Thermodynamic parameters (ΔH and ΔS) indicated the interaction to be hydrophobic in nature. While WPI-curcumin complex showed better aqueous solubility for curcumin than PPI-curcumin complex at varying pH (3, 5 & 7), the PPI-curcumin complex showed better solubility at higher temperature of 80 °C. The solubility of curcumin in WPI-curcumin and PPI-curcumin complex at pH 7 was 1.16 mg/g and 1.02 mg/g, respectively. The protein curcumin solutions were further spray dried and characterized for surface hydrophobicity, crystallinity, thermal properties, and surface morphology. Both the proteins showed a similar score for bioaccessibility of curcumin from their respective complexes. Thus PPI can be a good non-dairy protein alternative for curcumin delivery. © 2020 Elsevier Ltd

145) Abdel-Hafez, S.M., Hathout, R.M., Sammour, O.A.
Attempts to enhance the anti-cancer activity of curcumin as a magical oncological agent using transdermal delivery
(2021) *Advances in Traditional Medicine*, 21 (1), pp. 15-29.

Abstract
For the past few years, curcumin has drawn the attention of scientists in multidisciplinary fields related to oncology and therapeutics. However, despite its high potency, its delivery suffers from several limitations and challenges that hinders the complete benefit from this magical molecule. Accordingly, this review demonstrates the several attempts and endeavors that the scientists exerted in order to delivery this molecule successfully through the transdermal route. We believe that the transdermal route of delivery of drugs can pose a new platform of targeting solid tumors such as the breast carcinoma so that applying a transdermal patch over the skin or the membrane covering the solid tumor can provide a means of the cure. © 2020, Institute of Korean Medicine, Kyung Hee University.

146) Li, H.-K., Feng, N., Wang, W.-B., Li, J.-X., He, C.-F.
The mechanism of skin glycation reaction, influencing factors and the development status of anti-glycation in the cosmetics industry
(2021) *China Surfactant Detergent and Cosmetics*, 51 (2), pp. 153-160.

Abstract
The formation process of the advanced glycation end product (AGEs) and its effect on the skin were clarified in the paper through the introduction of the mechanism of skin glycation in details and the measures against the skin glycation and the mechanism of action were introduced too. The cosmetic brands and ingredients that claim anti-glycation effects at present were summarized, and the deficiencies in the development of antiglycation cosmetics in the market were analyzed in personal opinion. It aims to provide solid and scientific theoretical basis for the development of anti-glycation cosmetics. © 2021 Editorial Office China Surfactant Detergent and Cosmetics. All rights reserved.

147) Mullaj, K., Bulsara, K.K., Bulsara, K.R., Guha, A.
Commentary: Unintended perils of herbal supplements: Anticoagulation
(2021) *Operative Neurosurgery*, 20 (2), pp. E156-E158.

148) Hosseini-Zare, M.S., Sarhadi, M., Zarei, M., Thilagavathi, R., Selvam, C.
Synergistic effects of curcumin and its analogs with other bioactive compounds: A comprehensive review
(2021) *European Journal of Medicinal Chemistry*, 210, art. no. 113072, .

Abstract
Curcumin, as a natural compound, extracted from plant Curcuma longa, is abundant in the Indian subcontinent and Southeast Asia, and have been used in a diverse array of pharmacological activities. Although curcumin has some limitations like low stability and low bioavailability, it has been proved that this compound induced apoptosis signaling and is also known to block cell proliferation signaling pathway. Recently, extensive research has been carried out to study the

application of curcumin as a health improving agent, and devise new methods to overcome to the curcumin limitations and incorporate this functional ingredient into foods. Combinational chemotherapy is one of the basic strategies is using for 60 years for the treatment of various health problems like cancer, malaria, inflammation, diabetes and etc. Molecular hybridization is another strategy to make multi-pharmacophore or conjugated drugs with more synergistic effect than the parent compounds. The aim of this review is to provide an overview of the pharmacological activity of curcumin and its analogs in combination with other bioactive compounds and cover more recent reports of anti-cancer, anti-malarial, and anti-inflammatory activities of these analogs. © 2020

149) Pelikh, O., Eckert, R.W., Pinnapireddy, S.R., Keck, C.M.
Hair follicle targeting with curcumin nanocrystals: Influence of the formulation properties on the penetration efficacy
(2021) *Journal of Controlled Release*, 329, pp. 598-613.

Abstract
Nanocrystals are a universal formulation approach for improved drug delivery of poorly water-soluble drug substances. Besides oral application, also topical application of the nanocrystals is feasible, because the increased kinetic solubility of the nanocrystals results in an increased concentration gradient, thus fostering passive, dermal penetration. Nanocrystals are also promising for targeting drug substances into the hair follicle. After penetration into the hair follicle, the nanocrystals could form a depot from which the active is released into the hair follicle. Thus, leading to a long-lasting and very efficient dermal drug delivery. The efficacy of nanocrystals to penetrate the hair follicles and the influence of the vehicle in which the nanocrystals are suspended was not yet investigated. Therefore, in this study curcumin nanocrystals with a size of about 300 nm were produced and incorporated into gels with different properties. The efficacy to penetrate the hair follicles, as well as the passive, dermal penetration, was assessed on the ex-vivo pig ear model. Nanocrystals were efficiently taken up by the hair follicles and reached the lower part of the infundibulum. This region is optimal for efficient drug delivery because the barrier of the lower infundibulum is not fully developed and thus more permeable, which results in a less hindered passive diffusion of drug substances. The penetration efficacy of the nanocrystals into the hair follicles was not affected by the different types of vehicles, which represented either oleogels or hydrogels that varied in viscosity as well as in the type and the concentration of the gelling agent. All gels possessed a shear-thinning flow behavior and it is hypothesized that all gels fluidized during the skin massage, whereby leading to similarly low viscosities than the aqueous nanosuspension and thus to similar penetration results. The passive, dermal penetration of curcumin was different for the different gels and the main driving parameter leading to good passive diffusion was caused by good skin hydrating properties of the vehicle. The best passive penetration was achieved from hydrogels that contained a humectant. However, the addition of the humectant reduced the efficacy of the nanocrystals to penetrate the hair follicle. Data so far, therefore, suggest that hair follicle targeting with nanocrystals that are suspended in water or simple, shear-thinning gels is highly effective. However, the addition of other excipients, e.g. humectants, to these vehicles might cause changes in the penetration profiles. More research in this regard is needed to understand these observations in more detail. © 2020 Elsevier B.V.

150) Fadhlizil Fasihi Mohd Aluwi, M., Moyeenul Huq, A.K.M., Akil Hossain, M.
Role of turmeric and cinnamon spices in digestive, metabolic, and immune systems
(2021) *Nutrition and Functional Foods in Boosting Digestion, Metabolism and Immune Health*, pp. 209-217.

Abstract
Turmeric, a golden spice, and cinnamon have a long history of not only as a principal spice in Asian cuisine, but most importantly as medicinal purposes as well. Traditionally, these spices have been used as herbal remedy for variety of diseases related to skin, aches, pulmonary, liver disorder, and gastrointestinal problems such as stomach cramps, diarrhea, constipation, cough, and indigestion. Turmeric and cinnamon are also known as natural agents which modulate the immune system. Furthermore, modern science has shown that these spices and their major chemical constituents, curcumin and cinnamaldehyde, respectively, regulate many biological processes including enhanced metabolism process. Even to date, turmeric and cinnamon still become subject of interest to many medicinal chemists for their wide range of pharmacological properties such as antiinflammatory, antidiabetic, anticancer, antiangiogenesis, antioxidant, as well as anti-viral. This chapter summarizes the effects of turmeric and cinnamon on the digestion, metabolism, and immune system. In the nutshell, both are wonders spices that possess amazing health benefits that are absolutely needed by everyone.

151) Meghwal, M., Devu, S., Singh, H., Goswami, T.K.
Piperine and curcumin
(2021) *A Centum of Valuable Plant Bioactives*, pp. 589-612.

Abstract
Black pepper is known for its pungent constituent piperine. It has wide culinary uses and also possess certain preservative and medicinal properties. Piperine, beyond pungency, has been found to possess bio-transformative effects that can detoxify pathogen, prevent oxidation, and improve the bioavailability and absorption of various drugs. Piperine also shows immunomodulatory, antiasthmatic, anticarcinogenic, antiulcer, antiamoebic, antioxidant, antiinflammatory, and antiulcer properties. On the other hand, curcumin, the curcuminoid of turmeric, mainly found in rhizomes of Curcuma spp., helped to prevent skin cancers, duodenum, forestomach, and colon cancers in mice. In India and many other regions of the world, piperine and curcumin have been part of the folk formulations used for treating various ailments for centuries. In this

chapter, the recent developments regarding chemistry, extraction processes, pharmacological, and biological activities of both piperine and curcumin have been discussed. © 2021 Elsevier Inc.

152) Pattanayak, S.
Plants in Healthcare: Past, Present and Future
(2021) *Exploratory Animal and Medical Research*, 11 (2), pp. 140-144.

Abstract
Plants have been used as medicines or sources of medicines from a very ancient stage of human civilization. In the ancient days, the collected plant parts were used directly or in dried and preserved conditions. Afterward, the dried parts of the medicinal plants were used as medicine as single or poly-herbal mixtures with or without vehicle as used in present-day Ayurveda and alike medical systems. In homeopathy, the ethanol extracts of dried plant parts are used. Identification of active principles from the extracts of the dried plant parts has made the basis of laboratory synthesis of many drugs of modern medicine. Some novel types of healthcare techniques are proposed for further validation. Following a diet containing selected herbal foods (DIP diet) in an unprocessed state along with a change in lifestyle can control many diseases. Fruit pulp, fruit juice and other related food products can be prepared by using only herbal plant parts and also can be supplied without the addition of any synthetic chemicals. Similarly, medicines prepared from the succulent parts of the medicinal plants can effectively be used to prevent and cure many diseases. All these can be performed following some novel procedures of collection, chemical-free processing, packaging, storage, and transportation to the patients and consumers.

153) Atazadegan, M.A., Bagherniya, M., Fakheran, O., Sathyapalan, T., Sahebkar, A.
The Effect of Herbal Medicine and Natural Bioactive Compounds on Plasma Adiponectin: A Clinical Review
(2021) *Advances in Experimental Medicine and Biology*, 1328, pp. 37-57.

Abstract
Noncommunicable diseases (NCDs) are one of the major public health concerns globally. Most of the NCDs including insulin resistance, metabolic syndrome, type 2 diabetes mellitus, fatty liver disease, and coronary heart disease are related to obesity and are called obesity-related NCDs (OR-NCDs). However, adipocytes can reduce OR-NCDs by secreting adiponectin. Adiponectin has an inverse relationship with body fat. Obese people have impairment in differentiating pre-adipocytes to adipocytes, the process facilitated by adiponectin. Adiponectin directly increases insulin sensitivity and reduces obesity-related insulin resistance by down-regulating hepatic glucose production and increasing fatty acid (FA) oxidation in skeletal muscle. Considering the various beneficial effects of adiponectin on health, increasing adiponectin might be a promising approach to prevent and treat OR-NCDs. Recent studies have shown that nutraceuticals and medicinal compounds isolated from plants could prevent and treat various diseases, particularly cardiovascular diseases (CVDs), diabetes mellitus, obesity, and non-alcoholic fatty liver disease. However, to our knowledge, the effect of these natural products, including herbal supplements and functional foods on adiponectin, has not yet been fully reviewed. The main aim of this review is to summarize the effects of nutraceuticals and herbal bioactive compounds on plasma adiponectin concentrations based on clinical studies. It can be concluded that medicinal plants, and herbal bioactive compounds, particularly curcumin, anthocyanins, resveratrol, soy, walnut, and dihydromyricetin can be used as adjunct or complementary therapeutic agents to increase plasma adiponectin, which could potentially prevent and treat NCDs.

154) Waman, A.A., Bohra, P., Devi, K.R., Pixy, J.
In vitro multiplication protocol for Curcuma mangga: Studies on carbon, cytokinin source and explant size
(2021) *Journal of Horticultural Sciences*, 16 (1), pp. 69-76.

Abstract
Mango ginger (Curcuma mangga Valeton & Zijp.) is an underutilized rhizomatous species that has been valued in the tropical Asian countries as a source of vegetable, spice, salad, medicine and essential oil. This species is hardy and requires less care for obtaining good yields. Rhizomes are the commonly used propagules for the species, which are also the economic part of the crop. Huge quantity of seed rhizomes is required to promote this crop in larger area. Efficient in vitro multiplication protocol is one of the options to meet the planting material requirement. Effects of carbon source (glucose, fructose and sucrose) and concentration (1 and 3%, w/v), cytokinins (BAP and meta topolin) and concentration (1 mg/ L and 2 mg/L), size of explants (one/ two/ three bud) and IBA treatment (0, 250, 500 and 1,000 mg/L) for concurrent ex vitro rooting cum hardening were studied. Results revealed that for facilitating efficient multiplication, medium should be supplemented with glucose (3%) as carbon source and meta topolin (1 mg/L) as cytokinin. Two-bud explant should be used for subculture as it promoted superior shoot proliferation. Concurrent ex vitro rooting cum hardening was possible even without auxin treatment. The present protocol could be useful for large scale production of quality planting material of this underexploited tropical species.

155) Ahmad, W., Parveen, R., Yusuf, M., Amir, M., Wahab, S., Ansari, M.A., Mujeeb, M., Zaidi, S.A., Ahmad, S.
Antiurolithiatic activity of Didymocarpous pedicellata R. Br.
(2021) *South African Journal of Botany*, .

Abstract
Didymocarpous pedicellata R.Br. (Gesneriaceae), also known as stone flower, is a valuable medicinal plant growing in the subtropical Himalayas (India). It is traditionally used for treating kidney and bladder stones and is the main ingredient of herbal formulations used to treat kidney stones, such as Cystone and Safoof-e-Pathr Phori (SPP). The present study explored the antiurolithiatic effect of Didymocarpous pedicellata leaves (DPL) in urolithiasis caused by ethylene glycol in Wistar male rats. The EG-induced urolithiasis group exhibited significantly higher ($P < 0.001$) serum creatinine, blood urea nitrogen, tissue lipid peroxidation, and urinary calcium levels, and significantly lower ($P < 0.001$) urinary potassium and sodium levels than the standard control group. DPL treatment (200 and 300 mg/kg) exhibited significantly ($P < 0.001$) lower urine and serum markers than toxicant rats. The histological investigation demonstrated refractile crystals and extensive damage to proximal tubules causing dilation in EG-induced urolithiasis rats. However, Didymocarpous pedicellata treatment of 300 mg/kg exhibited the absence of crystals and reduced kidney tissue damage, thus protecting against urolithiasis and nephrotoxicity. Therefore, DPL (300 mg/kg) is useful in the management of urolithiasis. © 2021 SAAB

156) Nedzvetsky, V.S., Gasso, V.Y., Agca, C.A., Sukharenko, E.V.
Soluble curcumin ameliorates motility, adhesiveness and abrogate parthanatos in cadmium-exposed retinal pigment epithelial cells
(2021) *Biosystems Diversity*, 29 (3), pp. 235-243.

Abstract
Cadmium (Cd) is a nonessential transition metal and one of the most toxic environmental pollutants. Industrial, agricultural and urban activities are the main sources of Cd environmental contamination. Multiple deleterious effects of Cd exposure were reported for different cell types and living organisms in a great number of research papers. Cd bioaccumulation hazard is mediated by the relatively long half-life of this metal in an organism. For example, in mammals its half-life lasts for about 10–30 years. Cd exposure affects many tissues. However, some of them, including the central nervous system and sensory organs, are most susceptible to its toxicity. The harmful effects of Cd could be linked to oxidative stress generation and consequently intracellular signalling disruption. Since Cd induces redox imbalance the antioxidants could be a prospective tool to ameliorate Cd cytotoxicity. In present work, we have studied the protective efficacy of soluble curcumin on Cd-caused retinal pigment epithelium (RPE) cells viability, reactive oxygen species production, adhesive and extracellular matrix proteins expression, cell migration and parthanatos level. Low dose (5 μM) of soluble curcumin ameliorated all aforementioned indices of Cd-induced cytotoxicity. Curcumin has restored the RPE cells motility as well as fibronectin and E-cadherin expression. Therefore, the modulation of RPE adhesiveness could be regarded as a cytoprotective effect of curcumin. Furthermore, Cd-caused poly(ADP-ribose) polymerase-1 (PARP-1) suppression and cleaved PARP-1 upregulation were ameliorated by curcumin exposure. Therefore, the protective effect of soluble curcumin could be related, at least partially, to the modulation of PARP activity and inhibition of parthanatos flux. The observed results have demonstrated that low doses of soluble curcumin are a promising tool to protect RPE cells against Cd-caused retinal injury.

157) Rácz, L., Tomoaia-Cotișel, M., Rácz, C.-P., Bulieris, P., Grosu, I., Porav, S., Ciorîță, A., Filip, X., Martin, F., Serban, G., Kacsó, I.
Curcumin-whey protein solid dispersion system with improved solubility and cancer cell inhibitory effect
(2021) *Studia Universitatis Babes-Bolyai Chemia*, 66 (3), pp. 209-224.

Abstract
The solid dispersion system containing a high amount of the natural compound curcumin was prepared with whey protein concentrate by spray-drying method in 5:1 molar ratio. X-ray powder diffraction and DSC techniques show the formation of the solid dispersion system in amorphous state, and the presence of weak hydrogen bond type interactions between the components was established by FTIR analysis. SEM images show highly homogeneous donut-like spherical microparticles morphology for the system. The solubility of curcumin from the system was enhanced compared to practically insoluble raw curcumin, reaching a value of 70 μg/mL in aqueous buffer solution at pH=8 similar with intestinal environment. The synthesized material had better effects against skin melanoma cells, compared to lung adenocarcinoma cells, but in both cases the effect was promising, and through further and more complex analyses the antitumoral potential of CUC-WPC_SD could be exploited.

158) Cihan, Y.B.
Curcumin's antineoplastic, radiosensitizing and radioprotective properties [Antineoplastické, radiosenzibilizující a radioprotektivní vlastnosti kurkuminu]
(2021) *Klinicka Onkologie*, 34 (4), pp. 273-277.

Abstract
Background: Curcumin is an ingredient in the turmeric plant that gives yellow color to dishes and is used as a spice. It has been used locally/topically and systemically in the treatment of diseases in Far Eastern societies, especially in Indian and Chinese traditional medicine. Curcumin is a natural substance that does not show toxic properties in overdose. In addition to its anti-inflammatory, anti-oxidant, anti-neoplastic, anti-viral, anti-microbial, anti-angiogenic properties, platelet aggregation, apoptosis, and wound healing have been demonstrated in different studies. In recent years, it has been used as a radiosensitizing agent and a radioprotector in radiation therapy. Although curcumin has low bioavailability, it seems to be the ideal molecule due to its low molecular weight, high activity in inhibiting the growth of tumor cells and protecting normal

tissues from the side effects of radiation. Purpose: Curcumin in combination with radiotherapy was discussed in the light of the literature.

159) Stamenkovska, M., Hadzi-Petrushev, N., Nikodinovski, A., Gagov, H., Atanasova-Panchevska, N., Mitrokhin, V., Kamkin, A., Mladenov, M.
Application of curcumine and its derivatives in the treatment of cardiovascular diseases: a review
(2021) *International Journal of Food Properties*, 24 (1), pp. 1510-1528.

Abstract
Cardiovascular diseases are the leading cause of death in the world and scientists pay a lot of attention to identify and reveal the mechanisms of their occurrence. Recently, the attention of scientists is focused increasingly on plant derivatives, such as flavonoids and polyphenols, due to their specific biological effects. One of these compounds is curcumin, which has many biological properties. Numerous studies have been performed to understand the molecular basis of the therapeutic properties of curcumin. As a result of these studies, there is considerable evidence to suggest that curcumin may affect signaling pathways associated with the cell growth, proliferation, survival, inflammation, and gene transcription. Antioxidant and anti-inflammatory mechanisms are the two basic mechanisms to which many of the effects of curcumin in various conditions are attributed. Many factors influence the development of heart disease, but one of the main culprits in their occurrence is the inflammatory process. According to recent research, curcumin is an ingredient that could be used in the prevention or treatment of cardiovascular disease. Also, some studies have shown that it has beneficial effects in preventing vascular damage and ischemia. Despite its beneficial and biological properties, it has been proven that curcumin has relatively low bioavailability and low stability in the human body, which limits its therapeutic application. In this regard, several attempts have been made to synthesize curcumin derivatives with improved bioavailability. In this paper, we review the potential and possibilities of using curcumin and its derivatives in the treatment of cardiovascular disease, which would significantly reduce the mortality rate in the population. Based on all of the above, it can be concluded that further studies of animal models and humans are needed to verify current knowledge about the application of curcumin and its derivatives in the treatment of cardiovascular diseases. In this way through these studies more reliable data will be generated concerning the effects of curcumin and its analogs on cellular and subcellular/molecular levels. Prospectively, we believe that this will ground the basis for further improved synthesis of curcumin-analogs, appropriate for the treatment of cardiovascular diseases. © 2021, Published with license by Taylor & Francis Group, LLC. © 2021 Mimoza Stamenkovska, Nikola Hadzi-Petrushev, Aleksandar Nikodinovski, Hristo Gagov, Natalija Atanasova-Panchevska, Vadim Mitrokhin, Andre Kamkin and Mitko Mladenov.

160) Fakheran, O., Khademi, A., Bagherniya, M., Dehghannejad, M., Sathyapalan, T., Sahebkar, A.
Antibacterial Activity of Curcumin Against Periodontal Pathogens: A Systematic Review
(2021) *Advances in Experimental Medicine and Biology*, 1291, pp. 239-249.

Abstract
Periodontitis is a chronic inflammatory disease characterized by destruction of the supporting structures of teeth caused by development of dental plaques and accumulation of microorganism around the gingival tissue. Curcumin has been shown to improve clinical parameters in periodontal diseases. However, the efficacy of curcumin in the elimination of periodontal pathogens is not clearly defined. The purpose of this study was to carry out a systematic review of the antibacterial activity of curcumin against periodontal pathogens. An electronic literature search in Medline, Scopus, Science Direct, Web of Science, Cochrane library, and Google scholar was performed up to February 29, 2020, to identify studies assessing the antibacterial activity of curcumin against periodontal pathogens. From 1238 publications, three clinical trials and five in vitro studies met the eligibility criteria. All three clinical studies reported improvement in restoring gingival health in clinical and microbiological parameters, following adjunctive use of curcumin for treatment of periodontitis. All five in vitro studies showed that curcumin could inhibit the growth of bacterial strains. Three of the five in vitro studies evaluated the effect of curcumin on mixed biofilm of periopathogens, which showed a significant inhibitory effect of curcumin on periodontal biofilms. This systematic review found that curcumin has antibacterial activity against periopathogens. The anti-biofilm activity of curcumin is reported as one of the mechanisms for this phenomenon. Curcumin could improve the clinical parameters of periodontal tissue not only by inhibition of the pathogens but also by modulating the host response. © 2021, The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG.

161) Khodadadegan, M.A., Azami, S., Guest, P.C., Jamialahmadi, T., Sahebkar, A.
Effects of Curcumin on Depression and Anxiety: A Narrative Review of the Recent Clinical Data
(2021) *Advances in Experimental Medicine and Biology*, 1291, pp. 283-294.

Abstract
Depressive and anxiety disorders affect a significant proportion of the global population and constitute one of the highest disease burdens worldwide. Conventional pharmacological treatments are traditionally the first line of therapy for individuals affected by these conditions although these are only successful approximately half of the time and are often associated with undesirable side effects. This review describes the use of the natural substance curcumin as a potential alternative treatment of these mental disorders. With this in mind, we analyzed the effects of curcumin in eight clinical studies of depression and five studies of anxiety and assessed these using psychiatric symptom scores and molecular biomarker readouts. © 2021, The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG.

162) Gharibpour, F., Fakheran, O., Parvaneh, A., Shirban, F., Bagherniya, M., Sathyapalan, T., Sahebkar, A.
The Clinical Use of Curcumin for the Treatment of Recurrent Aphthous Stomatitis: A Systematic Review of Clinical Trials
(2021) *Advances in Experimental Medicine and Biology*, 1291, pp. 229-238.

Abstract
Recurrent aphthous stomatitis (RAS) lesions are inflammatory painful oral ulcers with uncertain etiology. Curcumin acts as an effective anti-inflammatory and antibacterial agent in the treatment of various oral diseases. This systematic review aimed to assess the effects of curcumin on RAS. A systematic search of the medical databases, PubMed, Scopus, ISI, Science Direct, and Google Scholar was performed up to March 30, 2020, to identify clinical trials assessing the effect of curcumin on aphthous ulcers. Nine studies comprising of 469 participants met all criteria and were analyzed. Treatment with curcumin significantly reduced aphthous ulcer size (seven studies), pain intensity (eight studies), number of aphthous ulcers (three studies), erythematous halo (one study), and erythema and exudate of the aphthous (one study). In four studies, the effect of curcumin on aphthous ulcer was assessed in comparison to the effects of the standard medication, triamcinolone. In all of these studies, curcumin had similar beneficial effects on the aphthous ulcer as measured by ulcer size, number, and pain. Only three studies were categorized as high quality using the Jadad scale. Within the limitations of this review, it can be concluded that curcumin may have a beneficial role in the treatment of recurrent aphthous ulcers. However, more randomized clinical trials are needed to validate these findings. © 2021, The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG.

163) Dharmalingam, K., Anandalakshmi, R., Shekhar, S.
Microwave-induced diffusion method for solid dispersion of curcumin in HPMC matrix using water as hydration carrier
(2021) *Journal of Dispersion Science and Technology*, 42 (10), pp. 1419-1430.

Abstract
In this study, a possible way of dispersing curcumin on hydroxypropylmethylcellulose (HPMC) at a nanoscale level using microwave-induced diffusion method is reported to enhance its solubility, release control and oral bioavailability. Different weight ratios of 1:1, 1:2 and 1:4 curcumin-HPMC solid dispersions (SDs) were prepared and characterized. The results of XRD and DSC indicated that obtained 1:4 SDs exhibited less crystalline and less fusion enthalpy (13.72 ± 1.19 J/g) compared to pure curcumin and other SDs. FESEM confirmed that size reduced curcumin nanoparticles were uniformly dispersed in HPMC. Dispersed curcumin nanoparticles of 20–40 nm were embedded in HPMC for 1:4 SDs as shown by AFM and TEM analysis. In vitro release test showed that this method was successful in achieving a higher dissolution rate of curcumin at pH 6.8 and 1.2. This study proposes that the prepared SDs favorably enhanced the solubility and sustained high dissolution rate of water-insoluble curcumin. © 2020 Taylor & Francis Group, LLC.

164) Fu, H., Ni, X., Ni, F., Li, D., Sun, H., Kong, H., Shan, Y., Dai, S.
Study of the Mechanism by Which Curcumin Cooperates with Sestrin2 to Inhibit the Growth of Pancreatic Cancer
(2021) *Gastroenterology Research and Practice*, 2021, art. no. 7362233, .

Abstract
Background. Pancreatic carcinoma is a malignant tumor with a high fatality rate, and the increased resistance of pancreatic carcinoma to chemotherapy has become a difficult problem in clinical practice. Hence, it is imperative to develop an effective treatment for pancreatic cancer. Sestrins are a class of stress-induced proteins that have antioxidation functions, regulating cell growth and metabolism. Curcumin is a natural pigment isolated from turmeric. Several studies have also suggested that this molecule has multiple pharmacological effects, such as anti-inflammatory, antioxidant, and antitumor effects. However, there are insufficient studies on curcumin cooperating with the sestrin family to inhibit tumors, and the mechanism is still unclear. Our aim was to observe the potential anticancer effects of curcumin combined with the sestrin family on pancreatic carcinoma and probe its possible molecular mechanisms. Methods. Lentiviral infection, real-time fluorescence quantitative PCR assays, Cell Counting Kit-8 assays, real-time cell analysis technology, colony formation assays, wound healing assays, Transwell invasion assays, protein extraction, and western blots (WBs) were used to evaluate the effect of curcumin combined with sestrin2 on the proliferation, invasion, and migration of pancreatic carcinoma cells. Results. The results revealed that curcumin cooperated with sestrin2 to significantly suppress pancreatic cancer. In addition, we determined that sestrin2 cooperated with curcumin to inhibit pancreatic cancer by specifically targeting Nrf2/Keap1/HO-1/NQO-1. Conclusion. These findings clarify that curcumin-mediated synergistic targeting of sestrin2 is a potentially valuable treatment for pancreatic cancer. © 2021 Haotian Fu et al.

165) Moezi, L., Ashjazadeh, N., Rezapanah, S., Pirsalami, F., Esmaeili, Z., Soukhaklari, R., Moosavi, M.
Anticonvulsant effect of acute curcumin nanoparticle on pentylenetetrazole-induced seizures in mice: non-involvement of jnk restoration
(2021) *Physiology and Pharmacology (Iran)*, 25 (1), pp. 36-46.

Abstract
Introduction: Although several animal studies have indicated the antiepileptic effect for curcumin, there are reports stating

the null antiepileptic effect of this substance. This inconsistency might be due to the low bioavailability of curcumin. Therefore, the current study aimed to assess the effect of oral bovine serum albumin (BSA)-based nanocurcumin on seizure caused by pentylenetetrazol (PTZ) in mice. Furthermore, due to the suggested involvement of JNK signaling in seizure pathology, the hippocampal pattern of JNK phosphorylation (activation) was evaluated. Methods: BSA based nanocurcumin was administered at doses of 50 and 100mg/kg oral gavage to male NMRI mice, one hour before PTZ administration. Intravenous PTZ paradigm was used to determine the threshold dose of PTZ to induce clonic seizures, while the intraperitoneal PTZ paradigm was applied to evaluate the latency for appearance of generalized clonus. Upon completion of intraperitoneal PTZ paradigm experiments, the hippocampi were removed and Western blot analysis was performed to determine the phosphorylated and total forms of JNK. Results: The results indicated that BSA-based nanocurcumin at the doses of 50 and 100mg/kg could significantly increase the threshold and latency of clonic seizure, which was a significant superior effect compared to natural curcumin. PTZ significantly increased the level of hippocampal JNK phosphorylation, but pretreatment of nanocurcumin did not modify this effect. Conclusion: The present study shows that converting curcumin to BSA-based nanocurcumin can increase its antiepileptic effect. Furthermore, the antiepileptic effect of nanocurcumin was not associated with a modification in PTZ-induced hippocampal JNK hyper activation.

166) Sohrevardi, S.M., Heydari, B., Azarpazhooh, M.R., Teymourzadeh, M., Simental-Mendía, L.E., Atkin, S.L., Sahebkar, A., Karimi-Zarchi, M.
Therapeutic Effect of Curcumin in Women with Polycystic Ovary Syndrome Receiving Metformin: A Randomized Controlled Trial
(2021) *Advances in Experimental Medicine and Biology*, 1308, pp. 109-117.

Abstract
Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility, for which the insulin sensitizer metformin has been used therapeutically. It has been shown that curcumin also exhibits insulin-sensitizing properties. Given that metformin acts as an ovulation inducing agent and both curcumin and metformin can reduce insulin resistance, the aim of the current study was to evaluate the effect of metformin with and without curcumin nanomicelles in the treatment of women with polycystic ovary syndrome. This clinical trial was conducted on 100 women with PCOS, diagnosed according to the Rotterdam criteria, who were sequentially recruited and randomly divided into two groups (n = 50 each). Group 1 received 500 mg metformin three times daily and group 2 received 80 mg/day capsule of curcumin nanomicelle and 500 mg metformin three times a day for 3 months. After collecting fasting blood samples, biochemical parameters including triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol, plasma glucose, alanine amino transferase (ALT) and aspartate aminotransferase (AST) were evaluated based on enzymatic methods. Hormonal parameters were assessed using immunoassay kits. Insulin resistance (HOMA-IR) and insulin-sensitivity check index (QUICKI) were also assessed. After treatment, fasting insulin, HOMA-IR, and total testosterone in group 2 were significantly lower than those in group 1 (p < 0.05). Post-treatment LDL-C levels in groups 1 and 2 were 117.9 ± 24 and 91.12 ± 19.46 mg/dL, respectively (p < 0.01). In addition, HDL-C levels were increased with curcumin (group 1: 38.1 ± 4.36 mg/dL; group 2: 44.12 ± 7.3 mg/dL, p < 0.05). Total cholesterol was decreased with curcumin level (group 1: 207.9 ± 39.84 mg/dL; group 2; 159.7 ± 48.43 mg/dL, p < 0.05), with a decrease in triglycerides levels (group 1: 141.6 ± 9.57; group 2: 97.5 ± 8.8 mg/dL, p < 0.01). This study showed that curcumin has a synergistic effect with metformin in the improvement of insulin resistance and lipid profile in patients with PCOS. Therefore, the combined use of metformin and curcumin may have therapeutic utility in patients with PCOS.

167) Chestnut, C., Subramaniam, D., Dandawate, P., Padhye, S., Taylor, J., III, Weir, S., Anant, S.
Targeting Major Signaling Pathways of Bladder Cancer with Phytochemicals: A Review
(2021) *Nutrition and Cancer*, 73 (11-12), pp. 2249-2271.

Abstract
Bladder cancer is the 9th most prevalent cancer worldwide and carries a protracted treatment course with significant patient expense, morbidity, and mortality. Over 95% of bladder cancers arise from the urothelium and invade into the underlying muscle layer before metastasizing. Trans-urethral resection and BCG therapy is the current first-line treatment for non-muscle invasive bladder cancer but carries a high rate of tumor recurrence and progression. The poor outcomes associated with advanced disease indicate the urgent need for new and improved treatment strategies. There is increasing investigation into the molecular signaling pathways involved in bladder cancer pathogenesis with the goal of uncovering potential therapeutic targets. This article reviews the major signaling pathways implicated in bladder cancer, including PI3K/AKT/mTOR, Ras/Raf/MEK/MAPK, NF-κB, Wnt/β-catenin, Notch, Hedgehog, Hippo, JAK/STAT, and TGF-β as well as major cellular receptors central to cancer pathophysiology, including EGFR, Her2, FGFR, and VEGF. We also discuss various naturally occurring phytochemicals that show evidence of targeting these molecular pathways including curcumin, resveratrol, green tea polyphenols, sulforaphane, erucin, genistein, genipin, baicalein, quercetin, isoquercitin, vitamin E, parthenolide, dioscin, triptolide, kaempferol, pterostilbene, isoliquiritigenin, and escin. This review highlights the potential use of these compounds in treatment of bladder cancer.

168) Gregory, J., Vengalasetti, Y.V., Bredesen, D.E., Rao, R.V.
Neuroprotective herbs for the management of alzheimer's disease
(2021) *Biomolecules*, 11 (4), art. no. 543, .

Abstract
Background—Alzheimer's disease (AD) is a multifactorial, progressive, neurodegenerative disease that is characterized by memory loss, personality changes, and a decline in cognitive function. While the exact cause of AD is still unclear, recent studies point to lifestyle, diet, environmental, and genetic factors as contributors to disease progression. The pharmaceutical approaches developed to date do not alter disease progression. More than two hundred promising drug candidates have failed clinical trials in the past decade, suggesting that the disease and its causes may be highly complex. Medicinal plants and herbal remedies are now gaining more interest as complementary and alternative interventions and are a valuable source for developing drug candidates for AD. Indeed, several scientific studies have described the use of various medicinal plants and their principal phytochemicals for the treatment of AD. This article reviews a subset of herbs for their antiinflammatory, antioxidant, and cognitive-enhancing effects. Methods—This article systematically reviews recent studies that have investigated the role of neuroprotective herbs and their bioactive compounds for dementia associated with Alzheimer's disease and pre-Alzheimer's disease. PubMed Central, Scopus, and Google Scholar databases of articles were collected, and abstracts were reviewed for relevance to the subject matter. Conclusions—Medicinal plants have great potential as part of an overall program in the prevention and treatment of cognitive decline associated with AD. It is hoped that these medicinal plants can be used in drug discovery programs for identifying safe and efficacious small molecules for AD. © 2021 by the authors. Licensee MDPI, Basel, Switzerland.

169) Abd El-Monem, D.D., Abdel Rahman, A.A.S., Elwakeel, S.H.B.
Nanocurcumin improves the therapeutic role of mesenchymal stem cells in liver fibrosis rats
(2021) *Biointerface Research in Applied Chemistry*, 11 (6), pp. 14463-14479.

Abstract
Nano-curcumin (Nano-Cur) is a promising therapeutic agent that has a wide array of effective medicinal potentials. Therefore, the present inquiry aimed to assess Nano-Cur's impact on the therapeutic effect of bone-marrow-derived mesenchymal stem cells (BM-MSCs) in the rat model of liver fibrosis prompted by carbon tetrachloride (CCl4). Liver fibrosis was developed in 30male Wistar albino rats which were divided into five groups, six animals each. The 1st group (CCl4 group) was sacrificed immediately after the induction of liver fibrosis. The 2nd group received a single iv injection of BM-MSCs and left for 4weeks, the3rd group received 100mg/kg b.w. Nano-Cur 3times/week for 4weeks, the 4th group received a single iv injection of 107 BM-MSCs accompanied with Nano-Cur 3times/week for 4weeks, and the 5th group left for 4weeks without any intervention. Data revealed that treatment with BM-MSCs plus Nano-Cur alleviated liver fibrosis through reducing liver oxidative stress and restoring both liver histological picture and enzymatic profile. Additionally, companied treatment resulted in reducing TGFβ1 levels and attenuating the expression of Smad 2,3 and collagen I, III genes. Conversely, most of the pathological lesions were still detected in the recovery group. Nano-Cur improves the therapeutic role of BM-MSCs in liver fibrosis rats. © 2021 by the authors.

170) Forouzanfar, F., Majeed, M., Jamialahmadi, T., Sahebkar, A.
Telomerase: A Target for Therapeutic Effects of Curcumin in Cancer
(2021) *Advances in Experimental Medicine and Biology*, 1286, pp. 135-143.

Abstract
Telomerases are attractive targets for development of new anticancer agents. Most tumors express the enzyme telomerase that maintains telomere length and thus ensures indefinite cell proliferation, a hallmark of cancer. Curcumin has been shown to be effective against several types of malignancies and has also been shown to have inhibitory effects on telomerase activity. Hence, the aim of this chapter is to review the available investigations of curcumin on telomerase activity. Based on the findings obtained from the different studies here, we conclude that the telomerase inhibitory effects of curcumin are integral to its anticancer activity, and thus curcumin may be useful therapeutically in the cancer field. © 2021, The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG.

171) Vimala, K., Kannan, S.
Phyto-drug conjugated nanomaterials enhance apoptotic activity in cancer
(2021) *Advances in Protein Chemistry and Structural Biology*, 125, pp. 275-305.

Abstract
Cancer continues to be one of the leading causes of death worldwide and is a major obstacle to increased life expectancy. However, survival has not improved significantly with average cancer standard treatment strategies over the past few decades; survival rates have remained low, with tumor metastasis, adverse drug reactions, and drug resistance. Therefore, substitute therapies are essential to treat this dreadful disease. Recently, research has shown that natural compounds in plants, such as phytochemicals, are extensively exploited for their anticarcinogenic potential. Phytochemicals may show their anticancer activity different cancer cell markers may alter molecular pathways, which promote in cellular events such as cell cycle arrest and apoptosis, regulate antioxidant status, cell proliferation, migration, invasion and toxicity. Although their outstanding anticancer activity, however, their pharmacological budding is hindered by their low aqueous solubility, poor bioavailability, and poor penetration into cells, hepatic disposition, narrow therapeutic index, and rapid uptake by normal tissues. In this situation, nanotechnology has developed novel inventions to increase the potential use of phytochemicals in anticancer therapy. Nanoparticles can improve the solubility and stability of phytochemicals, specific tumor cell/tissue targeting, enhanced cellular uptake, reduction of phytochemicals. Therapeutic doses of phytochemicals for a long time. Additional benefits include better blood stability, multifunctional design of nanocarriers and improvement in

countermeasures. This review summarizes the advances in the use of nanoparticles for the treatment of cancer, as well as various nano-drug deliveries of phytochemicals against cancer. In particular, we are introducing several applications of nanoparticles in combination with phyto-drug for the treatment of cancer. © 2021 Elsevier Inc.

172) Sabir, S.M., Zeb, A., Mahmood, M., Abbas, S.R., Ahmad, Z., Iqbal, N.
Phytochemical analysis and biological activities of ethanolic extract of curcuma longa rhizome [Análise fitoquímica e atividades biológicas do extrato etanólico do rizoma de curcuma longa]
(2021) *Brazilian Journal of Biology*, 81 (3), pp. 737-740.

Abstract
Curcuma longa is an important dietary plant which possess several pharmacological activities, including antioxidant, antimicrobial, anti-inflamatory, anticancer and anti clotting etc. The aim of the present study was to determine the phenolic profile of Curcuma longa and in vitro antioxidant and antidiabetic activities. In HPLC chromatogram of Curcuma longa rhizome extract 15 phenolic compounds were identified namely Digalloyl-hexoside, Caffeic acid hexoside, Curdione, Coumaric, Caffeic acid, Sinapic acid, Qurecetin-3-D-galactoside, Casuarinin, Bisdemethoxycurcumin, Curcuminol, Demethoxycurcumin, and Isorhamnetin, Valoneic acid bilactone, Curcumin, Curcumin-O-glucuronide respectively. The ethanolic extract displayed an IC50 value of 37.1±0.3 µg/ml against alpha glucosidase. The IC50 value of DPPH radical scavenging activity was 27.2 ± 1.1 µg/mL. It is concluded that ethanolic extract of Curcuma long is rich source of curcumin and contain several important phenolics. The in vitro antioxidant and alpha glucosidase inhibitory effect of the plant justifies its popular use in traditional medicine.

173) Hardwick, J., Taylor, J., Mehta, M., Satija, S., Paudel, K.R., Hans-Bro, P.M., Chellappan, D.K., Bebawy, M., Dua, K.
Targeting cancer using curcumin encapsulated vesicular drug delivery systems
(2021) *Current Pharmaceutical Design*, 27 (1), pp. 2-14.

Abstract
Curcumin is a major curcuminoid present in turmeric. The compound is attributed to various therapeutic properties, which include anti-oxidant, anti-inflammatory, anti-bacterial, anti-malarial, and neuroprotection. Due to its therapeutic potential, curcumin has been employed for centuries in treating different ailments. Curcu-min has been investigated lately as a novel therapeutic agent in the treatment of cancer. However, the mechanisms by which curcumin exerts its cytotoxic effects on malignant cells are still not fully understood. One of the main limiting factors in the clinical use of curcumin is its poor bioavailability and rapid elimination. Advancements in drug delivery systems such as nanoparticle-based vesicular drug delivery platforms have improved several parameters, namely, drug bioavailability, solubility, stability, and controlled release properties. The use of curcumin-encapsulated niosomes to improve the physical and pharmacokinetic properties of curcumin is one such approach. This review provides an up-to-date summary of nanoparticle-based vesicular drug carriers and their therapeutic applications. Specifically, we focus on niosomes as novel drug delivery formulations and their potential in improving the delivery of challenging small molecules, including curcumin. Overall, the applications of such carriers will provide a new direction for novel pharmaceutical drug delivery, as well as for biotechnology, nutraceutical, and functional food industries.

174) Solati, K., Karimi, M., Rafieian-Kopaei, M., Abbasi, N., Abbaszadeh, S., Bahmani, M.
Phytotherapy for wound healing: The most important herbal plants in wound healing based on iranian ethnobotanical documents
(2021) *Mini-Reviews in Medicinal Chemistry*, 21 (4), pp. 500-519.

Abstract
Wound healing is a process that starts with the inflammatory response after the occurrence of any damage. This process initiates by restoring the wound surface coating tissue, migrating fibro-blasts to form the required collagen, forming a healing tissue and finally, leading to contortion and extraction of the wound. Today, various drugs are used to heal wounds. However, the drugs used to repair wounds have some defects and side effects. In spite of all attempts to accelerate wound healing definitely, no safe drug has been introduced for this purpose. Therefore, the necessity to identify herbal plants in ethnopharmacology and ethnobotany documents with healing effects is essential. In this article, we tried to review and present effective Iranian medicinal plants and herbal compounds used for wound healing. Searching was performed on databases, including ISI Web of Science, PubMed, PubMed Central, Scopus, ISC, SID, Magiran and some other databases. The keywords used included wound healing, skin treatment, medicinal plants, ethnobotany, and phytotherapy. In this regard, 139 medicinal plants effective on wound healing were identified based on ethnopharmacology and ethnobotanical sources of Iran. Plants such as Salvia officinalis, Echium amoenum, Verbascum spp., G1ycyrrhiza glabra, Medicago sativa, Mentha pulegium, Datura stramonium L., Alhagi spp., Aloe vera, Hypericum perforatum, Pistacia atlantica and Prosopis cineraria are the most important and useful medicinal plants used for wound healing in Iran. These native Iranian medicinal plants are rich in antioxidants and biological compounds and might be used for wound healing and preparation of new drugs.

175) Tubsakul, A., Sangartit, W., Pakdeechote, P., Kukongviriyapan, V., Apaijit, K., Kukongviriyapan, U.
Curcumin mitigates hypertension, endothelial dysfunction and oxidative stress in rats with chronic exposure to

lead and cadmium
(2021) *Tohoku Journal of Experimental Medicine*, 253 (1), pp. 69-76.

Abstract
Lead (Pb) and cadmium (Cd) are environmental pollutants and nonessential elements in the body. Both metals induce the development of hypertension which is associated with oxidative stress. Curcumin (CUR) is a polyphenolic compound with strong antioxidant activity. The present study evaluated the effect of CUR on oxidative stress, alteration of vascular responsiveness and hypertension induced by exposure to either Pb, Cd or the combination of Pb and Cd. Male Sprague-Dawley rats were exposed to low level of lead acetate (100 mg/L) and/or cadmium chloride (10 mg/L) in the drinking water for 16 weeks. The control animals received deionized water as drinking water. CUR (100 mg/kg) or propylene glycol as vehicle was intragastrically administered once daily for the last 4 weeks. Exposure to Pb, Cd or the combination induced increases in blood pressure and peripheral vascular resistance, and decreased the blood pressure response to intravenous infusion to acetylcholine. Supplementation with CUR significantly reduced blood pressure, alleviated oxidative stress, and increased plasma nitrate/nitrite and glutathione in the blood. The effects of CUR were associated with the improvement of vascular responsiveness, upregulation of the endothelial nitric oxide synthase and downregulation of the NADPH oxidase expression. Furthermore, CUR reduced the metal levels in blood, aorta, liver and kidney. Altogether, exposure to the combination of Pb and Cd aggravated hypertension and oxidative stress, and CUR effectively ameliorated these adverse events in metal exposed animals. Data indicate that CUR may be useful as a dietary supplement for protection against the noxious effects of the heavy metals. © 2021 Tohoku University Medical Press.

176) Liu, S.-K., Xie, H.-X., Ge, Y.-X., Zhang, J., Jiang, C.-S.
An updated research of glycogen synthase kinase-3β inhibitors: a review
(2021) *Monatshefte fur Chemie*, 152 (1), pp. 19-33.

Abstract
Abstract: Glycogen synthase kinase-3β (GSK-3β) is a highly conserved multifunctional serine/threonine (Ser/Thr) protein kinase widely expressed in many tissues. GSK-3β inhibitors could be used in the treatment of human key diseases, such as cancer, Alzheimer's disease, Parkinson's disease, inflammation, type-II diabetes, and so on, due to the multi-role of GSK-3β in the hepatic glycolysis regulation, cell signaling pathways, and phosphorylation of various proteins. Recently, sets of diverse GSK-3β inhibitors have been prepared, and biologically evaluated in vitro and in vivo in different screening models. This review summarizes the latest developments in GSK-3β inhibitors unclosed from 2015 to 2019, including their structure–activity relationship and bioactivity studies. Graphic abstract: [Figure not available: see fulltext.] © 2021, Springer-Verlag GmbH Austria, part of Springer Nature.

177) Alikiaii, B., Bagherniya, M., Askari, G., Johnston, T.P., Sahebkar, A.
The role of phytochemicals in sepsis: A mechanistic and therapeutic perspective
(2021) *BioFactors*, 47 (1), pp. 19-40.

Abstract
Sepsis and septic shock are still a leading cause of mortality and morbidity in intensive care units worldwide. Sepsis is an uncontrolled and excessive response of the innate immune system toward the invading infectious microbes, characterized by the hyper-production of pro-inflammatory mediators such as interleukin (IL)-1β, IL-6, tumor-necrosis factor (TNF)-α, and high-mobility group box 1 (HMGB1). In severe sepsis, the overwhelming production of pro-inflammatory cytokines and reactive oxygen species may compromise organ function and lead to the induction of abnormal apoptosis in different organs, resulting in multiple organ dysfunction syndrome and death. Hence, compounds that are able to attenuate inflammatory responses may have therapeutic potential for sepsis treatment. Understanding the pathophysiology and underlying molecular mechanisms of sepsis may provide useful insights in the discovery and development of new effective therapeutics. Therefore, numerous studies have invested much effort into elucidating the mechanisms involved with the onset and development of sepsis. The present review mainly focuses on the molecules and signaling pathways involved in the pathogenicity of sepsis. Additionally, several well-known natural bioactive herbal compounds and phytochemicals, which have shown protective and therapeutic effects with regard to sepsis, as well as their mechanisms of action, are presented. This review suggests that these phytochemicals are able to attenuate the overwhelming inflammatory responses developed during sepsis by modulating different signaling pathways. Moreover, the anti-inflammatory and cytoprotective activities of phytochemicals make them potent compounds to be included as complementary therapeutic agents in the diets of patients suffering from sepsis in an effort to alleviate sepsis and its life-threatening complications, such as multi-organ failure. © 2020 International Union of Biochemistry and Molecular Biology

178) Aravind, S.R., Lakshmi, S., S, R., Krishnan, L.K.
Sustained release of curcumin from fibrin matrix induces cancer cell death and immunomodulation
(2021) *Biomedicine and Pharmacotherapy*, 133, art. no. 110967, .

Abstract
Despite the role of curcumin in controlling inflammation, angiogenesis, and cancer in human cells, its therapeutic use is limited. The reasons are quick metabolic breakdown, low aqueous solubility, and bioavailability. This study describes the advantages of clinical-grade curcumin-incorporated fibrin matrix either in lyophilized off-the-shelf wafer or injectable hydrogel forms, as a biodegradable local delivery system. To produce the curcumin-fibrin wafer, used clinical-grade fibrin sealant in a modified composition. To fabricate wafer, we premixed the curcumin with either fibrinogen or thrombin, before

clotting into a hydrogel. Sustained release of active curcumin from fibrin wafer, suspended in culture medium at 37 °C lasted for seven days. Upon premixing albumin with thrombin and subsequently adding curcumin into the mixture improved the loading concentration and stability. Dose- and time-dependent apoptotic function of curcumin on cancer cell lines upon release from fibrin wafer, were demonstrated in vitro. In vivo immuno-modulation and a nontoxic response to curcumin released from fibrin into the peritoneal cavity of mice were established. The cytotoxic effect of released curcumin was demonstrated; showing both a preventive and therapeutic role against tumor growth. In vivo studies used Dalton's Lymphoma Ascites (DLA) mice model. Both implanted fibrin wafer and injected hydrogel can breakdown by a physiological process and get cleared by the fibrinolytic mechanism. The lyophilized fibrin wafer could function as a hemostat, adhere to surgical cancer tissues, and arrest bleeding. The potential of curcumin in preventing solid tumor metastasis may be explored upon the sustained delivery of the molecule from the fibrin wafer. © 2020

179) Shi, W., Ling, D., Zhang, F., Fu, X., Lai, D., Zhang, Y.
Curcumin promotes osteogenic differentiation of human periodontal ligament stem cells by inducting EGR1 expression
(2021) *Archives of Oral Biology*, 121, art. no. 104958, .

Abstract
Objective: Human periodontal ligament stem cells (hPDLSCs) attract attention for the periodontal regeneration therapy. Curcumin may promote osteogenic differentiation of hPDLSCs. This research aims to elucidate whether Curcumin displays promoting osteogenic differentiation and its mechanism. Methods: The hPDLSCs were isolated from human periodontal ligament by immunomagnetic beads, identified with immumofluorescence. hPDLSCs were treated with 0, 5, 10, 20, 50, 100 μmol/L Curcumin. The early growth response gene 1 (EGR1) siRNA or plasmind were tranfected into the hPDLSCs. The viability, Alkaline Phosphatase (ALP) activity and mineralizaiton level of hPDLSCs were measured with 3-(4,5)-dimethylthiahiazo(-z-y1)-3,5-di-phenytetrazoliumromide (MTT) assay, ALP Assay Kit or Alizarin Red staining. The expression of EGR1, RUNX family transcription factor 2 (Runx2), bone gamma-carboxyglutamate protein (OC), secreted phosphoprotein 1 (OPN) and collagen type I alpha 1 chain (Collagen I), in hPDLSC were determined by Western blotting and quantitative reverse transcription-polymerase chain reaction. Results: The isolated hPDLSCs were spindle or irregular, arranged in radial shape and shown positive expression of STRO-1, CD146 and Vimentin. Curcumin 10 μmol/L treatment maximal promoting the cells viability, ALP activities, mineralization, and levels of Runx2, OC, OPN, Collagen I and EGR-1 in hPDLSCs. EGR-1 siRNA transfection inversed Curcumin's promoting effect on ALP activities, mineralization, and levels of Runx2, OC, OPN, Collagen I and EGR-1 in hPDLSCs. While the EGR-1 plasmid transfection enhanced Curcumin's promoting effect on these parameters of hPDLSCs. Conclusion: Curcumin promotes the osteogenic differentiation of hPDLSCs, which may work through the EGR1. Curcumin may be a promising medicine for periodontitis treatment and periodontal regeneration. © 2020 Elsevier Ltd

180) Mishra, R., Gupta, A.K.
CHAPTER 8: Biological Activities of Curcuminoids
(2021) *Food Chemistry, Function and Analysis*, 2021-January (25), pp. 172-195.

Abstract
Turmeric, a rhizomatous herb, contains curcuminoids and essential oil, which are two major classes of secondary metabolites. These compounds are largely responsible for the pharmacological effects of turmeric. The three major curcuminoids are curcumin, demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC). Curcumin is the most abundant curcuminoid present in turmeric rhizomes followed by demethoxycurcumin and bisdemethoxycurcumin. The curcuminoids' mixture, which we get on a commercial scale, contains 78% curcumin, 18% DMC and 4% BDMC. A brief account of the chemical compositions and natural analogues of turmeric has been discussed in this chapter. The composition of turmeric and natural analogues, their antioxidant activities and pharmacological activities are also presented in this chapter. © 2021 The Royal Society of Chemistry.

181) Campbell, M.S., Carlini, N.A., Fleenor, B.S.
Influence of curcumin on performance and post-exercise recovery
(2021) *Critical Reviews in Food Science and Nutrition*, 61 (7), pp. 1152-1162.

Abstract
Intense exercise, especially involving eccentric contractions, causes muscle damage concomitant with increased reactive oxygen species (ROS), which can lead to increased fatigue and decrements in physical performance. Additionally, inflammatory cytokines and advanced glycation end-products (AGEs) are produced as a result of eccentric exercise and may further lead to decreased exercise performance. Nutritional interventions may provide an avenue to respond to and reduce the symptoms associated with muscle damage. Of recent interest, curcumin, the main constituent in the spice turmeric, has been the focus of various studies considering post-exercise recovery. Curcumin has potent anti-oxidant and anti-inflammatory properties and can reduce the accumulation of AGEs. This review considers the current evidence for curcumin to impact muscle recovery following exercise to improve performance and the potential mechanisms of action. To date, clinical studies have considered the potential role of curcumin to reduce muscular damage following treadmill running (downhill and flat), conventional walking/running, cycling (acute and chronic), single-leg jumping (downhill), and eccentric muscular fitness exercises of the upper and lower body (single- and double-leg). Studies have been conducted in sedentary to highly active men and women, both young and old, with supplementation duration lasting from a single, acute dose to daily dosages for three months. Various curcumin-based interventions have improved self-perceived measures of pain and

tenderness, reduced evidence of muscle damage, ameliorated inflammatory markers, increased markers of antioxidant capacity, diminished markers of oxidative stress, reduced markers of AGEs, and attenuated loss in mean power of single-leg sprints. However, these findings have not been consistently reported. © 2020 Taylor & Francis Group, LLC.

182) Sobhani, M., Farzaei, M.H., Kiani, S., Khodarahmi, R.
Immunomodulatory; Anti-inflammatory/antioxidant Effects of Polyphenols: A Comparative Review on the Parental Compounds and Their Metabolites
(2021) *Food Reviews International*, 37 (8), pp. 759-811.

Abstract
Polyphenols are a big family of phytochemicals that includes a wide range of natural substances with various biological activities. Amongst these activities, the immunomodulatory property has significant importance due to the central and vital roles of the immune system in the human body. The biological activities of polyphenols depend crucially on the chemical structure and the biotransformation undergone in the body. The glycosylation state of polyphenols and its diversity have a significant impact on the immunomodulatory activity, while there is a lack of a comprehensive review paper in this concept. Hence, we aimed to review the body of literature to light the way for effective modulation of the immune system function using dietary polyphenols. However, due to the significant diversity in the structure and biotransformation of polyphenols, it is hard to draw a general pattern in this regard. The sugar moiety, type, position, and extent of glycosylation determine the antioxidant, anti-inflammatory, and generally the immunomodulatory activities of polyphenols. In conclusion, this study provides a new comparative approach regarding the immunomodulatory activities of polyphenols versus their metabolites. Moreover, we conclude that polyphenols can modulate the immune system, while each polyphenol has its structural relevance and should be assessed case by case. Abbreviations: BBC: brush border cell; GI: gastrointestinal tract; LPH: lactase-phlorizin hydrolase; CBG: cytosolic beta-glucosidase; CYP: cytochrome p450 enzymes; COMT: catechol-O-methyltransferases; SULT: sulphotransferases; UDPGT: uridine-5′-diphosphate glucuronosyl-transferases; ABC: ATP-binding cassette; ET: transporters, ellagitannin; EA: ellagic acid; EGCG: epigallocatechin-3- gallate; DC: dendritic cell; Th: T helper; NK: natural killer; Treg: cells, regulatory T cells; TGFβ: transforming growth factor β; Foxp3: forkhead box P3; T-bet: T-box transcription factor; RORγt: Retineic-acid-receptor-related orphan nuclear receptor gamma; STAT: Signal transducer and activator of transcription; AhR: aryl hydrocarbon receptor; XRE: xenobiotic-responsive elements; PWM: pokeweed mitogen; Igs: immunoglobulins; PGE2: prostaglandin E2; TNF-α: tumor necrosis factor α; COX-2: cyclooxygenase-2; iNOS: inducible nitric oxide synthase; LPS: lipopolysaccharide; ApoE: apolipoprotein E; NF-κB: nuclear factor kappa light chain enhancer of activated B cells; JNK: c-Jun N-terminal kinases; IκBα: IκB alpha; IKK: IκB kinase; hsCRP: high sensitivity C reactive protein; ICAM-1: Intracellular adhesion molecule-1; MCP-1: Monocyte chemoattractant protein-1; VCAM-1: vascular cellular adhesion molecule-1; M3Gal: myricetin 3-O-β-D-galactopyranoside; Q3Glc: quercetin 3-O-β-D-glucopyranoside; Q3Rut: quercetin 3-O-β-D-rutinoside; and Q3Gal: quercetin 3-O-β-D-galactopyranoside; ISR, 3-methyl metabolite of quercetin: isorhamnetin; TAM, 4'-O-methyl quercetin: tamarixetin; ConA: Concanavalin A; ROS: Reactive oxygen species; ROS: Reactive oxygen species; THC: tetrahydrocurcumin; DHC: dihydrocurcumin; OHC: octahydrocurcumin; HHC: hexahydrocurcumin; NaC: sodium curcuminate; TEC: triethyl curcumin; DAC: diacetyl curcumin; HHC: hexahydrocurcumin; PLA2: phospholipase A2; TDM: trimethoxydibenzoylmethane; DBM: dibenzoylmethane; cPLA2: cytosolic phospholipase A2; 5-LOX: 5-lipoxygenase; IC50: half maximal inhibitory concentration; PI3K: phosphatidylinositol-3-Kinase; 12-HHT: 12(S)-hydroxy(5Z,8E,10E)-heptadecatrienoic acid; TXB2: thromboxane B2; 12-HETE: 12(S)-hydroxy-(5Z,8Z,10E,14Z)-eicosatetraenoic acid; MIP-1a: macrophage inflammatory protein-1a; DHG: dihydrogenistein; DHD: dihydrodaidzein; O-DMA: O-desmethylangolensin; MnSOD: manganese superoxide dismutase; DP: degree of polymerization; MMPs: matrix metalloproteinases; EC: epicatechin; EGC: epigallocatechin; C3G: cyanidin-3-glucoside; MAPK: mitogen-activated protein kinase; PI3K/PKB: phosphoinositide-3-kinase/protein kinase B; PA: protocatechuic acid; BR: black rice; HHDP: hexahydroxydiphenoyl; AP-1: activator protein 1; TSP: thrombospondin; eNOS: endothelial-nitric oxide synthase; Nrf2: nuclear factor erythroid 2–related factor 2; PAI-1: plasminogen activator inhibitor-1; C–C motif: chemokine; CCL2: ligand 2; miR-155: microRNA-155; M-CSF: macrophage colony-stimulating factor; BMDM: bone marrow-derived macrophage; ORAC: oxygen radical absorbance capacity; PCL: photochemiluminescence; FRAP: ferric reducing antioxidant power; ABTS: 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid); TEAC: trolox equivalent antioxidant capacity; DPPH: 2,2-diphenyl-1- picrylhydrazyl; ESR: electron spin resonance spectroscopy; CAA: cell-based antioxidant assay; NADPH: nicotinamide adenine dinucleotide phosphate; GST: oxidase, glutathione S-transferase; GPX: glutathione peroxidase; Fe-NTA: ferric nitrilotriacetate; AAPH: 2,2- azobis(2-amidinopropane) dihydrochloride; LP: lipid peroxidation; LOX: lipoxygenase; XO: xanthine oxidase; Q7GA: quercetin-7-O-glucuronide; Q3′GA: quercetin-3′-O-glucuronide; Q4′GA: quercetin-4′-O-glucuronide; Q3S: quercetin-3-O-sulfate; DOPAC: 3,4-dihydroxyphenylacetic acid; protocatechuic acid, PCA: 3,4-dihydroxybenzoic acid; 3-OPAC: 3-hydroxyphenyl acetic acid; CYP1A1: cytoprotective enzyme (cytochrome P450 1A1); HO-1: heme oxygenase 1; QR1: quinone reductase; 1GST: glutathione S-transferase; GCLC: glutamate-cysteine ligase catalytic subunit; 3'ME7G: 3'-O-methyl-(-)-epicatechin-7-O-glucuronide; E3'G: (-)-epicatechin-3'-O-glucuronide; E7G: (-)-epicatechin-7-O-glucuronide; 4'ME3'G: 4'-O-methyl-(-)-epicatechin-3'-O-glucuronide; COPD: chronic obstructive pulmonary disease; LDL: low-density lipoprotein; NBT: nitroblue tetrazolium; PAMPs: pathogen-associated molecular patterns; DAMPs: damage-associated molecular patterns; PRRs: pattern recognition receptors; TLR4: toll-like receptor 4; ERK: extracellular signal-regulated protein kinases; LT: leukotrienes; Pg-3-glc: pelargonidin-3-O-glucoside; PGA: phloroglucinaldehyde; 4-HBA: 4-hydroxybenzoic acid; HUVECs: human umbilical vein endothelial cells; APC: antigen-presenting cells; MHC: major histocompatibility complex; TCR: T cell receptor; PCA: passive cutaneous anaphylaxis; FcεRI: high affinity Immunoglobulin E receptor; EGCG4″Me: (-)-epigallocatechin-3-O-(4-O-methyl)gallate; EGCG3″Me: (-)-epigallocatechin-3-O-(3-O-methyl)gallate; 67LR: 67 kDa laminin receptor; MRLC: myosin II regulatory light chain; CGA: chlorogenic acid; IFN-c: interferon-c; NGC: naringenin chalcone. © 2020 Taylor & Francis.

183) Ashrafizadeh, M., Zarrabi, A., Hushmandi, K., Zarrin, V., Moghadam, E.R., Hashemi, F., Makvandi, P., Samarghandian, S., Khan, H., Hashemi, F., Najafi, M., Mirzaei, H.

Toward Regulatory Effects of Curcumin on Transforming Growth Factor-Beta Across Different Diseases: A Review
(2020) *Frontiers in Pharmacology*, 11, art. no. 585413, .

Abstract
Immune response, proliferation, migration and angiogenesis are juts a few of cellular events that are regulated by transforming growth factor-β (TGF-β) in cells. A number of studies have documented that TGF-β undergoes abnormal expression in different diseases, e.g., diabetes, cancer, fibrosis, asthma, arthritis, among others. This has led to great fascination into this signaling pathway and developing agents with modulatory impact on TGF-β. Curcumin, a natural-based compound, is obtained from rhizome and roots of turmeric plant. It has a number of pharmacological activities including antioxidant, anti-inflammatory, anti-tumor, anti-diabetes and so on. Noteworthy, it has been demonstrated that curcumin affects different molecular signaling pathways such as Wnt/β-catenin, Nrf2, AMPK, mitogen-activated protein kinase and so on. In the present review, we evaluate the potential of curcumin in regulation of TGF-β signaling pathway to corelate it with therapeutic impacts of curcumin. By modulation of TGF-β (both upregulation and down-regulation), curcumin ameliorates fibrosis, neurological disorders, liver disease, diabetes and asthma. Besides, curcumin targets TGF-β signaling pathway which is capable of suppressing proliferation of tumor cells and invading cancer cells. © Copyright © 2020 Ashrafizadeh, Zarrabi, Hushmandi, Zarrin, Moghadam, Hashemi, Makvandi, Samarghandian, Khan, Najafi and Mirzaei.

184) Hercz, D., Jiang, S.H., Webster, A.C.
Interventions for itch in people with advanced chronic kidney disease
(2020) *Cochrane Database of Systematic Reviews*, 2020 (12), art. no. CD011393, .

Abstract
Background: Itch in patients with chronic kidney disease (CKD) is common, often very distressing and associated with depression, reduced quality of life, and increased death. The most common first-line treatment has been the use of antihistamines despite the lack of substantial evidence for its use for uraemic itch. Few recommendations and guidelines exist for treatment. Objectives: We aimed to determine: 1) the benefits and harms (both absolute and relative) of all topical and systemic interventions for the treatment of uraemic itch, either alone or in combination, when compared with placebo or standard care; and, 2) the dose strength or frequency, stage of kidney disease or method of dialysis used (where applicable) in cases where the effects of these interventions vary depending on co-interventions. Search methods: We searched the Cochrane Kidney and Transplant Register of Studies up to 17 December 2019 through contact with the Information Specialist using search terms relevant to this review. Studies in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov. Selection criteria: Randomised controlled trials (RCTs) in adults with CKD stages 4 or 5 comparing treatments (pharmacological, topical, exposure, dialysis modality) for CKD associated itch to either placebo or other established treatments. Data collection and analysis: Two authors independently abstracted study data and assessed study quality. Data were analysed using a random effects meta-analysis design estimating the relative effects of treatment versus placebo. Estimates of the relative effects between treatments are included where possible. For continuous measures of severity of itch up to three months, mean difference (MD) or standardised mean difference (SMD) were used. When reported, adverse effects were tabulated. The certainty of the evidence was estimated using GRADE. Main results: Ninety-two RCTs, randomising 4466 participants were included. Fifty-eight studies (3285 participants) provided sufficient data to be meta-analysed. Of these, 30 compared an intervention to a placebo or control. The 10 cm Visual Analogue Scale (VAS) was the dominant instrument utilized for itch reporting and the Duo score was used in a minority of studies. GABA analogues including, gabapentin and pregabalin, reduce itch in patients with CKD (5 studies, 297 participants: 4.95 cm reduction, 95% CI 5.46 to 4.44 lower in VAS compared to placebo; high certainty evidence). Kappa opioid agonists, including nalfurafine also reduced itch in this population (6 studies, 661 participants: 1.05 cm reduction, 95% CI 1.40 to 0.71 lower in VAS compared to placebo; high certainty evidence). Ondansetron had little or no effect on itch scores (3 studies, 183 participants: 0.38 cm reduction, 95% CI 1.04 lower to 0.29 higher in VAS compared to placebo; high certainty evidence). Reduction in the severity of itch was reported with oral montelukast, turmeric, zinc sulfate and topical capsaicin. For all other interventions, the certainty of the evidence was low to moderate, and the interventions had uncertain effects on uraemic pruritus. Six studies have disclosed significant financial support from their respective manufacturers, six were affected by lack of blinding, and 11 studies have 15 participants or less. Older, smaller RCTs often failed to follow intention-to-treat protocols with unexplained dropouts after randomisation. Adverse effects were generally poorly and inconsistently reported across all RCTs. No severe adverse events were reported for any intervention. Authors' conclusions: The RCTs of this meta-analysis contain a large array of interventions with a diverse set of comparators. For many interventions, trials are sparse. This served to make informative meta-analysis challenging. Of all treatments for uraemic pruritus, gabapentinoids (gabapentin and pregabalin) were the most studied and show the greatest reduction in itch scores. Further RCTs, even of the scale of the largest trials included in this review, are unlikely to significantly change this finding. Kappa-opioid agonists (mainly nalfurafine) also may reduce itch, but indirect comparison suggests a much more modest effect in comparison to GABA analogues. Evidence for oral montelukast, turmeric, zinc sulfate, and topical capsaicin also showed an itch score reduction. However, these reductions were reported in small studies, and warrant further investigation. Ondansetron did not reduce itch. It is somewhat unlikely that a further study of ondansetron will change this result. Copyright © 2020 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

185) Saha, T., Singha, S., Kumar, S., Das, S.
Spectroscopy driven DFT computation for a structure of the monomeric Cu2+-Curcumin complex and thermodynamics driven evaluation of its binding to DNA: Pseudo-binding of Curcumin to DNA
(2020) *Journal of Molecular Structure*, 1221, art. no. 128732, .

Abstract
In an attempt to overcome limitations of Curcumin from being an important molecule in biology and medicine, a monomeric

complex of CuII [Cu(Cur)(OCOCH3)(H2O)] was prepared. Physico-chemical studies in solution using copper acetate and Curcumin indicate formation of a 1:2 CuII:Curcumin species. However, attempts to prepare it always led to the formation of a 1:1 CuII:Curcumin species, if CuII-acetate was used as the starting material. In the absence of a single crystal or an appropriate powder X ray diffraction data that would allow solving of the structure, it was arrived at by spectroscopy guided DFT calculations. Unlike Curcumin, the prepared complex was stable under physiological conditions, an advance achieved through complex formation. Effective binding of the complex to DNA with an ability to enhance cellular uptake owing to the presence of CuII are other benefits of complex formation that might increase its cytotoxic potential. The complex has a reasonably strong affinity for DNA realized from binding constant values obtained with calf thymus DNA at different temperatures in the range 25 °C–35 °C. This enabled an evaluation of thermodynamic parameters (ΔH, ΔS and ΔG), that helped in determining the mode of binding between the complex and DNA as realized from a correlation of thermodynamic signatures to binding types. The study may be considered a case of pseudo-binding of Curcumin to DNA since the complex containing a Curcumin bound the metal ion does not dissociate in solution under physiological conditions, i.e. remains as one unit. Hence binding of the complex to DNA is also the binding of Curcumin to it present as one “single unit”, a major advancement based on a biophysical approach. Besides, aspects like stability of the complex in solution, prevention of degradation of Curcumin in aqueous buffer or biological milieu, binding with mammalian DNA are other aspects that are significant for use of the complex on biological targets. © 2020 Elsevier B.V.

186) Henriques, M.C., Faustino, M.A.F., Braga, S.S.
Curcumin innovative delivery forms: Paving the ‘yellow brick road’ of antitumoral phytotherapy
(2020) *Applied Sciences (Switzerland)*, 10 (24), art. no. 8990, pp. 1-30.

Abstract
This review deals with the various aspects involved in the medicinal action of curcumin, from the photosensitivity and its relevance to storage and shelf-life, to the different routes of administration, which influence the bioavailability. The focus of the review is on the antitumor properties of curcumin and the currently available solutions for their amelioration. The work starts by presenting a brief historical perspective on the origins and uses of curcumin, from early days until the present time. The following sections describe the physico-chemical properties of curcumin and their impact on the biological activity and pharmacokinetics, raising awareness to the need for formulations able to improve the bioavailability. The last section is focused on research efforts being made to circumvent curcumin’s instability and low availability due to the extensive hepatic first pass metabolism, describing innovative scientific advances and new patented formulations and emerging products on the market. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

187) Saeed, M., Mirzadeh, H., Zandi, M., Barzin, J.
PEGylated curcumin-loaded nanofibrous mats with controlled burst release through bead knot-on-spring design
(2020) *Progress in Biomaterials*, 9 (4), pp. 175-185.

Abstract
APEGylatedcurcumin (PCU) loaded electrospuns based on poly(ε-caprolactone) (PCL) andpolyvinyl alcohol (PVA) were fabricated for wound dressing applications. The main reason for this wound dressing design is antibacterialactivity enhancement, and wound exudates management. PEGylation increases curcuminsantibacterial properties and PVA can help exudates management. For optimal wound dressing, first, response surface methodology (RSM) was applied to optimize the electrospinning parameters to achieve appropriate nanofibrous mats. Then a three-layer electrospun was designed by considering the water absorbability, PCU release profile as well as antibacterial and biocompatibility of the final wound dressing. The burst release in controlled release systems could be evaluated for prevention of the higher initial drug release and control the effective life time. The PCU release results illustrated that the bead knot plays a positive role in controlling the release profile andby increase in the number of beads per unit area from 3000 to 9000 mm−2,the PCU burst release will be reduced; Also in vitro studies show that optimized three-layer dressing based on PCL/PVA/PCU can support water vapour transmission rate in optimal range and also absorb more than three times exudates in comparison with mono-layerdressing. Antibacterial tests show that the electrospun wound dressing containing 5% PCU exhibits100% antibacterial activityas well as cell viability level within an acceptable range. © 2020, Islamic Azad University.

188) Humadi, A.A., Al-Kaisei, B.I., Hameed, M.S.
Pathological and hormonal effects of 2,3,7,8-tetrachloro-dibenzo-p-dioxin (Tcdd) versus antioxidant activity of curcumin in sprague dawley male rats
(2020) *Veterinary Practitioner*, 21 (2), pp. 439-443.

Abstract
Current experiment was designed to evaluate the chronic effects of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) intoxicant effects and Curcumin antioxidant effects on pathological and hormonal assay in Sprague Dawley male rats at day 90. Thirty male rats divided randomly and equally into 3 groups, control group (negative control) received only normal pellet and corn oil, 2nd group (positive group) act as TCDD group received orally weekly for 90 day by stomach tube (2 µg/kg), while 3rd group received weekly by stomach tube (2 µg/kg) TCDD with (100 mg/kg) daily Curcumin for 90 day. Testosterone hormone and sperm analysis (viability, number and abnormality) assay significantly decrease (P<0.05) at 2nd group when compare with control and 3rd group, while pathological changes indicated at 2nd group testicular carcinoma characterized by pleomorphic and polyhydral of leydig cells and sertoli cells.The histopathological examination refer to leydig and sertoli cells carcinoma (testis carcinoma). © 2020, Veterinary Practitioner. All rights reserved.

189) Hahn, D., Shin, S.H., Bae, J.S.
Natural antioxidant and anti-inflammatory compounds in foodstuff or medicinal herbs inducing heme oxygenase-1 expression
(2020) *Antioxidants*, 9 (12), art. no. 1191, pp. 1-40.

Abstract
Heme oxygenase-1 (HO-1) is an inducible antioxidant enzyme that catalyzes heme group degradation. Decreased level of HO-1 is correlated with disease progression, and HO-1 induction suppresses development of metabolic and neurological disorders. Natural compounds with antioxidant activities have emerged as a rich source of HO-1 inducers with marginal toxicity. Here we discuss the therapeutic role of HO-1 in obesity, hypertension, atherosclerosis, Parkinson's disease and hepatic fibrosis, and present important signaling pathway components that lead to HO-1 expression. We provide an updated, comprehensive list of natural HO-1 inducers in foodstuff and medicinal herbs categorized by their chemical structures. Based on the continued research in HO-1 signaling pathways and rapid development of their natural inducers, HO-1 may serve as a preventive and therapeutic target for metabolic and neurological disorders. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

190) Kupnik, K., Primožič, M., Kokol, V., Leitgeb, M.
Nanocellulose in drug delivery and antimicrobially active materials
(2020) *Polymers*, 12 (12), art. no. 2825, pp. 1-40.

Abstract
In recent years, nanocellulose (NC) has also attracted a great deal of attention in drug delivery systems due to its unique physical properties, specific surface area, low risk of cytotoxicity, and excellent biological properties. This review is focused on nanocellulose based systems acting as carriers to be used in drug or antimicrobial delivery by providing different but controlled and sustained release of drugs or antimicrobial agents, respectively, thus showing potential for different routes of applications and administration. Microorganisms are increasingly resistant to antibiotics, and because, generally, the used metal or metal oxide nanoparticles at some concentration have toxic effects, more research has focused on finding biocompatible antimicrobial agents that have been obtained from natural sources. Our review contains the latest research from the last five years that tested nanocellulose-based materials in the field of drug delivery and antimicrobial activity. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

191) Trochopoulos, A.G.X., Zaharieva, M.M., Marinova, M.H., Yoncheva, K., Tibi, I.P.-E., Berger, M.R., Konstantinov, S.M.
Antineoplastic effect of a novel nanosized curcumin on cutaneous T cell lymphoma
(2020) *Oncology Letters*, 20 (6), art. no. 304, .

Abstract
Cutaneous T cell lymphomas (CTCLs) are a group of heterogeneous, life-threatening, extra-nodal and lympho- proliferative T cell neoplasms. Since chronic inflammation serves a key role in CTCL progression, curcumin, a natural pigment with proven anti-inflammatory and antineoplastic properties, as well as minimal toxicity, may be used as a therapeutic agent. In the present study, two formulations of curcumin (standard ethanolic and a Pluronic®P-123/F-127 micellar solution) were compared regarding their cytotoxic efficacy and speed of internalization in three CTCL cell lines, namely HuT-78, HH and MJ. In addition, the modulating effect of curcumin on selected proteins involved in the prolif- eration and progression of the disease was determined. The results indicated the superiority of the Pluronic®P-123/F-127 micellar curcumin over the standard ethanol solution in terms of cellular internalization efficiency as determined by spectrophotometric analysis. Notably, the presence of commonly used media components, such as phenol red, may interfere when interpreting the cytotoxicity of curcumin, due to their overlapping absorbance peaks. Therefore, it was concluded that phenol red-free media are superior over media with phenol red in order to correctly measure the cytotoxic efficacy and cell penetration of curcumin. Depending on the cell line, the IC50 values of micellar curcumin varied from 29.76 to 1.24 μM, with HH cells demonstrating the highest sensitivity. This cell line had the lowest expression levels of the Wilms' tumor-1 transcription factor. Performing western blot analyses of treated and untreated CTCL cells, selective signal transduction changes were recorded for the first time, thus making curcumin nano-formulation an attractive and prospective option with therapeutic relevance for CTCL as a rare orphan disease. © 2020 Spandidos Publications. All rights reserved.

192) Ismail, A.A., Abdel-Khalek, A.-K.E., Khalil, W.A., Yousif, A.I., Saadeldin, I.M., Abomughaid, M.M., El-Harairy, M.A.
Effects of mint, thyme, and curcumin extract nanoformulations on the sperm quality, apoptosis, chromatin decondensation, enzyme activity, and oxidative status of cryopreserved goat semen
(2020) *Cryobiology*, 97, pp. 144-152.

Abstract
Goat semen cryopreservation is a challenging process as it results in reduced motility, vitality, and fertility of spermatozoa after freezing. In this study, we evaluated the effects of different herbal extract nanoformulations (NFs) [mint (MENFs), thyme (TENFs), and curcumin (CENFs)], supplemented at either 50 or 100 μg into Tris-extender on the cryopreserved goat semen quality. The hydrothermal squeezing method was used for the preparation of the NFs extracts. The morphological

evaluation of the NFs extracts was conducted by transmission electron microscopy. All NFs supplements improved ($p < 0.05$) the progressive motility, vitality, and plasma membrane integrity of sperm compared with the control extender after equilibration (5 °C for 2 h) and thawing (37 °C for 30 s), but had no effect on sperm abnormality and acrosome integrity. All NFs supplements decreased ($p < 0.05$) the apoptosis, malondialdehyde level, and chromatin decondensation of sperm cells, while increased ($p < 0.05$) the total antioxidant capacity and catalase activity in the frozen/thawed extender. Particularly, CENFs at a level of 100 μg showed improvement of sperm parameters and antioxidant status during cryopreservation of goat semen more than TENFs and MENFs. The CENFs improved the quality of goat spermatozoa in post-thawed semen in terms of preventing cryodamage and promoting the cryotolerance of spermatozoa when compared with TENFs and MENFs. Therefore, supplementation of Tris-extender with CENFs could enhance goat semen processing during cryopreservation. © 2020 Elsevier Inc.

193) Alqahtani, M.S., Alqahtani, A., Kazi, M., Ahmad, M.Z., Alahmari, A., Alsenaidy, M.A., Syed, R.
Wound-healing potential of curcumin loaded lignin nanoparticles
(2020) *Journal of Drug Delivery Science and Technology*, 60, art. no. 102020, .

Abstract
The emergence of new material platforms, focused on nanotechnology, have resulted in a growing interest in their application to healing skin wounds. The skin forms an effective barrier against the external environment and consequently, rapid healing of wound tissue after injury is essential. Curcumin (diferuloylmethane) is a promising small molecule for the treatment of wounds based on its wound-healing activity and antioxidant and anti-inflammatory properties. However, its therapeutic application is limited by the poor skin permeability and bioavailability due to its poor solubility and low stability. Herein, curcumin loaded LNPs was prepared and characterized for their wound healing activity. Cytotoxicity assays indicated that curcumin-free and loaded nanoparticles were biocompatible with skin keratinocytes with no cytotoxic effects, suggesting that they did not interfere with cell proliferation during wound healing. Curcumin loaded LNPs exhibited potent in vitro antibacterial activity against gram-positive bacterial pathogens, particularly against Staphylococcus aureus, the most common wound bacterium. Fibroblast cell migration was observed using a scratch assay; upon treatment with curcumin loaded LNPs, wounded keratinocytes exhibited increased cell migration, which is a key feature of wound healing. The in vivo results showed that wounded rats treated with curcumin loaded LNPs exhibited enhanced dermal wound closure compared with the untreated control. After 12 days, the wounds treated with curcumin loaded LNPs achieved nearly full wound contraction compared with the untreated control, which had a wound size reduction of approximately 43%. Curcumin-loaded LNPs treated wounds showed advanced granulation tissue formation, characterized by greater collagen deposition. They also had lower myeloperoxidase activity, which is indicative of less inflammatory infiltration. Lower expression of matrix metalloproteinases (MMPs), especially MMP9, was characteristic of wounds treated with curcumin loaded LNPs. Overall, the results from this study highlight the advantages of using lignin as a nanocarrier to accelerate wound healing. © 2020 Elsevier B.V.

194) Zahran, R.F., Geba, Z.M., Tabll, A.A., Mashaly, M.M.
Therapeutic potential of a novel combination of Curcumin with Sulfamethoxazole against carbon tetrachloride-induced acute liver injury in Swiss albino mice
(2020) *Journal of Genetic Engineering and Biotechnology*, 18 (1), art. no. 13, .

Abstract
Background: In the current study, we have investigated the effect of each of curcumin (CUR) and sulfamethoxazole (SMX) either separate or mixed together (CUR + SMX) on biochemical, hematological and histological alternations associated with carbon tetrachloride (CCl4)-induced liver fibrosis in mice. Results: CCl4, caused changes of several biomarkers, proving its hepatotoxic effects, such as an increase in aminotransferases liver enzymes alanine and aspartate transaminases (ALT, AST), malondialdehyde (MDA), and nitric oxide (NO) formation, with a decrease in superoxide dismutase (SOD), glutathione reductase (GSSG), total antioxidant capacity (TAO), glutathione (GSH), total protein, and albumin, compared to a negative control mice group. Compared to the CCl4 group of mice, the CUR and SMX separate and/or together (CUR + SMX) treatments showed significance in (p < 0.001), ameliorated liver injury (characterized by an elevation of (ALT, AST) and a decrease (p < 0.001) in serum albumin and total protein), antioxidant (characterized by a decrease in (p < 0.001) MDA, NO; an increase (p < 0.001) SOD, GSSG, TAO; and reducing GSH), hematological changes (characterized by a decrease (p < 0.001) in white blood cells count and an increase (p < 0.001) in platelets count, hematocrit levels, hemoglobin concentration, and (p < 0.05) red blood cells count), SDS-PAGE electrophoresis with a decrease in protein synthesis and changes in histological examinations. Conclusions: CUR and SMX either separate or together (SUR + SMX) may be considered promising candidates in the prevention and treatment of liver fibrosis. © 2020, The Author(s).

195) Ramaholimihaso, T., Bouazzaoui, F., Kaladjian, A.
Curcumin in Depression: Potential Mechanisms of Action and Current Evidence—A Narrative Review
(2020) *Frontiers in Psychiatry*, 11, art. no. 572533, .

Abstract
Major depressive disorder (MDD) is one of the most prevalent and debilitating disorders. Current available treatments are somehow limited, so alternative therapeutic approaches targeting different biological pathways are being investigated to improve treatment outcomes. Curcumin is the main active component in the spice turmeric that has been used for centuries in Ayurvedic medicine to treat a variety of conditions, including anxiety and depressive disorders. In the past decades, curcumin has drawn researchers' attention and displays a broad range of properties that seem relevant to depression

pathophysiology. In this review, we break down the potential mechanisms of action of curcumin with emphasis on the diverse systems that can be disrupted in MDD. Curcumin has displayed, in a number of studies, a potency in modulating neurotransmitter concentrations, inflammatory pathways, excitotoxicity, neuroplasticity, hypothalamic–pituitary–adrenal disturbances, insulin resistance, oxidative and nitrosative stress, and endocannabinoid system, all of which can be involved in MDD pathophysiology. To date, a handful of clinical trials have been published and suggest a benefit of curcumin in MDD. With evidence that is progressively growing, curcumin appears as a promising alternative option in the management of MDD.

196) Carrizzo, A., Izzo, C., Forte, M., Sommella, E., Di Pietro, P., Venturini, E., Ciccarelli, M., Galasso, G., Rubattu, S., Campiglia, P., Sciarretta, S., Frati, G., Vecchione, C.
A novel promising frontier for human health: The beneficial effects of nutraceuticals in cardiovascular diseases
(2020) *International Journal of Molecular Sciences*, 21 (22), art. no. 8706, pp. 1-40.

Abstract
Cardiovascular diseases (CVDs) such as hypertension, atherosclerosis, myocardial infarction, and diabetes are a significant public health problem worldwide. Although several novel pharmacological treatments to reduce the progression of CVDs have been discovered during the last 20 years, the better way to contain the onset of CVDs remains prevention. In this regard, nutraceuticals seem to own a great potential in maintaining human health, exerting important protective cardiovascular effects. In the last years, there has been increased focus on identifying natural compounds with cardiovascular health-promoting effects and also to characterize the molecular mechanisms involved. Although many review articles have focused on the individual natural compound impact on cardiovascular diseases, the aim of this manuscript was to examine the role of the most studied nutraceuticals, such as resveratrol, cocoa, quercetin, curcumin, brassica, berberine and Spirulina platensis, on different CVDs. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

197) Pelikh, O., Keck, C.M.
Hair follicle targeting and dermal drug delivery with curcumin drug nanocrystals—essential influence of excipients
(2020) *Nanomaterials*, 10 (11), art. no. 2323, pp. 1-25.

Abstract
Many active pharmaceutical ingredients (API) possess poor aqueous solubility and thus lead to poor bioavailability upon oral administration and topical application. Nanocrystals have a well-established, universal formulation approach to overcome poor solubility. Various nanocrystalbased products have entered the market for oral application. However, their use in dermal formulations is relatively novel. Previous studies confirmed that nanocrystals are a superior formulation principle to improve the dermal penetration of poorly soluble API. Other studies showed that nanocrystals can also be used to target the hair follicles where they create a drug depot, enabling long acting drug therapy with only one application. Very recent studies show that also the vehicle in which the nanocrystals are incorporated can have a tremendous influence on the pathway of the API and the nanocrystals. In order to elucidate the influence of the excipient in more detail, a systematic study was conducted to investigate the influence of excipients on the penetration efficacy of the formulated API and the pathway of nanocrystals upon dermal application. Results showed that already small quantities of excipients can strongly affect the passive dermal penetration of curcumin and the hair follicle targeting of curcumin nanocrystals. The addition of 2% ethanol promoted hair follicle targeting of nanocrystals and hampered passive diffusion into the stratum corneum of the API, whereas the addition of glycerol hampered hair follicle targeting and promoted passive diffusion. Propylene glycol was found to promote both pathways. In fact, the study proved that formulating nanocrystals to improve the bioefficacy of poorly soluble API upon dermal application is highly effective. However, this is only true, if the correct excipient is selected for the formulation of the vehicle. The study also showed that excipients can be used to allow for a targeted dermal drug delivery, which enables to control if API should be delivered via passive diffusion and/or as drug reservoir by depositing API in the hair follicles. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

198) Sundararajan, R., Mittal, L., Camarillo, I.G.
Electrochemotherapy modulates mammary tumor growth in rats on a western diet supplemented with curcumin
(2020) *Biomedicines*, 8 (11), art. no. 498, pp. 1-15.

Abstract
In the US, every 12 min, six women are diagnosed with breast cancer and one dies. This highlights a critical need for developing alternate therapies using natural compounds, which are cost effective and with less side effects. Curcumin, the yellow pigment of turmeric has been found to suppress initiation, progression, and metastasis of a variety of tumors. Multiple clinical trials highlight the efficacy of curcumin in treating breast cancer and other diseases. Our in vitro studies have demonstrated that the electrical pulse (EP) application can further enhance the effectiveness of curcumin against breast cancer cells in a therapy called electrochemotherapy (ECT). In a direct extension of these results, we studied the effect of ECT coupled with intratumoral curcumin administration (EP+Cur) on N-methyl-N-nitrosourea (MNU) induced mammary tumors in female Sprague Dawley rats. Beginning at the weaning and throughout the study, rats were fed either western diet (West) or western diet, supplemented with 1% curcumin (W+Cur). Our results showed that EP+Cur treatment led to a reduced growth rate in rats fed with W+Cur diet compared to West diet (57.14% vs. 16.67% in West diet). These results provide a foundation for further studies towards utilizing it in clinical practice. © 2020 by the authors. Licensee MDPI, Basel, Switzerland.

199) Pandey, A., Chaturvedi, M., Mishra, S., Kumar, P., Somvanshi, P., Chaturvedi, R.
Reductive metabolites of curcumin and their therapeutic effects
(2020) *Heliyon*, 6 (11), art. no. e05469, .

Abstract
Curcumin, a secondary metabolite from the turmeric plant is one of the most promising natural products, which has been studied extensively for decades. It has demonstrated several pharmacological activities in vitro and in vivo. Various studies have indicated that the pharmacological activity of curcumin is contributed by its metabolites. The aim of this review is to present an overview of metabolic products of curcumin produced upon its reduction like di, tetra, hexa and octa-hydrocurcumin. In addition, this paper has systematically analyzed the current information regarding medicinal use of reduced metabolites of curcumin and identified the limitations which have hindered its widespread usage in the medical world. Several diverse therapeutic effects have shown to be exhibited by reduced metabolites of curcumin such as antioxidant, anti-cancerous, anti-inflammatory and immunoregulatory activities. The potential underlying molecular mechanisms of the biological activities of reduced metabolites of curcumin have also been highlighted, which may provide insight into the principle of effectiveness of curcumin. © 2020 The Authors

200) Miñano, J., Puiggalí, J., Franco, L.
Effect of curcumin on thermal degradation of poly(glycolic acid) and poly(ε-caprolactone) blends
(2020) *Thermochimica Acta*, 693, art. no. 178764, .

Abstract
The influence of curcumin on the thermal stability and degradation kinetics of poly(glycolic acid) (PGA), poly-ε-caprolactone (PCL) and their blend has been investigated in detail using thermogravimetric analysis. A 50/50 ratio was chosen for the blend and the effect caused by the addition of different percentages of curcumin (CUR) was evaluated. The thermogravimetric analysis was carried out under an atmosphere of inert nitrogen, operating in a dynamic regime at six different heating rates between 3 and 30 °C/min. The results obtained from the degradation on a blend of PCL and PGA concluded that CUR hardly affects to the decomposition of PCL but instead, it significantly influences the stability of PGA. To observe this effect in detail, a more complete degradation study was carried out for the system formed by PGA incorporating 5% of the drug. The activation energy could be determined accurately using Kissinger and isoconversional methods like KAS and Friedman, without previously assuming a reaction model. Coats-Redfern method and generalized master curves were adopted to determine the optimal mechanism of degradation. Results showed a F1 model as suitable mechanism able to describe the degradation process of PGA with curcumin in a range of conversions between 20 and 60 %. Incorporation of CUR did not change the degradation mechanism of PGA but had a dramatic effect on the activation energy that was significantly lowered. © 2020 Elsevier B.V.