

# Emphasizing the Anti-Inflammatory and Antioxidant Properties of Bioactive Constituents in Herbal Foods

V. VERMA<sup>1\*</sup>, ROOPAL MITTAL<sup>1</sup>, PRERNA GOEL<sup>2</sup> AND A. MITTAL<sup>3,4</sup>

Department of Pharmacy, I.K. Gujral Punjab Technical University, Jalandhar, Punjab 144601, <sup>1</sup>RKSD College of Pharmacy, Kaithal, Haryana 136027, <sup>2</sup>School of Medical and Allied Sciences, GD Goenka University, Gurugram, Haryana 122103, <sup>3</sup>Department of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, Punjab 144411, <sup>4</sup>Desh Bhagat University, Mandi Gobindgarh, Punjab 147301, India

## Verma *et al.*: Anti-Inflammatory and Antioxidant Properties of Herbal Foods

In daily life, nutrition is crucial in maintaining health in all parts of the world. Utilizing foods with medicinal characteristics simultaneously can change the body's pathological and physiological processes. Inflammation is a consequence of a pathophysiological process that leads to cellular damage with the release of inflammatory mediators. Several foods containing bioactive constituents such as phenolics, flavanoids, catechins, tannins, vitamins and non-sodium minerals were reported to possess pharmacological activity that improves the health status of an individual. A range of plant-derived foods such as turmeric (*Curcuma longa*), green tea (*Camellia sinensis*), tomato (*Solanum lycopersicum*), chili pepper (*Capsicum annum*) and nuts such as almond (*Prunus dulcis*) and hazelnuts (*Corylus avellana*) showed the anti-inflammatory and antioxidant activity. In this review article, the knowledge regarding food-derived plants are compiled and systematically presented in terms of morphological characters, major active constituents, antioxidant and anti-inflammatory activity because bioactive constituents show low bioavailability, emphasising nanotechnology in the administration has been made in the past to improve targeted drug delivery. These foods may be consumed in a routine balanced diet and also be a good choice that may lead to our healthiness.

**Key words:** Inflammation, *Curcuma longa*, balanced diet, antioxidant, superoxide radicals

Nutrition has great value for maintaining health in daily life worldwide. Simultaneously use of food that possesses medicinal properties can alter the body's physiological and pathological mechanism<sup>[1]</sup>. The significant changes in lifestyles such as dietary, physical activity, smoking, alcohols and work stress are the undeniable determinants that lead to oxidative stress and consequently causes inflammation upon long-term exposure<sup>[2]</sup>. Since classical times, these plants were consumed for medicinal benefits in the Ayurvedic and Unani systems due to easy accessibility and cheap value with minimal side effects. The plants encompass a wide array of bioactive compounds of flavanoids, glycosides, sesquiterpenes, tannins, fatty acids and essential oil components. The versatile spices and condiments in daily life can be used multiaxial in gastroenterology<sup>[3]</sup>, migraine, reproductive dysfunctioning<sup>[4]</sup>, endocrine disorders (diabetes)<sup>[5]</sup>, anxiety and depression<sup>[6]</sup>, hepatic disorders<sup>[7]</sup> and chronic disease (cancer,

cardiovascular and neurodegenerative diseases). In this review we highlight various medicinal herbs having anti-inflammatory, antioxidant and immunomodulatory activity. This review was conducted by searching keywords such as anti-inflammatory, antioxidant, curcumin, lycopene, capsaicin, nuts and herbal plants separately in various databases such as a Web of Science, PubMed, Google Scholar and Google. Articles in the English language were included in this study. A domain of food including turmeric (*Curcuma longa*), green tea (*Camellia sinensis*), tomato (*Solanum lycopersicum*), chili pepper (*Capsicum frutescens*) and nuts such as almond (*Prunus amygdalus*) and hazelnuts

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms

\*Address for correspondence

E-mail: vivekverma.verma23@gmail.com

Accepted 14 October 2024

Revised 26 June 2024

Received 22 December 2023

Indian J Pharm Sci 2024;86(5):1529-1541

(*Corylus avellana*) showing the anti-inflammatory and antioxidant activity are discussed briefly. The bioactive compound rich plant possesses a variety of pharmacological activity with therapeutic benefits proving in pre-clinical and clinical trials<sup>[8]</sup>. In this review article, the knowledge regarding food-derived plants are compiled and systematically presented in terms of morphological characters and major active constituent with anti-inflammatory and antioxidant activity. Considering the fact that bioactive constituents show low bioavailability, emphasising nanotechnology in the administration has been made in the past to improve targeted drug delivery.

## PLANTS WITH ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTIES

### Turmeric:

Turmeric is well known as “Indian saffron” and used from ancient times. In India, it is used as a carminative, condiment, coloring agent and flavoring agent having digestive properties. Indian food preparations are not completed without the use of turmeric. The botanical name of turmeric is *Curcuma longa* L. belongs to the family Zingiberaceae<sup>[9]</sup>. The most frequently used part is the rhizomes of *Curcuma longa*. Turmeric is a perennial herbaceous plant tall up to 3 feet. The rhizomes are branching, cylinder-shaped, yellow to orange in color and aromatic in character. The leaves

are placed in two rows and are alternated. They are mainly divided into petiole, leaf blade and leaf sheath. The false stem is formed from leaf sheaths. The length of the petiole is up to 50-115 cm. The length of simple leaf blades are up to 100-230 cm. The width of leaf is nearly 45 cm with a narrowing tip<sup>[10]</sup>. Various chemical constituents found in turmeric was curcumin, eugenol, vitamin A,  $\beta$ -sitosterol, curcuminone, cineole, calcium, phosphorous, sodium, iron, potassium, etc.<sup>[11]</sup>. Turmeric has curcumin as the main important constituent with various medicinal uses, but it is also a rich source of nutrients such as fiber, carbohydrates, proteins, fats with minerals such as vitamins, calcium, magnesium, potassium and phosphorous in quantitative value<sup>[12]</sup>. The structure of chemical constituents present in *Curcum longa* L. has been shown in fig. 1.

**Active constituent of turmeric:** Major bioactive constituents isolated from turmeric are mainly the curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin) out of which curcumin is the most important bioactive constituent that is obtained majorly from the rhizomes of turmeric. Curcumin is used as a biological active compound in many diseases such as in asthmatic inflammation<sup>[13]</sup>, Alzheimer's disease<sup>[14]</sup> and possess anticancer<sup>[16]</sup>, antiviral (hepatitis C, HIV, chikungunya and zika virus)<sup>[16-18]</sup>, wound healing<sup>[19,20]</sup>, anti-inflammatory<sup>[21]</sup>, antioxidant<sup>[22]</sup> and anti-diabetic activity<sup>[23]</sup>.

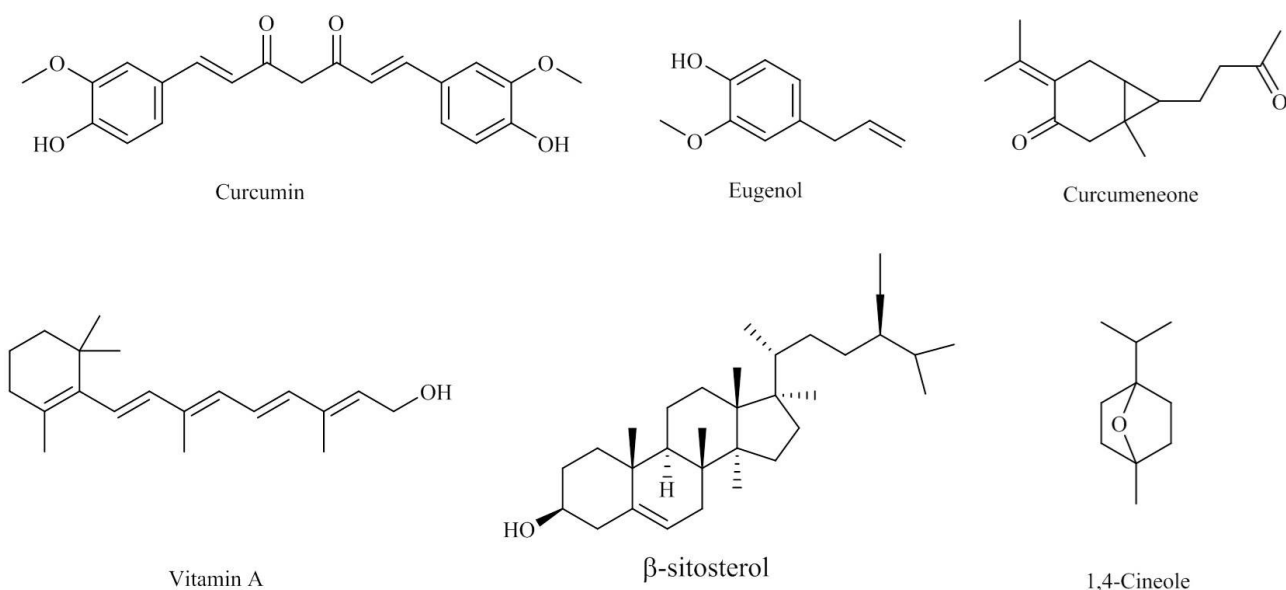


Fig. 1: Structures of chemical constituents reported in *Curcuma longa* L.

Jagetia *et al.*<sup>[24]</sup>, concluded the antioxidant activity of curcumin in mice when exposed to  $\gamma$ -irradiation at a dose of 2 Gy/d for 5-20 d below the rib cage. The drug curcumin was administered orally and skin biopsies were collected for the biochemical estimations of groups (curcumin-treated and untreated), results showed that the curcumin administration before irradiation increased the glutathione concentration and enhanced activity of glutathione peroxidase and superoxide dismutase whereas decrease in the lipid peroxidation indicated that curcumin increased the antioxidant activity on mouse exposed to  $\gamma$ -radiation due to free radical scavenging and upregulation of Nuclear factor erythroid 2-related factor 2 (Nrf2) expression<sup>[24]</sup>. Curcumin also acts by inhibiting Cyclooxygenase-2 (COX-2), Lipoxygenase (LOX), inducible Nitric Oxide Synthase (iNOS), arachidonic acid metabolites, cytokines (Interleukins (IL)), Nuclear Factor-kappa B (NF- $\kappa$ B) and Tumor Necrosis Factor- $\alpha$  (TNF- $\alpha$ )<sup>[20]</sup>. Curcumin inhibits inflammation in acute pulmonary injury by a decline in the concentration of cytokines TNF- $\alpha$ , IL-1 $\beta$ , IL-6 and IL-17A<sup>[25]</sup>. However, diclofenac sodium has beneficial efficacy on various oxidative stress parameters such as Malondialdehyde (MDA), the indirect assessment of Nitric Oxide synthesis (NOx), Total Oxidative Status (TOS), total Thiols (SH), Total Antioxidant Capacity (TAC) and Oxidative Stability Index (OSI) but the combination of diclofenac sodium with curcumin nanoparticles showed a better effect on antioxidant parameters (TAC and SH) and pro-oxidant parameters (MDA, NOx, TOS and OSI) experimental acute inflammation due to its increased bioavailability<sup>[26]</sup>. Curcumin combination with 6-shogaol and 10-shogaol acts synergistically as an anti-inflammatory by suppressing NF- $\kappa$ B translocation and down regulation of Toll-Like Receptor (TLR4), TNF receptor associated factor 6 and Mitogen-Activated Protein Kinase (MAPK) pathway<sup>[27]</sup>. Curcumin shows neuralgia in Lipoteichoic Acid (LTA)-stimulated microglial cells by inhibiting inflammatory cytokine TNF- $\alpha$ , Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), NO, iNOS and COX-2. Curcumin showed an anti-inflammatory effect mainly due to the inhibition of NF- $\kappa$ B and Microtubule-Associated Protein Kinase (MAPKs) signaling<sup>[28]</sup>. The antioxidant activities of quercetin and curcuminoids in the mixture in a ratio of 3:1 were tested by assay methods such as 2,2-diphenyl-1-picrylhydrazyl and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) free radical scavenging and showed the best formulation for wound healing due to antioxidant and antimicrobial activities<sup>[29]</sup>.

Curcumin with vitamin E showed anti-inflammatory

and antioxidant efficacies by improving oxidative stress such as TAC and MDA and inflammatory high sensitivity C-Reactive Protein (CRP) biomarkers in healthy postmenopausal women and aids in improving arthritis conditions<sup>[30]</sup>. Curcumin showed anti-inflammatory and antioxidant effects cooperatively by inhibiting MAPKs/NF- $\kappa$ B phosphorylation and promoting the Nrf2 pathway on arsenic-induced injury in kidney and liver of mice<sup>[31]</sup>.

Curcumin with ferrous sulphate assisted to reduce oxidative stress and inflammation on 155 healthy participants by placebo-controlled randomized study. The anti-inflammatory and antioxidant effect showed a significant reduction in IL-6, TNF- $\alpha$  increased Thiobarbituric Acid Reactive Substance (TBARS) levels in plasma<sup>[32]</sup>. Curcumin and punicalagin showed the anti-inflammatory action by suppressing TNF-induced pro-inflammatory cytokine (IL-1A, IL-1B and IL-6) and chemokines (CCL2-4, CXCL1, CXCL5 and CXCL8) in human placenta<sup>[33]</sup>. Currently, new nano-formulations of curcumin were developed that showed better bioavailability and enhanced anti-inflammatory and antioxidant efficacies<sup>[34]</sup>.

#### Green tea:

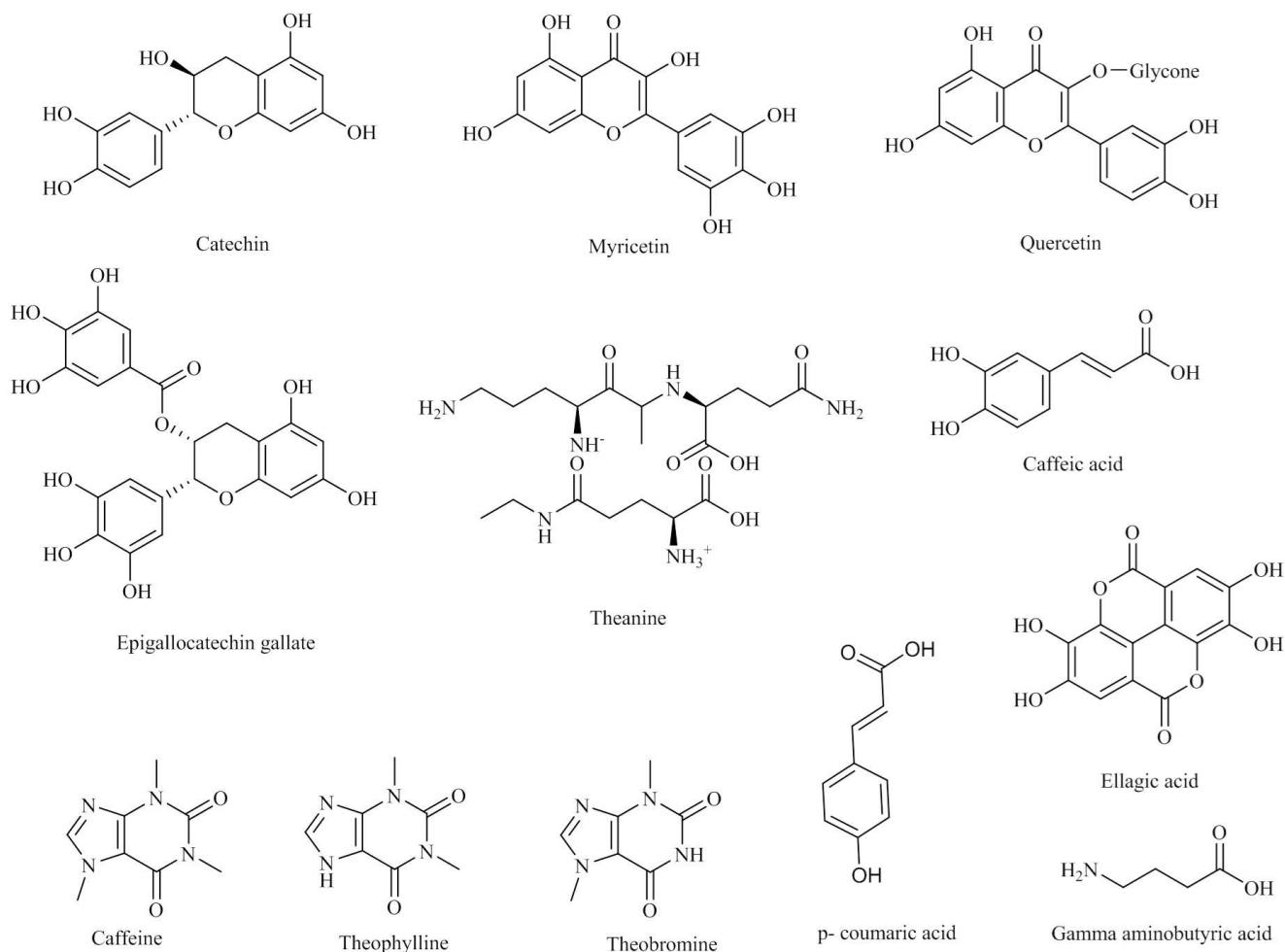
Green tea obtained from the fresh leaves of *Camellia sinensis*, belongs to the family Theaceae. As the most popular non-alcoholic beverage in the world, green tea is consumed by nearly 3 billion people worldwide and is available in a variety of forms. It can be produced from the leaves, buds, or delicate stems of the plant. *Camellia sinensis* evergreen shrub having a large number of branches generally 1-3 m tall. The leaves appears green and the young leaves appears silver, flowers are axillary and solitary are 2.5-3.5 cm in diameter and the seeds are brown, sub-globose with 1-1.4 cm in diameter<sup>[35]</sup>. Various chemical constituents of green tea are polyphenols (20 %-30 %), catechins, flavonoids, phenolic acids, caffeine, theanine, alkaloids etc. Polyphenols were the main ingredients of green tea whereas in black tea tannins were the main. It is also an excellent source of nutrients as carbohydrates, amino acids and minerals<sup>[36,37]</sup>. The leaves are commercially used to make green, oolong and black teas having antiobesity, anticancer, anti-inflammatory, anti-diabetic and neuroprotective activity<sup>[38]</sup>. Fig. 2 represents the structures of chemical constituents reported in *Camellia sinensis*.

**Active constituent of tea:** Tea polyphenols include catechins, flavanoids and phenolic acids were the main

bioactive compounds in green tea. Tea polyphenols acted as an anti-inflammatory and decreased the inflammation-induced obesity by inhibiting the Lipopolysaccharides (LPS)-activated TLR4/NF- $\kappa$ B pathway and decreasing systemic LPS levels in high-fat diet obese mice<sup>[39]</sup>.

The inflammatory response was inhibited by tea polyphenols by improving myeloperoxidase activity, increase in the levels of IL-10, lowering the levels of IL-6, IL-2 and TNF- $\alpha$  and deactivating NF- $\kappa$ B. Tea polyphenols are antioxidant against free radicals and oxidants and also acts as an anti-inflammatory agent by managing intracellular transductions (Nrf2, NF- $\kappa$ B, AP-1 and STATs)<sup>[40]</sup>. In D-galactose-induced liver aging in mice polyphenols from green tea showed antioxidant and anti-inflammatory activity by decreasing the oxidative stress, pro-inflammatory cytokines level and 8-hydroxy-2'-deoxyguanosine and advanced glycation end products levels in liver regulating through Nrf2 signaling pathways<sup>[41]</sup>.

Green tea polyphenols reduces the oxidative stress and inflammation by preserving Reactive Oxygen Species (ROS) and inflammatory balance (TNF- $\alpha$ , IL-6 and IL-1 $\beta$ ), intracellular redox balance by activating the Nrf2 pathway and Extracellular signal-Regulated Kinase (ERK1/2) pathway in bovine mammary epithelial cells<sup>[42]</sup>. Nguyen *et al.*<sup>[43]</sup> reported the polyphenol catechins from green tea i.e., Epigallocatechin-3-Gallate (EGCG) reduces inflammatory mediators (IL-1 $\beta$  and TNF- $\alpha$ ) relating pathways in zebrafish model by abolishing neutrophil migration speed<sup>[43]</sup>. EGCG reported for antioxidant activity by reduction of MDA and GSH and anti-inflammatory activity by reducing TNF- $\alpha$ , NF- $\kappa$ B, IL-1 $\beta$  and TGF- $\beta$  in chloroform-induced hepatotoxicity in rats<sup>[44]</sup>. Kim *et al.*<sup>[45]</sup> reported that EGCG possessed both anti-inflammatory and antioxidant efficacies by inhibiting NF- $\kappa$ B pathway and enhancing Nrf-2/HO-1 pathway in cobalt chloride-stimulated BV2 microglial cells.



**Fig. 2: Structures of chemical constituents reported in *Camellia sinensis***

## Tomato:

Tomato is a significant vegetable that is grown commercially over the world and has numerous health advantages that are beneficial in preventing diseases that affect people. It is regarded as a healthy diet regimen because it has low-fat content but no detrimental cholesterol. Tomatoes are fruits obtained from the plant *Solanum lycopersicum* L. belongs to the family Solanaceae. Tomato a perennial plant that can grow upto 1-3 m, stems are green having trichomes. Spiral leaves with ovate leaflets having hairs. The clusters of flowers are called truss. The shape of the fruit varies among cultivars and may be round, pear-shaped, or ovate. Botanically, tomato is known as a berry and

nutritionally classified in the category of vegetables. Fruit is composed of placental tissue, seeds and pericarp. The various chemical constituents in tomato reported were phenolic compounds (phenolic acids, ferulic acid, caffeic acid, sinapic acid, p-coumaric acid and chlorogenic acid), flavanoids (quercetin, rutin and kaempferol), carotene and its derivatives (lycopene, lutein, phytoene,  $\beta$ -carotene,  $\alpha$ -carotene,  $\gamma$ -carotene,  $\delta$ -carotene and neurosporene). Various nutrients like fat and water-soluble vitamins (A, B, C and E), potassium and folic acid analogues are present in appropriate concentrations in tomatoes<sup>[46,47]</sup>. Fig. 3 represents the structures of chemical constituents reported in *Solanum lycopersicum* L.

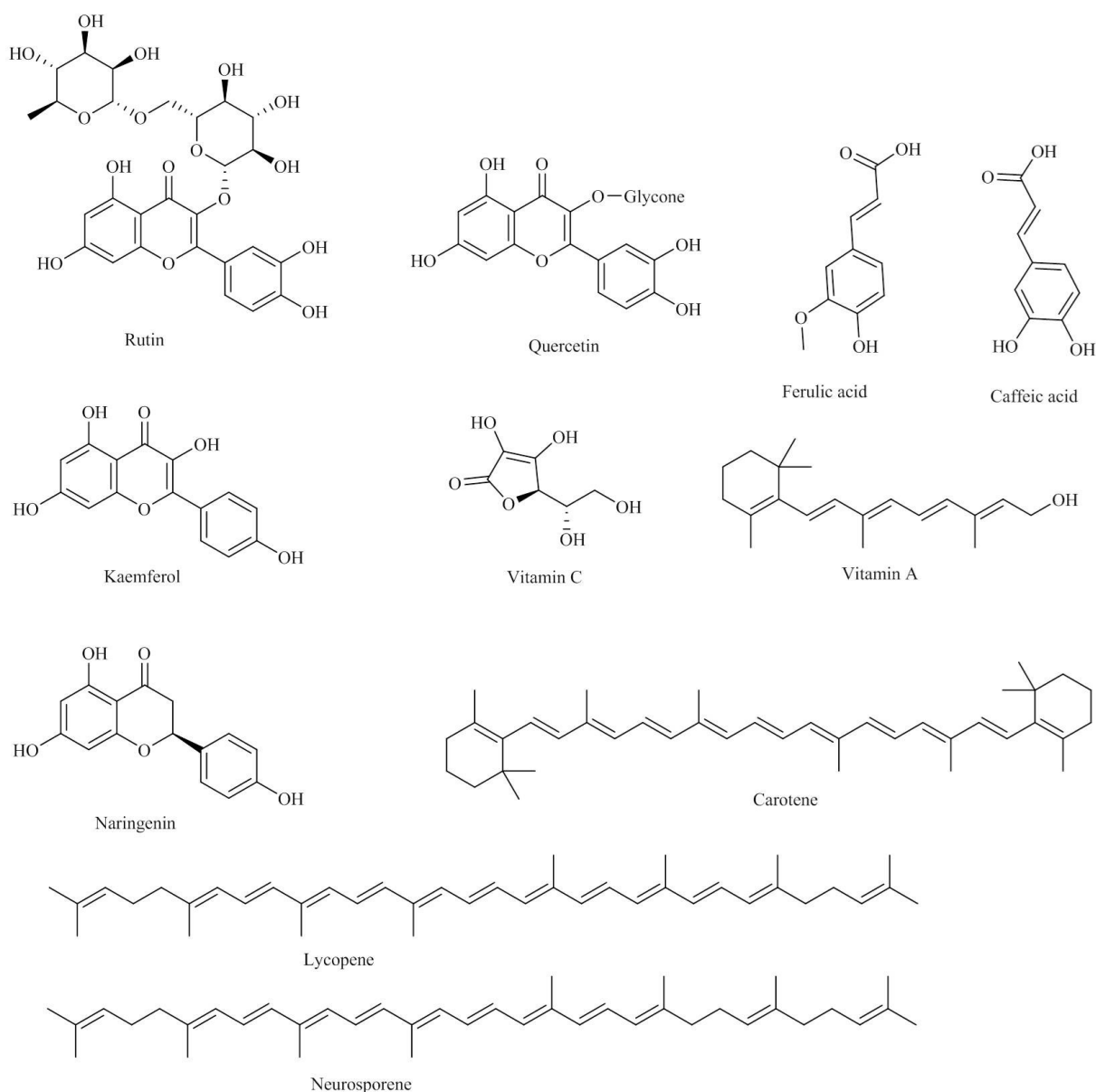


Fig. 3: Structures of chemical constituents reported in *Solanum lycopersicum* L.

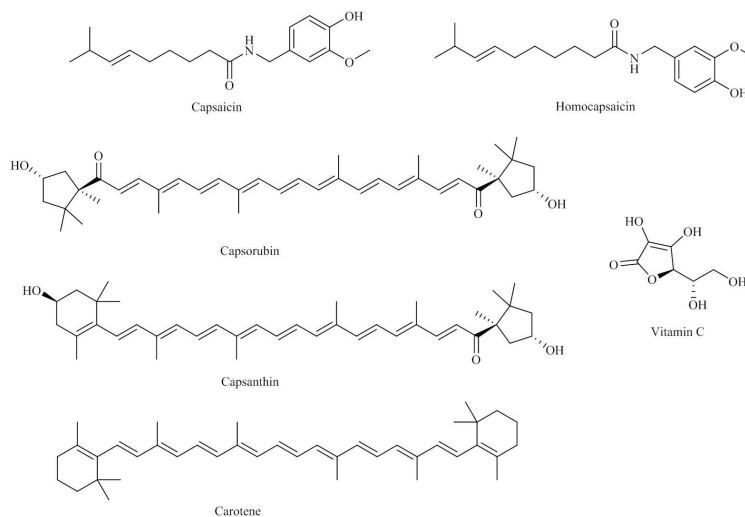
**Active constituent of tomato:** Liu *et al.*<sup>[48]</sup> reported anti-inflammatory and antioxidant efficacies of lycopene in finishing pigs as dietary supplements at a dose of 0.1 g/kg and 0.2 g/kg. Antioxidant and anti-inflammatory effects were observed in the duodenum by decreasing MDA (0.1 g/kg and 0.2 g/kg) and IL-1 $\beta$ , NF- $\kappa$ B and TNF- $\alpha$  (0.2 g/kg)<sup>[48]</sup>. Lycopene possesses antioxidant activity by strengthening the Nrf2 antioxidant pathway and antioxidant response genes HO-1 and Nicotinamide Adenine Dinucleotide Phosphate Hydrogen (NADPH) Quinone Oxidoreductase-1 (NQO1), anti-inflammatory activity was due to inhibition of MAPK and NF- $\kappa$ B pathways by D-galactose-induced mitochondrial dysfunction and insulin signaling impairment in mouse kidneys and livers<sup>[49]</sup>. Lycopene (20 mg/kg) exerts an anti-inflammatory effect by reducing NF- $\kappa$ B and TLR4, and an antioxidant effect by increasing levels through the Nrf2 pathway in LPS-induced acute kidney injury<sup>[50]</sup>. The phenolic acids, carotenoids, flavonoids and tannins extracted from tomato pomace have the highest radical scavenging activities and carotenoids extracted in ethyl acetate have anti-inflammatory effects<sup>[51]</sup>. Pancreatic inflammation due to LPS and ethanol is prevented through lycopene-rich food diet. The inflammation due to alcoholic pancreatitis might be a consequence of increasing ROS levels in pancreatic cells. The anti-inflammatory activity of lycopene was due to stimulation of Nrf2/NQO1-HO-1 pathway by reducing levels of IL-6, ROS in pancreatic acinar cells<sup>[52]</sup>. Major components of tomato are  $\beta$ -carotene, lycopene and fatty acids. These were extracted in various solvents like bioethanol and ethyl acetate could be used in pharmaceutical, cosmetic and food industries due to their potent antioxidant activity<sup>[53]</sup>. The tomato *sofrito* is a sauce made with ingredients such as olive oil, garlic, and onion, which showed a significant

anti-inflammatory effect in healthy individuals by decreasing CRP and TNF- $\alpha$  levels. A single dose of 240 g/70 kg of tomato *sofrito* indicated that not only lycopene but also the combination with other bioactive constituents (carotenoids and polyphenols) contributed to this effect<sup>[54, 55]</sup>.

### Chili pepper:

Chili peppers are cultivated across the world and originated in Mexico. It is widely used as a spice and condiment in the world due to its pungency and special flavour. It is consumed in dried forms, in vegetables, as a spice and also in salad. It is obtained as fruits from the plant *Capsicum annuum* belongs to the family Solanaceae. It is a small shrub cultivated in the Americas and throughout the world. *Capsicum annuum* is a small spreading annual shrub that can grow up to 1.8 m in height. The leaves are of varying shapes and simple but with smooth margins. The flowers are approximately 1.5 cm in diameter of white colour may be in groups. The fruit are multi-seeded berries that are long, cylindrical in shape, but with no sutures; turns red when ripe and have shiny surface. The fruit is up to 250 mm in length and 7 mm in width, with a characteristic odour and pungent taste.

Various chemical constituents of chili pepper (capsaicin (46 %), dihydrocapsaicin (41 %), nordihydrocapsaicin (7 %), norcapsaicin (7 %), homocapsaicin (3 %), homodihydrocapsaicin (2 %)), carotenoids (capsanthin, capsorubin, and  $\beta$ -carotene), phenolic compounds, and flavonoid. It is also composed of fat, proteins, carbohydrates, fibers, and vitamin C as nutrients with minerals such as sodium, potassium, calcium, and zinc, etc.,<sup>[56-59]</sup>. Fig. 4 represents structure of chemical constituents reported in *Capsicum annuum*.



**Fig. 4: Structures of chemical constituents reported in *Capsicum annuum***

**Active constituents of chili pepper:** Chili pepper contained capsaicinoids (capsaicin, dihydrocapsaicin, nordihydrocapsaicin and norcapsaicin) as the major active constituents. Capsaicin is most active constituent as compared to other and in good amount. Capsaicin is responsible for the pungent odor of chili pepper<sup>[60]</sup>. Capsaicinoids are reported for their various bioactivities such as anti-inflammatory, anticancer, analgesic, antioxidant, weight control, cardioprotective, anti-lithogenic effects<sup>[61,62]</sup>.

Antioxidant effect of capsaicin (150 mg/kg) and curcumin (1500 mg/kg HFD) were due to reduced levels TBARS, ROS of testicular and hepatic oxidative stress on rats on high fat diet<sup>[63]</sup>. Bioavailable acyclic cucurbitencapsulated capsaicin were developed with improved antioxidant and anti-inflammatory properties by significantly increasing the inhibition rate of Nitric Oxide (NO) and IL-1 $\beta$  in human gastric mucosal cell<sup>[64]</sup>. Capsaicin and phenolic compounds obtained from cellulose supported extracts of Habanero chili pepper seeds showed anti-inflammatory effects by reducing the concentration of inflammation cytokines with potential immunostimulant effects depends upon the cellulase treatment time<sup>[65]</sup>. Capsaicinoids (capsaicin and dihydrocapsaicin) showed anti-inflammatory and antioxidant effects by abolished TNF- $\alpha$  induced expression of the adhesion molecules Vascular Cell Adhesion Molecule (VCAM)-1, Intercellular Adhesion Molecule (ICAM)-1, IL-6 and reducing NO in human vascular endothelial cell cultures<sup>[66]</sup>. Capsaicin revealed anti-inflammatory effect by decreasing the level of inflammatory cytokines (TNF- $\alpha$ , IL-1 and IL-6) by suppressing NF- $\kappa$ B and MAPKs signaling pathways in mice LPS-induced inflammation and LPS-stimulated BV 2 microglia cells<sup>[67-69]</sup>. Capsaicin with topical Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in patches having considerable effect on inflammation<sup>[56,70]</sup>. The formulation of Solid Liquid Nanoparticles (SLNs) of curcumin, capsaicin and linolenic acid employ an anti-inflammatory effect by reducing IL-6 level even in the presence of TNF- $\alpha$  in skin cells<sup>[71]</sup>.

### Nuts (almonds, hazelnuts):

Nuts are widely used worldwide due to their health benefits. Now a days the oils obtained from various nuts are widely used in foods due their flavor, nut oils are also used in formulation of cosmetics in cosmetic industry and also used as health promoting diet. The health benefits of nuts components depends on their

bioavailability and the amount ingested. Here in this review we describe only two nuts; they are almonds and hazelnuts, obtained from the plants *Prunus dulcis* and *Corylus avellana*, belong to the families Rosaceae and Betulaceae, respectively. Nuts were common in some features such as good oil content and big seed size as compared to other oil seed varieties<sup>[72,73]</sup>. As chemically similar nuts; almonds and hazelnuts are highly nutritious contains phytochemicals such as caffeic acid, gallic acid, ellagic acid, catechin, epicatechin, epigallocatechin, EGCG, isorhamnetin, quercetin, kaempferol, myricetin, proanthocyanidin, stilbenes, hydrolysable tannins, lignans, proanthocyanidins, carotenoids, coumestans, phytates and phytoestrogens with macronutrients (protein, fat and carbohydrate), micronutrients (minerals and vitamins) and essential oils<sup>[74]</sup>. Fig. 5 represents the structure of chemical constituents reported in nuts.

**Active constituents of nuts:** Nuts are used as healthy and nutritious diet worldwide are dry fruits obtained from trees. Nuts contain carbohydrates, vitamins, minerals and bioactive constituents such as polyphenols, flavonoids, fatty acids<sup>[75-77]</sup>. Nuts were reported for many bioactivities such as antioxidant, prebiotic<sup>[78]</sup>, anxiolytic<sup>[79]</sup>, sedative and hypnotics<sup>[80]</sup>, anti-inflammatory<sup>[81]</sup>, antimicrobial<sup>[82]</sup>, cardiometabolic protective<sup>[83]</sup>, anticancer and memory enhancing effects<sup>[84,85]</sup>. Fatty acids (oleic acid and linoleic acids) showed the antioxidant and *in vitro* anti-inflammatory activity with better results than diclofenac<sup>[86]</sup>. Formulation of acetonc lyophilized almond skin extract showed the anti-inflammatory activity by inhibiting TNF- $\alpha$  in intestine with good bioavailability of active constituents<sup>[87]</sup>. A potential antioxidant property of roasted hazelnut skin was reported due flavonoids, tannins and phenolic acids as a good nutraceutical<sup>[88]</sup>. Hydroxytyrosol (HT) and almond polyphenols were reported for antioxidant and anti-inflammatory effects on Low Density Lipoproteins (LDL) in moderately hypercholesterolemic patients<sup>[89]</sup>. Hazelnut extract encapsulated nano-structured lipid carriers showed the antioxidant property through ROS scavenging effects on Human Dermal Fibroblast (HDF) cells with increased stability and prolonged bioactivity<sup>[90]</sup>. Table 1 showed the comprehensive view of pharmacological activities reported by the active constituent in the food of daily use.

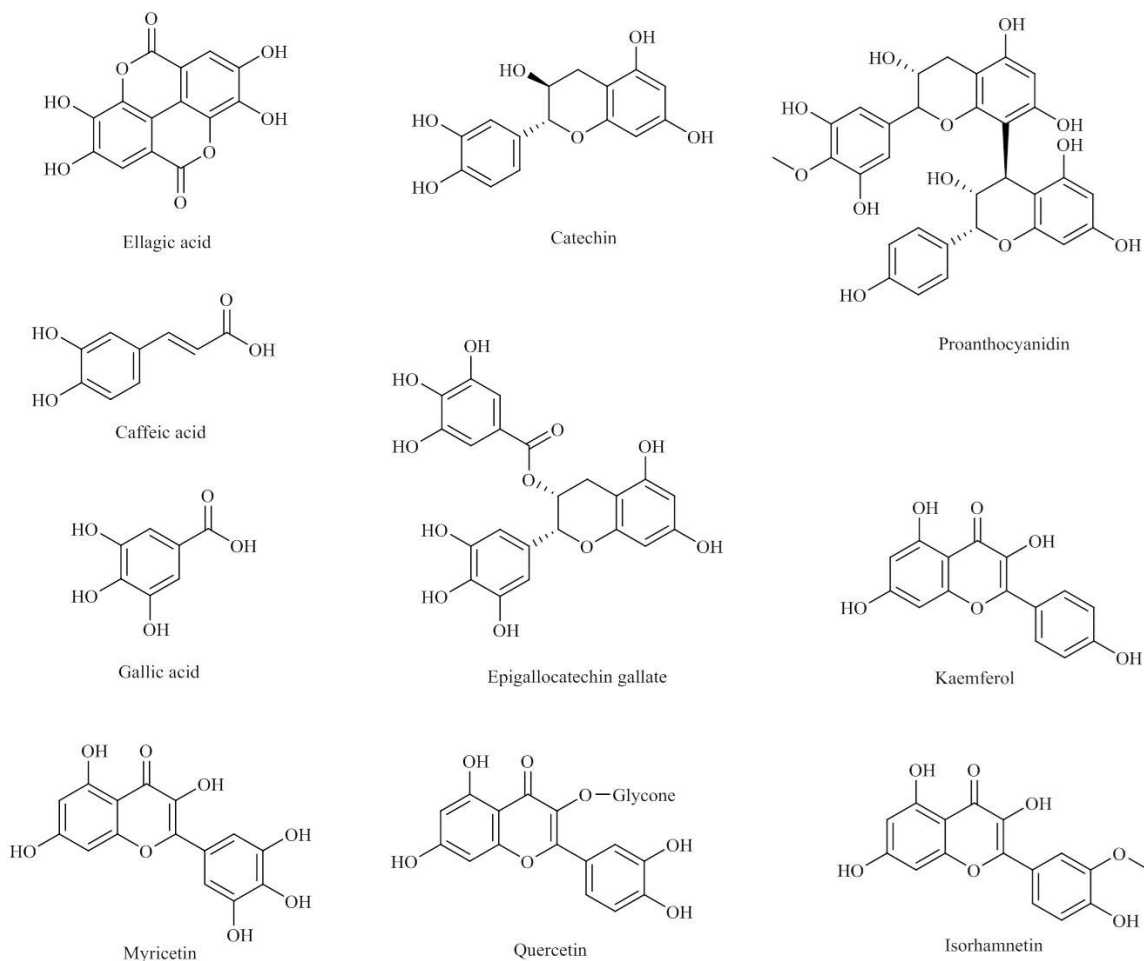


Fig. 5: Structures of chemical constituents reported in nuts

TABLE 1: THE LIST OF PHARMACOLOGICAL ACTIVITIES OF PLANTS USED AS FOOD

S. No	Plant	Family	Major bioactive constituents	Pharmacological activity	Reference
1	Tumeric	Zingiberaceae	Curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin)	Antibacterial, anti-malarial, anticancer, antiviral, wound healing agent, anti-nociceptive, anti-diabetic, cardiovascular diseases	[91-95]
2	Green tea	Theaceae	Catechins (EGCG, epigallocatechin, epicatechin gallate and epicatechin)	Immunomodulatory, anticancer, weight loss, antibacterial, cardiovascular diseases, antiviral	[96-99]
3	Tomato	Solanaceae	Carotenoids (lycopene, $\alpha$ -carotene, $\beta$ -carotene, $\gamma$ -carotene and $\delta$ -carotene)	Anticancer, cardiovascular diseases, antibacterial, anti-diabetic	[100-103]
4	Chili pepper	Solanaceae	Capsaicinoids (capsaicin, dihydrocapsaicin, nordihydrocapsaicin and norcapsaicin)	Antimicrobial, antiviral, cardiovascular diseases. anti-obesity, anticancer, anti-diabetic	[104-107]
5	Nuts	Rosaceae	Caffeic acid, gallic acid, ellagic acid, catechins, isorhamnetin, quercetin, kaempferol, myricetin, proanthocyanidin	Cardiovascular, memory enhancing agent, antimicrobial, anticancer, sedative and hypnotics, anxiolytic	[79,80,82,83,85,108]



## DISCUSSION

The modern lifestyle, food, lack of exercise and exposure to various chemicals will lead to oxidative stress and consequently inflammation<sup>[2,109]</sup>. Bioactive constituents obtained from plants such as curcumin, tea polyphenols, lycopene, capsaicin and nut polyphenols showed impressive anti-inflammatory and antioxidant activities. Curcumin is an important bioactive constituent of turmeric, a promising dietary compound with potential anti-inflammatory activity. The metabolites of curcumin tetrahydrocurcumin and octahydrocurcumin have superior anti-inflammatory by suppressing TAK1-NF- $\kappa$ B Pathway. Curcumin shows poor absorption, chemical instability, rapid metabolism and rapid systemic elimination due to this delivery system nanoparticle formulations have been developed to improve bioavailability, stability and prolonged systemic action<sup>[110]</sup>. Curcumin used in synergism also used to increase efficacy of traditional NSAIDs<sup>[26]</sup>.

Green tea polyphenols are bioactive compounds used to control weight and is very powerful antioxidant. Nanoparticle formulations of tea polyphenols have been developed with increased bioavailability<sup>[111]</sup>. There are a few side effects of green tea that are firstly, caffeine sensitive patients may experience insomnia, anxiety, irritability, nausea, upset stomach. Secondly, high concentration of green tea may lead to liver damage. Thirdly, stimulant drug with green tea could increase blood pressure. Tea supplements are not regulated by Food and Drug Administration (FDA) as they may contain other substances that may be unsafe for health with unproven health benefits.

Lycopene the most abundantly compound found in tomato reported for reducing risks of cancer, diabetes, hepatic disorders. Carotene, its derivatives in tomato such as lycopene and  $\beta$ -carotene are precursor for vitamin A helps the vision effect<sup>[112]</sup>. Lycopene consumption is extremely safe. High concentration of lycopene may lead to skin discoloration. Recently various nanoparticles formulation has been developed to overcome the solubility issues by increasing bioavailability<sup>[113]</sup>.

Capsaicin is major bioactive constituent of capsicum having anti-diabetic, anti-obesity and antimicrobial effects. Capsaicin with topical NSAIDs reported for their anti-inflammatory activities by synergistic action. Nanoparticles formulations have been developed for the capsaicin alone and with combination of curcumin also to improve bioavailability<sup>[71,114]</sup>. Nuts such as almonds and hazelnuts were consumed in worldwide for their

beneficial health effects. Nuts are used from ancient times to improve the mental health as they contain choline a precursor for the synthesis for acetylcholine. Nut polyphenols were extracted and reported for their bioactivities. Nuts are generally consumed by soaking overnight for improved systemic absorption. Nanoparticles formulation of bioactive compounds extracted from nuts have been developed with improved bioavailability<sup>[90]</sup>.

## CONCLUSION

The diets having nutritious value with medicinal uses are thought to be good choice foods. Here we discussed the foods that are very commonly used in India as well as in the whole world from ancient times for their medicinal uses. The major bioactive constituents that are curcumin, tea polyphenols, lycopene, capsaicin and nut polyphenols extracted from plants were discussed for their anti-inflammatory and antioxidant activities. Furthermore it was noted that due to low solubility the bioavailability of these compounds are low, to overcome this recently new delivery systems has been developed such as nanoparticles formulations with improved bioavailability, stability and prolonged action in low dose. The nanoparticles formulations of these active compounds with NSAIDs showed the synergistic effect. The nanoparticles may be the good choice of formulations for these compounds and also for pharmaceutical industry.

## Acknowledgements:

The authors are thankful to Amar Shaheed Baba Ajit Singh Jujhar Singh Memorial (ASBASJSM) College of Pharmacy, Bela, Ropar (Punjab), School of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Punjab) and RKSD College of Pharmacy, Kaithal (Haryana).

## Conflict of interest:

The authors declared no conflict of interests.

## REFERENCES

1. Kooti W, Servatyari K, Behzadifar M, Asadi-Samani M, Sadeghi F, Nouri B, *et al.* Effective medicinal plant in cancer treatment, part 2: Review study. *J Evid Based Complement Altern Med* 2017;22(4):982-95.
2. Peluso I, Palmery M, Yarla NS, Perry G, Kamal MA. From oxidative stress to ageing *via* lifestyle, nutraceuticals, polypharmacy, and neuropsychological factors. *Oxid Med Cell Longev* 2018;2018: 6352689.
3. Bahmani M, Zargaran A, Rafieian-Kopaei M. Identification of medicinal plants of Urmia for treatment of gastrointestinal disorders. *Rev Bras Farmacogn* 2014;24(4):468-80.

4. Kooti V, Ghasemiboroon M, Ahangarpour A, Hardani A, Amirzargar A, Asadi-Samani M, *et al.* The effect of hydro-alcoholic extract of celery on male rats in fertility control and sex ratio of rat offspring. *J Babol Univ Med Sci* 2014;16(4):43-9.
5. Kabiri N, Ahangar-Darabi M, Setorki M, Rafieian-kopaei M. The effect of silymarin on liver injury induced by thioacetamide in rats. *J Herb Med Pharmacol* 2013;2(2):29-33.
6. Saki K, Bahmani M, Rafieian-Kopaei M, Hassanzadazar H, Dehghan K, Bahmani F, *et al.* The most common native medicinal plants used for psychiatric and neurological disorders in Urmia city, Northwest of Iran. *Asian Pac J Trop Dis* 2014;4:S895-901.
7. Nasri H, Rafieian-kopaei M, Shirzad M, Rafieian M, Sahinfard N, Rafieian S. Effects of *Allium sativum* on liver enzymes and atherosclerotic risk factors. *J Herb Med Pharmacol* 2013;2:23-8.
8. Sharifi-Rad J, Quispe C, Shaheen S, El Haouari M, Azzini E, Butnariu M, *et al.* Flavonoids as potential anti-platelet aggregation agents: From biochemistry to health promoting abilities. *Crit Rev Food Sci Nutr* 2022;62(29):8045-58.
9. Nair KP. Turmeric (*Curcuma longa* L.) and ginger (*Zingiber officinale* Rosc.)-World's invaluable medicinal spices: The agronomy and economy of turmeric and ginger. Springer International Publishing; 2019.
10. Brinckmann JA, Kathe W, Berkhoudt K, Harter DE, Schippmann U. A new global estimation of medicinal and aromatic plant species in commercial cultivation and their conservation status. *Econ Bot* 2022;76(3):319-33.
11. Upadhyay S, Pandey MM. Therapeutic potential and phytoconstituents of traditionally used Indian spices. *J Pharmacogn Phytochem* 2022;11(5):146-9.
12. Ahmad RS, Hussain MB, Sultan MT, Arshad MS, Waheed M, Shariati MA, *et al.* Biochemistry, safety, pharmacological activities, and clinical applications of turmeric: A mechanistic review. *Evid Based Complement Alternat Med* 2020;2020(1):7656919.
13. Casula L, Lai F, Pini E, Valenti D, Sinico C, Cardia MC, *et al.* Pulmonary delivery of curcumin and beclomethasone dipropionate in a multicomponent nanosuspension for the treatment of bronchial asthma. *Pharmaceutics* 2021;13(8):1300-13.
14. Wang Y, Zhang H, Hua L, Wang Z, Geng S, Zhang H, *et al.* Curcumin prevents Alzheimer's disease progression by upregulating JMD3. *Am J Transl Res* 2022;14(8):5280-94.
15. Sharifi-Rad J, Quispe C, Kumar M, Akram M, Amin M, Iqbal M, *et al.* *Hyssopus* essential oil: An update of its phytochemistry, biological activities, and safety profile. *Oxid Med Cell Longev* 2022;2022(1):8442734-43.
16. Mounce BC, Cesaro T, Carrau L, Vallet T, Vignuzzi M. Curcumin inhibits Zika and Chikungunya virus infection by inhibiting cell binding. *Antiviral Res* 2017;142:148-57.
17. Nabila N, Suada NK, Denis D, Yohan B, Adi AC, Veterini AS, *et al.* Antiviral action of curcumin encapsulated in nanoemulsion against four serotypes of dengue virus. *Pharm Nanotechnol* 2020;8(1):54-62.
18. Naseri S, Darroudi M, Aryan E, Gholoobi A, Rahimi HR, Ketabi K, *et al.* The antiviral effects of curcumin nanomicelles on the attachment and entry of hepatitis C virus. *Iran J Virol* 2017;11(2):29-35.
19. Shefa AA, Sultana T, Park MK, Lee SY, Gwon JG, Lee BT. Curcumin incorporation into an oxidized cellulose nanofiber-polyvinyl alcohol hydrogel system promotes wound healing. *Mater Des* 2020;186:108313-40.
20. Urošević M, Nikolić L, Gajić I, Nikolić V, Dinić A, Miljković V. Curcumin: Biological activities and modern pharmaceutical forms. *Antibiotics* 2022;11(2):135-61.
21. Ferguson JJ, Abbott KA, Garg ML. Anti-inflammatory effects of oral supplementation with curcumin: A systematic review and meta-analysis of randomized controlled trials. *Nutr Rev* 2021;79(9):1043-66.
22. Haryuna TS, Fauziah D, Anggraini S, Harahap M, Harahap J. Antioxidant effect of curcumin on the prevention of oxidative damage to the cochlea in an ototoxic rat model based on malondialdehyde expression. *Int Arch Otorhinolaryngol* 2022;26:119-24.
23. Kostrzewa T, Przychodzen P, Gorska-Ponikowska M, Kuban-Jankowska A. Curcumin and cinnamaldehyde as PTP1B inhibitors with antidiabetic and anticancer potential. *Anticancer Res* 2019;39(2):745-9.
24. Jagetia GC, Rajanikant GK. Curcumin stimulates the antioxidant mechanisms in mouse skin exposed to fractionated  $\gamma$ -irradiation. *Antioxidants* 2015;4(1):25-41.
25. van Veen MM, Kooij JS, Boonstra AM, Gordijn MC, van Someren EJ. Delayed circadian rhythm in adults with attention-deficit/hyperactivity disorder and chronic sleep-onset insomnia. *Biol Psychiatry* 2010;67(11):1091-6.
26. Boarescu I, Boarescu PM, Pop RM, Bocşan IC, Gheban D, Râjnoveanu RM, *et al.* Curcumin nanoparticles enhance antioxidant efficacy of diclofenac sodium in experimental acute inflammation. *Biomedicines* 2021;10(1):61-74.
27. Zhou X, Al-Khazaleh A, Afzal S, Kao MH, Münch G, Wohlmuth H, *et al.* 6-shogaol and 10-shogaol synergize curcumin in ameliorating proinflammatory mediators via the modulation of TLR4/TRAF6/MAPK and NF $\kappa$ B translocation. *Biomol Ther* 2023;31(1):27-39.
28. Yu Y, Shen Q, Lai Y, Park SY, Ou X, Lin D, *et al.* Anti-inflammatory effects of curcumin in microglial cells. *Front Pharmacol* 2018;9:386-95.
29. Chittasupho C, Manthaisong A, Okonogi S, Tadtong S, Samee W. Effects of quercetin and curcumin combination on antibacterial, antioxidant, *in vitro* wound healing and migration of human dermal fibroblast cells. *Int J Mol Sci* 2021;23(1):142.
30. Farshbaf-Khalili A, Ostadrahimi A, Mirghafourvand M, Ataei-Almanghadim K, Dousti S, Iranshahi AM. Clinical efficacy of curcumin and vitamin E on inflammatory-oxidative stress biomarkers and primary symptoms of menopause in healthy postmenopausal women: A triple-blind randomized controlled trial. *J Nutr Metabol* 2022;2022(1):6339715-26.
31. Xu G, Gu Y, Yan N, Li Y, Sun L, Li B. Curcumin functions as an anti-inflammatory and antioxidant agent on arsenic-induced hepatic and kidney injury by inhibiting MAPKs/NF- $\kappa$ B and activating Nrf2 pathways. *Environ Toxicol* 2021;36(11):2161-73.
32. Lorinczova TH, Begum G, Temouri L, Renshaw D, Zariwala MG. Co-administration of iron and bioavailable curcumin reduces levels of systemic markers of inflammation and oxidative stress in a placebo-controlled randomised study. *Nutrients* 2022;14(3):712-32.
33. Nguyen-Ngo C, Willcox JC, Lappas M. Anti-inflammatory effects of phenolic acids punicalagin and curcumin in human placenta and adipose tissue. *Placenta* 2020;100:1-2.
34. Józsa L, Vasvári G, Sinka D, Nemes D, Ujhelyi Z, Vecsernyés

- M, *et al.* Enhanced antioxidant and anti-inflammatory effects of self-nano and microemulsifying drug delivery systems containing curcumin. *Molecules* 2022;27(19):6652.
35. Shrivastava RR, Pateriya PP, Singh MS. Green tea-A short review. *Int J Indig Herbs Drugs* 2018;3(2):12-21.
  36. Prasanth MI, Sivamaruthi BS, Chaiyasut C, Tencomnao T. A review of the role of green tea (*Camellia sinensis*) in antiphotaging, stress resistance, neuroprotection, and autophagy. *Nutrients* 2019;11(2):474-97.
  37. Zhao T, Li C, Wang S, Song X. Green tea (*Camellia sinensis*): A review of its phytochemistry, pharmacology, and toxicology. *Molecules* 2022;27(12):3909-31.
  38. Afzal O, Dalhat MH, Altamimi AS, Rasool R, Alzarea SI, Almalki WH, *et al.* Green tea catechins attenuate neurodegenerative diseases and cognitive deficits. *Molecules* 2022;27(21):7604-25.
  39. Zvereva EE, Vandyukova II, Vandyukov AE, Katsyuba SA, Khamatgalimov AR, Kovalenko VI. IR and Raman spectra, hydrogen bonds, and conformations of N-(2-hydroxyethyl)-4, 6-dimethyl-2-oxo-1, 2-dihydropyrimidine (drug Xymedone). *Russ Chem Bull* 2012;61:1199-206.
  40. Truong VL, Jeong WS. Antioxidant and anti-inflammatory roles of tea polyphenols in inflammatory bowel diseases. *Food Sci Human Wellness* 2022;11(3):502-11.
  41. Azarcoya-Barrera J, Wollin B, Veida-Silva H, Makarowski A, Goruk S, Field CJ, *et al.* Egg-phosphatidylcholine attenuates T-cell dysfunction in high-fat diet fed male wistar rats. *Front Nutr* 2022;9:811469-78.
  42. Ma Y, Ma X, An Y, Sun Y, Dou W, Li M, *et al.* Green tea polyphenols alleviate hydrogen peroxide-induced oxidative stress, inflammation, and apoptosis in bovine mammary epithelial cells by activating ERK1/2–NFE2L2–HMOX1 pathways. *Front Vet Sci* 2022;8:804241-53.
  43. Nguyen T, Payan B, Zambrano A, Du Y, Bondesson M, Mohan C. Epigallocatechin-3-gallate suppresses neutrophil migration speed in a transgenic zebrafish model accompanied by reduced inflammatory mediators. *J Inflamm Res* 2019;12:231-9.
  44. Mostafa-Hedeab G, Hassan ME, Halawa TF. Epigallocatechin gallate ameliorates tetrahydrochloride-induced liver toxicity in rats *via* inhibition of TGFβ/p-ERK/p-Smad1/2 signaling, antioxidant, anti-inflammatory activity. *Saudi Pharm J* 2022;30(9):1293-300.
  45. Kim SR, Seong KJ, Kim WJ, Jung JY. Epigallocatechin gallate protects against hypoxia-induced inflammation in microglia *via* NF-κB suppression and Nrf-2/HO-1 activation. *Int J Mol Sci* 2022;23(7):4004-18.
  46. Chaudhary P, Sharma A, Singh B, Nagpal AK. Bioactivities of phytochemicals present in tomato. *J Food Sci Technol* 2018;55(8):2833-49.
  47. Padmanabhan P, Cheema A, Paliyath G. Solanaceous fruits including tomato, eggplant, and peppers. *The Encyclopedia of Food and Health*. Oxford: Academic Press; 2016. p.24-32.
  48. Liu A, Chen X, Huang Z, Chen D, Yu B, Chen H, *et al.* Effects of dietary lycopene supplementation on intestinal morphology, antioxidant capability and inflammatory response in finishing pigs. *Anim Biotechnol* 2022;33(3):563-70.
  49. Wang J, Li T, Li M, Shi D, Tan X, Qiu F. Lycopene attenuates D-galactose-induced insulin signaling impairment by enhancing mitochondrial function and suppressing the oxidative stress/inflammatory response in mouse kidneys and livers. *Food Funct* 2022;13(14):7720-9.
  50. Salari S, Ghorbanpour A, Marefati N, Baluchnejadmojarad T, Roghani M. Therapeutic effect of lycopene in lipopolysaccharide nephrotoxicity through alleviation of mitochondrial dysfunction, inflammation, and oxidative stress. *Mol Biol Re* 2022;49(9):8429-38.
  51. Jamaledine A, de Caro P, Bouajila J, Evon P, Haddad JG, El-Kalamouni C, *et al.* *In vitro* bioactivities of extracts from tomato pomace. *Front Biosci* 2022;27(9):259.
  52. Lee J, Lim JW, Kim H. Lycopene inhibits IL-6 expression by upregulating NQO1 and HO-1 *via* activation of Nrf2 in ethanol/lipopolysaccharide-stimulated pancreatic acinar cells. *Antioxidants* 2022;11(3):519-38.
  53. Popescu M, Iancu P, Plesu V, Todasca MC, Isopencu GO, Bildea CS. Valuable natural antioxidant products recovered from tomatoes by green extraction. *Molecules* 2022;27(13):4191-211.
  54. Hurtado-Barroso S, Martínez-Huélamo M, Alvarenga RJF, Quifer-Rada P, Vallverdú-Queralt A, Pérez-Fernández S, *et al.* Acute effect of a single dose of tomato *sofrito* on plasmatic inflammatory biomarkers in healthy men. *Nutrients* 2019;11(4):851-82.
  55. Chernyshova MP, Pristenskiy DV, Lozbiakova MV, Chalyk NE, Bandaletova TY, Petyaev IM. Systemic and skin-targeting beneficial effects of lycopene-enriched ice cream: A pilot study. *J Dairy Sci* 2019;102(1):14-25.
  56. Batiha GE, Alqahtani A, Ojo OA, Shaheen HM, Wasef L, Elzeiny M, *et al.* Biological properties, bioactive constituents, and pharmacokinetics of some *Capsicum* spp. and capsaicinoids. *Int J Mol Sci* 2020;21(15):5179-213.
  57. Kulkarni YA, Suryavanshi SV, Auti ST, Gaikwad AB. *Capsicum*: A natural pain modulator. *InNutritional modulators of pain in the aging population* 2017;107-19.
  58. Maroon JC, Bost JW, Maroon A. Natural anti-inflammatory agents for pain relief. *Surg Neurol Int* 2010;1:80-89.
  59. Saleh BK, Omer A, Teweldemedhin BJ. Medicinal uses and health benefits of chili pepper (*Capsicum* spp.): A review. *MOJ Food Process Technol* 2018;6(4):325-8.
  60. Giuriato G, Venturelli M, Matias A, Soares EM, Gaetgens J, Frederick KA, *et al.* Capsaicin and its effect on exercise performance, fatigue and inflammation after exercise. *Nutrients* 2022;14(2):232-46.
  61. Lu M, Chen C, Lan Y, Xiao J, Li R, Huang J, *et al.* Capsaicin—the major bioactive ingredient of chili peppers: Bio-efficacy and delivery systems. *Food Funct* 2020;11(4):2848-60.
  62. Rosca AE, Iesanu MI, Zahiu CD, Voiculescu SE, Paslaru AC, Zagrean AM. Capsaicin and gut microbiota in health and disease. *Molecules* 2020;25(23):5681-703.
  63. Tanrikulu-Küçük S, Başaran-Küçükgergin C, Seyithanoğlu M, Dođru-Abbasođlu S, Koçak H, Beyhan-Özdaş Ş, *et al.* Effect of dietary curcumin and capsaicin on testicular and hepatic oxidant–antioxidant status in rats fed a high-fat diet. *Appl Physiol Nutr Metab* 2019;44(7):774-82.
  64. Zhou J, Zhang R, Lv P, Zhang S, Zhang Y, Yang J, *et al.* Acyclic cucurbit [n] urils-based supramolecular encapsulation for enhancing the protective effect of capsaicin on gastric mucosa and reducing irritation. *Int J Pharm* 2022;626:122190.
  65. Cortés-Ferré HE, Martínez-Avila M, Antunes-Ricardo M, Guerrero-Analco JA, Monribot-Villanueva JL, Gutiérrez-Urbe JA. *In vitro* evaluation of anti-inflammatory activity of “Habanero” chili pepper (*Capsicum Chinense*) seeds extracts pretreated with cellulase. *Plant Foods Hum Nutr*

- 2023;78(1):109-16.
66. Thongin S, Den-Udom T, Uppakara K, Sriwantana T, Sibmoo N, Laolob T, *et al.* Beneficial effects of capsaicin and dihydrocapsaicin on endothelial inflammation, nitric oxide production and antioxidant activity. *Biomed Pharmacother* 2022;154:113521-30.
  67. Li J, Wang H, Zhang L, An N, Ni W, Gao Q, *et al.* Capsaicin affects macrophage anti-inflammatory activity *via* the MAPK and NF- $\kappa$ B signaling pathways. *Int J Vitam Nutr Res* 2021;93(4):289-97.
  68. Zheng Q, Sun W, Qu M. Anti-neuro-inflammatory effects of the bioactive compound capsaicin through the NF- $\kappa$ B signaling pathway in LPS-stimulated BV2 microglial cells. *Pharmacogn Mag* 2018;14(58):489-94.
  69. Singh SA, Uddin MO, Khan MM, Singh SA, Chishti AS, Bhat UH. Therapeutic properties of capsaicin: A medicinally important bio-active constituent of chilli pepper. *Asian J Pharm Clin Res* 2022;15(7):47-58.
  70. Persson MS, Stocks J, Walsh DA, Doherty M, Zhang W. The relative efficacy of topical non-steroidal anti-inflammatory drugs and capsaicin in osteoarthritis: A network meta-analysis of randomised controlled trials. *Osteoarthritis Cartilage* 2018;26(12):1575-82.
  71. Cassano R, Serini S, Curcio F, Trombino S, Calviello G. Preparation and study of solid lipid nanoparticles based on curcumin, resveratrol and capsaicin containing linolenic acid. *Pharmaceutics* 2022;14(8):1593-610.
  72. Fernandes GD, Gómez-Coca RB, Pérez-Camino MD, Moreda W, Barrera-Arellano D. Chemical characterization of major and minor compounds of nut oils: Almond, hazelnut and pecan nut. *J Chem* 2017;2017(1):2609549-59.
  73. Barreca D, Nabavi SM, Sureda A, Rasekhan M, Raciti R, Silva AS, *et al.* Almonds (*Prunus dulcis* Mill. DA webb): A source of nutrients and health-promoting compounds. *Nutrients* 2020;12(3):672-93.
  74. Gorji N, Moeini R, Memariani Z. Almond, hazelnut and walnut, three nuts for neuroprotection in Alzheimer's disease: A neuropharmacological review of their bioactive constituents. *Pharmacol Res* 2018;129:115-27.
  75. Chang SK, Alasalvar C, Bolling BW, Shahidi F. Nuts and their co-products: The impact of processing (roasting) on phenolics, bioavailability, and health benefits—A comprehensive review. *J Functional Foods* 2016;26:88-122.
  76. Alasalvar C, Bolling BW. Review of nut phytochemicals, fat-soluble bioactives, antioxidant components and health effects. *Br J Nutr* 2015;113(S2):S68-78.
  77. Alalwan TA, Mohammed D, Hasan M, Sergi D, Ferraris C, Gasparri C, *et al.* Almond, hazelnut, and pistachio skin: An opportunity for nutraceuticals. *Nutraceuticals* 2022;2(4):300-10.
  78. Rocchetti G, Bhumireddy SR, Giuberti G, Mandal R, Lucini L, Wishart DS. Edible nuts deliver polyphenols and their transformation products to the large intestine: An *in vitro* fermentation model combining targeted/untargeted metabolomics. *Food Res Int* 2019;116:786-94.
  79. Sahib ZH. Assessment of anxiolytic activity of nuts of *Prunus amygdalus Dulcis* (almond) in mice. *Med J Babylon* 2014;11(4):817-24.
  80. Abdollahnejad F, Mosaddegh M, Kamalinejad M, Mirnajafi-Zadeh J, Najafi F, Faizi M. Investigation of sedative and hypnotic effects of *Amygdalus communis* L. extract: Behavioral assessments and EEG studies on rat. *J Nat Med* 2016;70:190-7.
  81. Müller AK, Schmözl L, Wallert M, Schubert M, Schlörmann W, Gleis M, *et al.* *In vitro* digested nut oils attenuate the lipopolysaccharide-induced inflammatory response in macrophages. *Nutrients* 2019;11(3):503-15.
  82. Dhingra N, Kar A, Sharma R, Bhasin S. *In vitro* antioxidative potential of different fractions from *Prunus dulcis* seeds: Vis a vis antiproliferative and antibacterial activities of active compounds. *South Afr J Bot* 2017;108:184-92.
  83. Bhardwaj R, Dod H, Sandhu MS, Bedi R, Dod S, Konat G, *et al.* Acute effects of diets rich in almonds and walnuts on endothelial function. *Indian Heart J* 2018;70(4):497-501.
  84. Vázquez-Carrillo MG, Aparicio-Eusebio LA, Salinas-Moreno Y, Buendía-Gonzalez MO, Santiago-Ramos D. Nutraceutical, physicochemical, and sensory properties of blue corn polvorones, a traditional flour-based confectionery. *Plant Foods Hum Nutr* 2018;73:321-7.
  85. Sireesha D, Reddy BS, Reginald BA, Samatha M, Kamal F. Effect of amygdalin on oral cancer cell line: An *in vitro* study. *J Oral Maxillofac Pathol* 2019;23(1):104-7.
  86. Kouacheur KGE, Cherif HS, Saidi F, Bensouici C, Fauconnier ML. *Prunus amygdalus* var. amara (bitter almond) seed oil: Fatty acid composition, physicochemical parameters, enzyme inhibitory activity, antioxidant and anti-inflammatory potential. *J Food Meas Charact* 2023;17(1):371-84.
  87. Lauro MR, Marzocco S, Rapa SF, Musumeci T, Giannone V, Picerno P, *et al.* Recycling of almond by-products for intestinal inflammation: Improvement of physical-chemical, technological and biological characteristics of a dried almond skins extract. *Pharmaceutics* 2020;12(9):884-98.
  88. Pelvan E, Olgun EÖ, Karadağ A, Alasalvar C. Phenolic profiles and antioxidant activity of Turkish Tombul hazelnut samples (natural, roasted, and roasted hazelnut skin). *Food Chem* 2018;244:102-8.
  89. Fonollá J, Maldonado-Lobón JA, Luque R, Rodríguez C, Banuelos O, López-Larramendi JL, *et al.* Effects of a combination of extracts from olive fruit and almonds skin on oxidative and inflammation markers in hypercholesterolemic subjects: A randomized controlled trial. *J Med Food* 2021;24(5):479-86.
  90. Emanet M, Şen Ö, Pignatelli F, Lavarello C, Petretto A, Ciofani G. Hazelnut extract-loaded nanostructured lipid carriers and evaluation of their antioxidant properties. *Front Bioeng Biotechnol* 2022;10:953867-78.
  91. Balasubramanian A, Pilankatta R, Teramoto T, Sajith AM, Nwulia E, Kulkarni A, *et al.* Inhibition of dengue virus by curcuminoids. *Antiviral Res* 2019;162:71-8.
  92. Tyagi P, Singh M, Kumari H, Kumari A, Mukhopadhyay K. Bactericidal activity of curcumin I is associated with damaging of bacterial membrane. *PloS one* 2015;10(3):e0121313-5.
  93. Liu HT, Ho YS. Anticancer effect of curcumin on breast cancer and stem cells. *Food Sci Hum Wellness* 2018;7(2):134-7.
  94. Li H, Zhong C, Wang Q, Chen W, Yuan Y. Curcumin is an APE1 redox inhibitor and exhibits an antiviral activity against KSHV replication and pathogenesis. *Antiviral Res* 2019;167:98-103.
  95. Zakerikhoob M, Abbasi S, Yousefi G, Mokhtari M, Noorbakhsh MS. Curcumin-incorporated crosslinked sodium alginate-g-poly (N-isopropyl acrylamide) thermo-responsive hydrogel as an *in situ* forming injectable dressing for wound healing: *In vitro* characterization and *in*

- vivo* evaluation. Carbohydr Polym 2021;271:118434.
96. Calgarotto AK, Longhini AL, de Souza PFV, Duarte AS, Ferro KP, Santos I, *et al.* Immunomodulatory effect of green tea treatment in combination with low-dose chemotherapy in elderly acute myeloid leukemia patients with myelodysplasia-related changes. Integr Cancer Ther 2021;20:1-12.
  97. Lee PM, Ng CF, Liu ZM, Ho WM, Lee MK, Wang F, *et al.* Reduced prostate cancer risk with green tea and epigallocatechin 3-gallate intake among Hong Kong Chinese men. Prostate Cancer Prostatic Dis 2017;20(3):318-22.
  98. Chen IJ, Liu CY, Chiu JP, Hsu CH. Therapeutic effect of high-dose green tea extract on weight reduction: A randomized, double-blind, placebo-controlled clinical trial. Clin Nutr 2016;35(3):592-9.
  99. Hattarki SA, Bogar C, Bhat KG. Green tea catechins showed antibacterial activity on *Streptococcus mutans*—An *in vitro* study. Indian J Dental Res 2021;32(2):226-9.
  100. Barigela A, Bhukya B. Probiotic *Pediococcus acidilactici* strain from tomato pickle displays anti-cancer activity and alleviates gut inflammation *in vitro*. Biotech 2021;11(1):23-33.
  101. Wolak T, Sharoni Y, Levy J, Linnewiel-Hermoni K, Stepsky D, Paran E. Effect of tomato nutrient complex on blood pressure: A double blind, randomized dose–response study. Nutrients 2019;11(5):950.
  102. Lee W, Lee DG. Lycopene-induced hydroxyl radical causes oxidative DNA damage in *Escherichia coli*. J Microbiol Biotechnol 2014;24(9):1232-7.
  103. Figueiredo ID, Lima TF, Inácio MD, Costa MC, Assis RP, Brunetti IL, *et al.* Lycopene improves the metformin effects on glycemic control and decreases biomarkers of glycoxidative stress in diabetic rats. Diabetes Metab Syndr Obes 2020;3117-35.
  104. Careaga M, Fernández E, Dorantes L, Mota L, Jaramillo ME, Hernandez-Sanchez H. Antibacterial activity of *Capsicum* extract against *Salmonella typhimurium* and *Pseudomonas aeruginosa* inoculated in raw beef meat. Int J Food Microbiol 2003;83(3):331-5.
  105. Liang YT, Tian XY, Chen JN, Peng C, Ma KY, Zuo Y, *et al.* Capsaicinoids lower plasma cholesterol and improve endothelial function in hamsters. Eur J Nutr 2013;52:379-88.
  106. Baek J, Lee J, Kim K, Kim T, Kim D, Kim C, *et al.* Inhibitory effects of *Capsicum annuum* L. water extracts on lipoprotein lipase activity in 3T3-L1 cells. Nutr Res Pract 2013;7(2):96-102.
  107. Friedman JR, Nolan NA, Brown KC, Miles SL, Akers AT, Colclough KW, *et al.* Anticancer activity of natural and synthetic capsaicin analogs. J Pharmacol Exp Ther 2018;364(3):462-73.
  108. Batool Z, Sadir S, Liaquat L, Tabassum S, Madiha S, Rafiq S, *et al.* Repeated administration of almonds increases brain acetylcholine levels and enhances memory function in healthy rats while attenuates memory deficits in animal model of amnesia. Brain Res Bull 2016;120:63-74.
  109. Sharifi-Rad M, Kumar ANV, Zucca P, Varoni EM, Dini L, Panzarini E, *et al.* Lifestyle, oxidative stress, and antioxidants: Back and forth in the pathophysiology of chronic diseases. Front Physiol 2020;11:694-714.
  110. Nocito MC, de Luca A, Prestia F, Avena P, Padula D, Zavaglia L, *et al.* Antitumoral activities of curcumin and recent advances to improve its oral bioavailability. Biomedicines 2021;9(10):1476-513.
  111. Davatgaran-Taghipour Y, Masoomzadeh S, Farzaei MH, Bahramsoltani R, Karimi-Soureh Z, Rahimi R, *et al.* Polyphenol nanoformulations for cancer therapy: Experimental evidence and clinical perspective. Int J Nanomed 2017:2689-702.
  112. Imran M, Ghorat F, Ul-Haq I, Ur-Rehman H, Aslam F, Heydari M, *et al.* Lycopene as a natural antioxidant used to prevent human health disorders. Antioxidants 2020;9(8):706-32.
  113. Carvalho GC, de Camargo BA, de Araújo JT, Chorilli M. Lycopene: From tomato to its nutraceutical use and its association with nanotechnology. Trends Food Sci Technol 2021;118:447-58.
  114. Fattori V, Hohmann MS, Rossaneis AC, Pinho-Ribeiro FA, Verri Jr WA. Capsaicin: Current understanding of its mechanisms and therapy of pain and other pre-clinical and clinical uses. Molecules 2016;21(7):844-76.