Chapter

Spices-Reservoir of Health Benefits

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Abstract

Spices contribute to the quality, nutritive value, and flavor of food. Since ancient times, they hold a great medicinal value. Their antimicrobial, antiviral, antibacterial, anti-inflammatory, and other numerous properties have made them a potent source of therapeutic agents. Phytochemical analysis revealed presence of active constituents such as eugenol, curcumin, carotenoids in clove, turmeric, saffron respectively that explains the efficacious nature of these spices. Owing to their easy availability and consumption, it is advised to make spices daily part of our diet though in balanced amount as sometimes excess usage bear few consequences. Evaluating multiple benefits offered by these as immunity boosters especially in times of pandemic and incorporating them in our routine diet would improve disease management strategies. This chapter discusses the reservoir of activities exhibited by few spices along with the components responsible for these activities. Here, we also discussed their negative effects if at all.

Keywords: curcumin, spices, antiviral, clove, immune booster

1. Introduction

Spices are plant-derived substances and play a crucial role in cooking. They are responsible for bringing out complex and rich flavors of food with their color, taste, aroma and making a cuisine distinct and popular. Without them kitchen looks empty and food gives a feeling of Stone Age. But do these spices just provide aroma or piquancy to food? Or is there any underlying advantage behind their regular consumption with food. Moreover, their usage depends upon habitat, time, and weather conditions. It is evident from both traditional as well as modern literature that vast medicinal properties offered by the spices makes them legendary and a vital part of daily diet. Pharmacological and molecular studies revealed that oils and alkaloids produced by most of the spices possess antimicrobial, anti-parasitic, immune booster, antioxidant and other important biological properties [1–4]. Their antioxidant and bactericidal activities prevents rancidity thereby increasing storage life of food [5]. Turmeric, with curcumin as principle ingredient, has been quite extensively used in the treatment of disorders such as amenorrhea, inflammation, hepatitis, arthritis [6, 7]. Clove, cinnamon, are rich source of antioxidants exhibiting wide range of pharmacological effects [8].

As spices are rich in immunity boosting ingredients, their daily consumption would lead to development of long-lasting immune protection and might maintain

safe drug bullets at a certain basal level in blood stream to tackle the infection. Since the outbreak of COVID-19, the first line of defense is body's immune system. Therefore, regular usage of spices not only enhances the body's immunity to fight against the infection but also provides a prophylactic therapy to prevent and minimize the chances of infection. Out of wide variety of spices, pharmaco-potential of some of them has been discussed here.

2. Turmeric

Turmeric (rhizome of *Curcuma longa* L.), native to Tropical South Asia, is used as a condiment, food preservative and a traditional remedy for various diseases. This spice of Zingiberaceae family is widely cultivated in tropics and is known by different names such as Haldi, bhadra, pitika, mehagni, terre merite etc. To date various compounds of turmeric have been identified such as monoterpenes, sesquiterpenes, curcuminoids, alkaloids, sterols. Among these, most abundant is curcumin (77%) which is responsible for characteristic yellow color of turmeric and exhibits a wide spectrum of biological effects viz. antidiabetic, antimicrobial, anti-inflammatory, etc. (**Figure 1**) [9].

Anti-inflammatory and antioxidant effects of curcumin have proved to be beneficial against neurological diseases. Curcumin has the ability to bind amyloid β (Aβ) inhibiting fibrils formation [10] and, also enhance its cellular uptake [11], circumvent plaque deposition [12] thereby preventing Alzheimer's disease. Furthermore, curcumin is capable of decreasing Aβ serum levels and attenuating inflammation in Alzheimer's disease mouse models [13] along with rescuing altered neuritic morphology around Aβ plaques [14]. Additionally, studies have shown that curcumin decreased Huntington protein aggregation [15], suppressed cell death relieving disease symptoms [16]; modulated accumulation of α-synuclein which is the prime reason for Parkinson's disease [17]. It has been reported that intravenous and oral administration of curcumin modulates dopamine related damage, induces microglial activation, and improves locomotion [18]. Curcumin has, further, shown to increase docosahexaenoic acid (DHA) levels [19]; improve learning and mental ability in

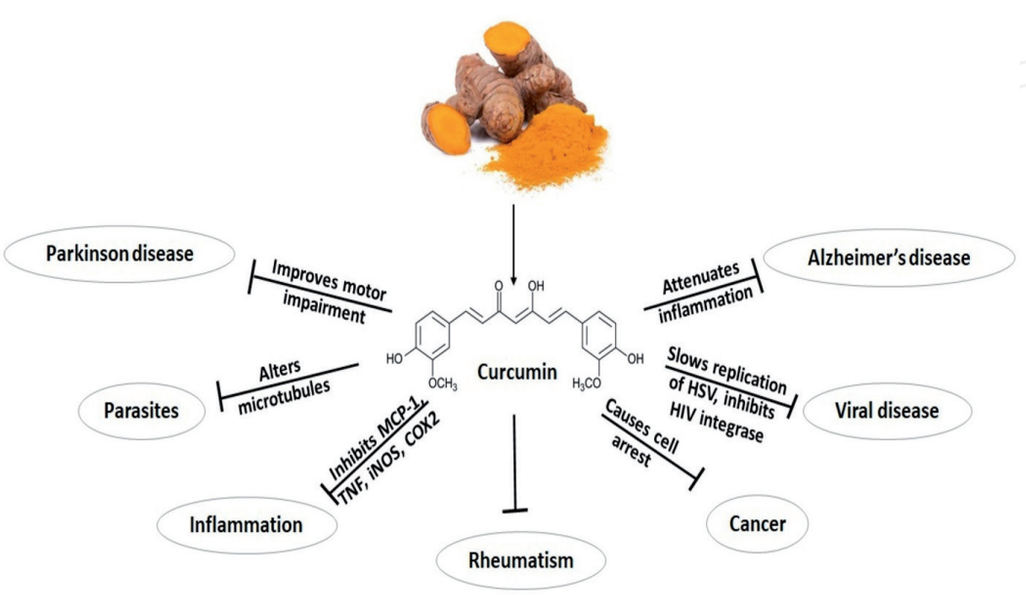

Figure 1.
Biological properties and chemical constituents of Turmeric.

scopolamine induced amnesia in mice [20]. Moreover, numerous other compounds with potent antioxidant activity have also been isolated from turmeric [21].

Curcumin has been known to downregulate production of inflammatory cytokines such as MCP- 1, TNF α, IL6, IL-1β both in vitro and in vivo [22–24]. However, recent study have suggested that efficacy to reduce levels of pro-inflammatory cytokines is enhanced on administering liposomal curcumin [25]. Studies have reported upregulation of heme oxygenase-1 reducing oxidative stress and providing protection against acute vascular inflammation in vitro as well as in vivo [26, 27].

Anti-rheumatic effects of curcumin have also been reported as curcumin decreased β3 and β7 integrins expression (adhesion molecules) ultimately decreasing joint inflammation; downregulated expression of chemokines, pro-inflammatory cytokines and growth-related oncogene/keratinocyte chemoattractant [28]. Further, randomized trials have also shown the efficacy of oral administration of curcumin in treatment of Rheumatoid Arthritis [29, 30].

Curcumin is effective in the management of virus infections as it inhibited Zika and Chikungunya virus at a concentration of 5 μM (IC50 = 1.9 and 3.89 μM respectively) [31], herpes simplex virus [32] and dengue virus [33]. Further, it inhibited human immunodeficiency virus (HIV) integrase and protease suggesting its protective effects against AIDS [34, 35]. The pandemic, COVID-19 related mortality is mainly due to acute respiratory distress syndrome with extensive cytokine storm. It has been reported that curcumin upregulates peroxisome proliferator-activated receptor-γ induction leading to inhibition of nuclear factor-κB (NFkb) signaling eventually decreasing cytokine storm [36] which suggests that curcumin might ameliorate COVID associated symptoms. Bioinformatic analysis have further shown ability of curcumin to interact with ACE2 receptor [37] and main protease [38] thereby fighting against COVID-19.

Curcumin displays antiparasitic and anti-cancer effects too. At a dose of 5 μM, it altered *P. falciparum* microtubules leading to reduction of 70–90% of parasitemia (IC_{50} = 50 μM) [39] and further at 100 mg/kg showed 80–90% decrease in *P. berghei* parasitemia [40]. Curcumin, in synergistic effect with Mitomycin C (5 μmol/L) arrested growth of MCF 7 breast cancer cell lines at G_0/G_1 phase of the cell cycle at a concentration of 40 μmol/L [41], decreased sensitivity of NFκB in human pancreatic cells lines BxPC-3, Capan-1, Capan-2, ASPC-1, and HS766-T (73–95% inhibition) [42], induced apoptosis [43]; inhibited cyclo-oxygenase 2 (COX 2- its overexpression leads to carcinogenesis) production in HT-29 colon cancer cell lines [44]. This prompts the requirement of detailed investigation to understand the potential of curcumin in cancer biology. Apart from curcumin, non-curcuminoids have also been reported to exhibit potential anticancer activities too [45].

Regardless of its demonstrated efficacy, purified curcumin has also been reported as pan assay interference compounds (PAINS) that show activity by interfering with assay readouts [46]. Curcumin exhibits PAIN properties such as fluorescence interference [47], aggregation [48], metal chelation [49], redox reactivity [50]. It is a highly unstable compound as it degrades rapidly in alkaline solutions [51]. Another drawback of curcumin is its poor bioavailability, however, number of formulations of curcumin with enhanced bioavailability and absorption are now available such as BioPerine-20x [52], BCM-95CG [52], Longvida-67x [53], Meriva-29x [54]. Furthermore, it is advised, traditionally, to consume turmeric powder with warm milk and ghee (Milk fat) as it is believed that this combination boosts immunity, purifies blood, beats everyday fatigue and anxiety, relieves cold and cough, which all are requirement to fight against COVID-19. Moreover, this combination might also enhance bioavailability of curcumin due to the constituents of milk and ghee such as casein, fats, iodine, phosphorus, calcium, vitamins etc.

3. Cinnamon

Cinnamon has a sweet, warm taste and is derived from dried central part of bark of *Cinnamomum zeylanicum* Blume (family Lauraceae). It is native to the Caribbean, South America, and Southeast Asia and is used throughout the world for its astounding properties such as anti-inflammatory, antidiabetic, antimicrobial, anticarcinogenic effects (**Figure 2**) [55]. Biochemical investigation of cinnamon revealed presence of camphor, linalool, cinnamaldehyde (major constituent), terpinen-4-ol, 1,8-cineole, α-cadiene, safrole, α-cadinol, germacrene D, γ-muurolene, α- terpineol, eugenol, 1,6-octadien-3-ol, 3,7-dimethyl,1-phenyl-propanr-2,2-diol diethanoate, etc. [56].

Cinnamon has been reported to exhibit antioxidant effects. In vitro studies showed free radical scavenging activity of methanolic extracts of cinnamon against 2,20 -azinobis- 3-ethylbenzothiazoline-6-sulphonic acid (ABTS) radical and Diphenylpicrylhydrazyl (DPPH) radical cations [57]. Intake of 100 mg/30 ml of cinnamon tea for 2 weeks showed reduction in the levels of 2-thiobarbituric acid reactive substances (TBARS) in plasma by 38% and increase in total antioxidant power 21% in a clinical study [58].

Antidiabetic and cholesterol lowering effects of aqueous extracts of cinnamon (AEC) have also been reported where it reduced fasting glucose levels (at 250 mg) from 1.14 mg/ml to 1.02 mg/ml in patients with impaired fasting glucose [59]; at a dose of 500 mg/kg for two months decreased glucose levels ($p < 0.005$) along with increasing in insulin sensitivity [60] and at 200 mg/kg reduced levels of LDL cholesterol, triglycerides and total cholesterol and increased levels of HDL-cholesterol in diabetic rats and hyper-lipidemic albino rabbits [61]. Further, decline in gastric acid secretion by 60% and reduction in gastric hemorrhagic lesions in rats was observed on pre-treatment with 250 mg/kg and 500 mg/kg of AEC [62].

Peterson et al., reported cinnamon as a potent anti-alzheimer agent as AEC inhibited tau aggregation (aggregation destabilizes microtubules causing Alzheimer's disease) [63].

In addition, cinnamon possesses antimicrobial and anticancer activities. Ethanolic extracts of cinnamon exhibited anti-microbial properties against

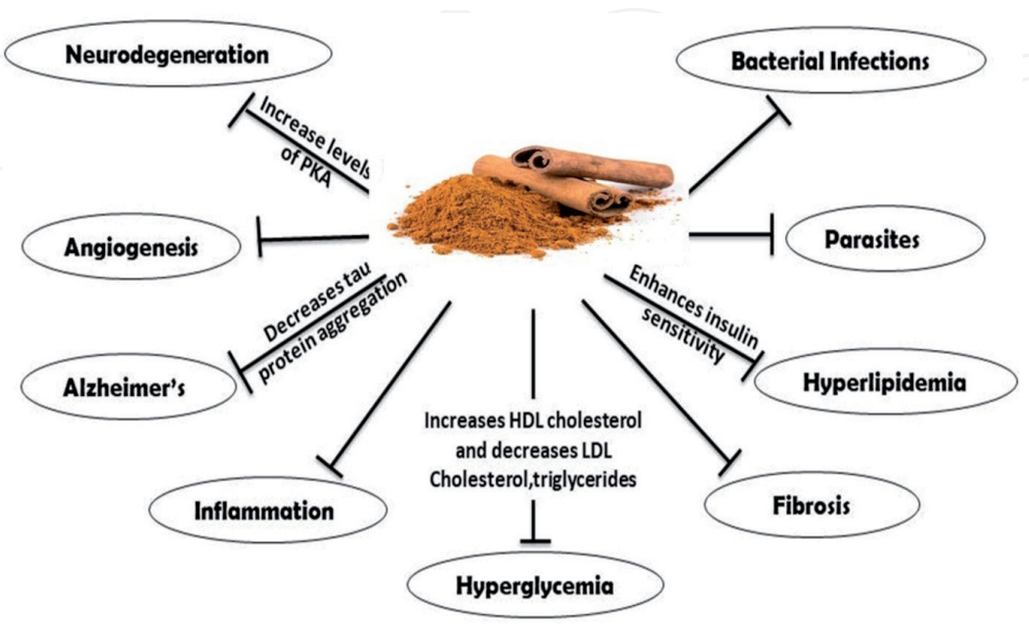

Figure 2.
Biological properties of Cinnamon.

Listeria monocytogenes (MIC 0.4 mg/ml other MICs) [64]. Further, essential oil of cinnamon also showed inhibitory effects against *Candida albicans* (MIC 7.81 μl/ml) [65]; nosocomial *P. aeruginosa* isolate (MIC- 1.9 μl/ml) [66]; *Anopheles tessellatus* (LD50: 0.33 μg/mL) and *Culex quinquefasciatus* (LD50: 0.66 μg/mL) [67]. Furthermore, AEC inhibited vascular endothelial growth factor (VEGF) and induced growth of vessels in aortic ring of rat ex vivo at a dose of 25 and 50 μg/ml suppressing angiogenesis [68]. Constituents of cinnamon essential oil, trans-cinnamaldehyde and its analogue - 4-hydroxy-3-methoxy-trans-cinnamaldehyde are effective inhibitors of bacterial acetyl-CoA carboxylase [69].

Cinnamon is considered as a strong immunity booster. At a dosage of 10 mg/kg, it significantly increased serum immunoglobulin levels whereas at 100 mg/kg dosage, along with boosting humoral immunity, cinnamon increased antibody titer and phagocytic index too thereby increasing cell-mediated immunity [70]. Cinnamon reportedly exhibits immunomodulatory properties as well. Studies have suggested that cinnamon decreased fibrotic symptoms and pro-inflammatory cytokines on treatment with 4.5 ml/kg dose [71] and 0.8 g/kg dose for 12 weeks [72] respectively in colitis infected mice models. Suppression of pro-inflammatory cytokines such as TNF-a, IL-1b, and IL-6 along with inhibition of nitric oxide secretion were also observed in BV 2 microglial cells on treatment with 50 μg/ml of ethanolic cinnamon extract [73]. Further, cinnamon bark is capable of decreasing in IFN-γ levels, enhancing of IL2 secretion thereby inhibiting cell death [74]. Studies have also suggested that cinnamaldehyde inhibits PI3K, NF-B activation and PDK1 thereby regulating monocyte\macrophage-mediated immune responses [74].

Recent bioinformatic analysis showed the possible effectiveness of molecules isolated from cinnamon against COVID-19 [75]. The ability to reduce pro-inflammatory cytokines and strong in silico investigation suggests the probable potential of cinnamon in fight against COVID-19.

Though cinnamon exhibits a wide range of health benefits, it is important to keep a check on the quantity of cinnamon consumed. A large amount can cause a dramatic drop in the blood sugar levels. In addition, high levels of cinnamon can cause rapid increase in heart rate, liver toxicity [76, 77].

4. Fennel

Fennel (seeds of *Foeniculum vulgare* Mill), originally cultivated in Mediterranean region, is used throughout the world for its licorice-like flavor. Belonging to class Magnoliopsida and family Apiaceae, fennel is known by different names such as suanf, sweet fennel, florence fennel, finocchio and is a concentrated source of minerals. This perennial herb is long loved for its culinary use. The essential oil of fennel constitutes anethole, estragole as major components and limonene, fenchone and others as minor components (**Figure 3**) [78, 79].

Fennel has been used for a long time for medicinal purposes (**Figure 3**) [80, 81]. It is a potent antioxidant agent. Essential oil of fennel seeds (FS) showed 45.05% DPPH radical scavenging activity along with 48.80–70.35% inhibition of peroxidation [81]. Ethanol and water extracts of FS (100 μg/ml) inhibited peroxidation in linoleic acid system by 77.5 and 99.1% respectively [82]. Parejo et al., isolated phenolic compounds from fennel viz. rosmarinic acid, kaempferol-3- O-glucoside, eriodictyol-7-Orutinoside, caffeoylquinic acid, quercetin-3-O-galactoside and observed decrease in absorbance of DPPH by 50% (IC50 in μg/mL = 1.17, 8.21, 24.78, 3.82, 7.52 respectively) [83].

Further, essential oil from fennel fruit showed inhibitory effects on growth of *Paenibacillus* larvae (MIC = 250 μg/ml) [84] and mycelial growth of *S. sclerotiorum*

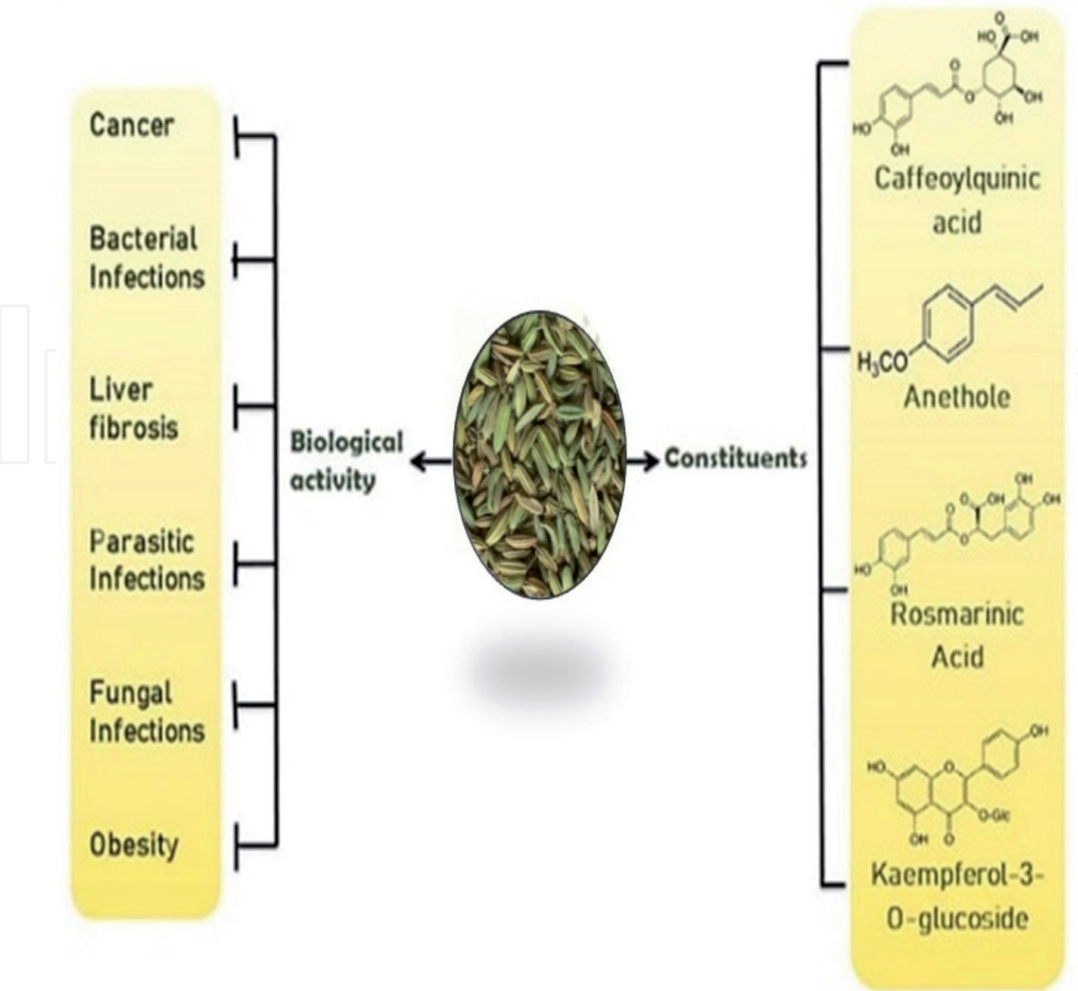

Figure 3.
Biological properties and chemical constituent of Fennel.

(MIC = 0.2 μg/ml) [85]. Similar inhibitory effects were observed against *C. quinquefasciatus* (LC_{50} = 70.85); *A. gambiae* (LC_{50} = 44.74) [86] and larvae of *C. pipiens* (90% inhibition at 60 mg/L) [87]. Hexane extracts of FS showed potent inhibitory effects against *E. coli* (MIC = 12.5 μg/mL), *S. typhi* (MIC =15 μg/mL), *S. aureus* (MIC = 10 μg/mL) [88].

Recent study reported that 300 μg/μl FS ethanolic extract inhibited Influenza virus H5N1 by 82.8% [89]. Moreover, Alazadeh et al., showed that oral administration of FS extract in capsular form ameliorated knee ostroarthritis [90]. In addition, methanol extract of FS showed significant anticancer potential against liver cancer cell line Hepg-2 (IC50 = 27.96 μg/mL) and breast cancer cell line MCF-7 (IC50 = 15.78 μg/mL) [80]. Özbek et al., 2003 studied hepatoprotective effects of fennel and observed that a dose of 0.4 ml/kg of fennel oil showed significant protective role against liver fibrosis (CCl4 induced) in rats [91].

It is safe to consume fennel and since it provides protection against flu, cough, it is advised to take fennel with warm milk.

5. Clove

Clove [*Syzygium aromaticum* (L.) Merr. & L.M. Perry] is one of the most valuable spices of family Myrtaceae and is a native of Indonesia, albeit found all around the globe. Major bioactive component of clove is eugenol. Other components

include phenolic acids such as gallic acid, gallic acid derivatives, caffeic acids, salicylic acids; flavonoids such as quercetin, kaempferol (**Figure 4**) [92].

Traditionally used to prevent nausea, enhance blood circulation and liver function, clove is commonly applied for toothache relief and has been long known as a medicine for numerous ailments (**Figure 4**). Miyazawa & Hisama, isolated dehydrodieugenol and trans-coniferyl aldehyde from ethyl acetate extract of clove bud and observed significant activity of both, at a concentration of 0.6 μmol/mL and 1.2 μmol/ml respectively, against mutagens 4-nitroquinolin 1-oxide and N-methyl-N′-nitro-N-nitrosoguanidine [93]. Furthermore, eugenol and eugenol acetate extracted from aroma extract of clove buds inhibited 99% of hexanal oxidation [94].

Eugenol also exhibits remarkable antimicrobial, antiparasitic, antiviral activities. Essential oil of clove has reportedly inhibited growth of *S. aureus, H. influenzae* (MIC = .0125 ml/ml each), *K. pneumoniae* (MIC = .050 ml/ml) [95], *C. albicans* (MIC = 2.5 μg/ml), *L. monocytogenes* (MIC = 5 μg/ml), *Y. enterocolitica* (MIC = 2.5 μg/ml) [96]. It has been reported that clove decreases ergosterol (cell membrane component) inhibiting growth of *C. albicans* (MIC = 0.64 μg/ml) [97]. Methanol extract, ether soluble fraction (ES), ethyl acetate soluble fraction (EAS) and acetone soluble fraction (AS) of clove buds showed inhibitory effects on *Bacillus cereus* (MIC =250 μg/disc each). Further, EAS and AS also inhibited *Micrococcus luteus* and *Shigella dysenteriae* respectively (MIC = 62.5 μg/disc each) [98]. In addition, antiparasitic effects were reported by Bagavan et al., who observed growth inhibition of chloroquine resistant *P. falciparum* on treatment with ethyl acetate and methanol extracts of clove (IC50 = 13 μg/ml and 6.25 μg/ml

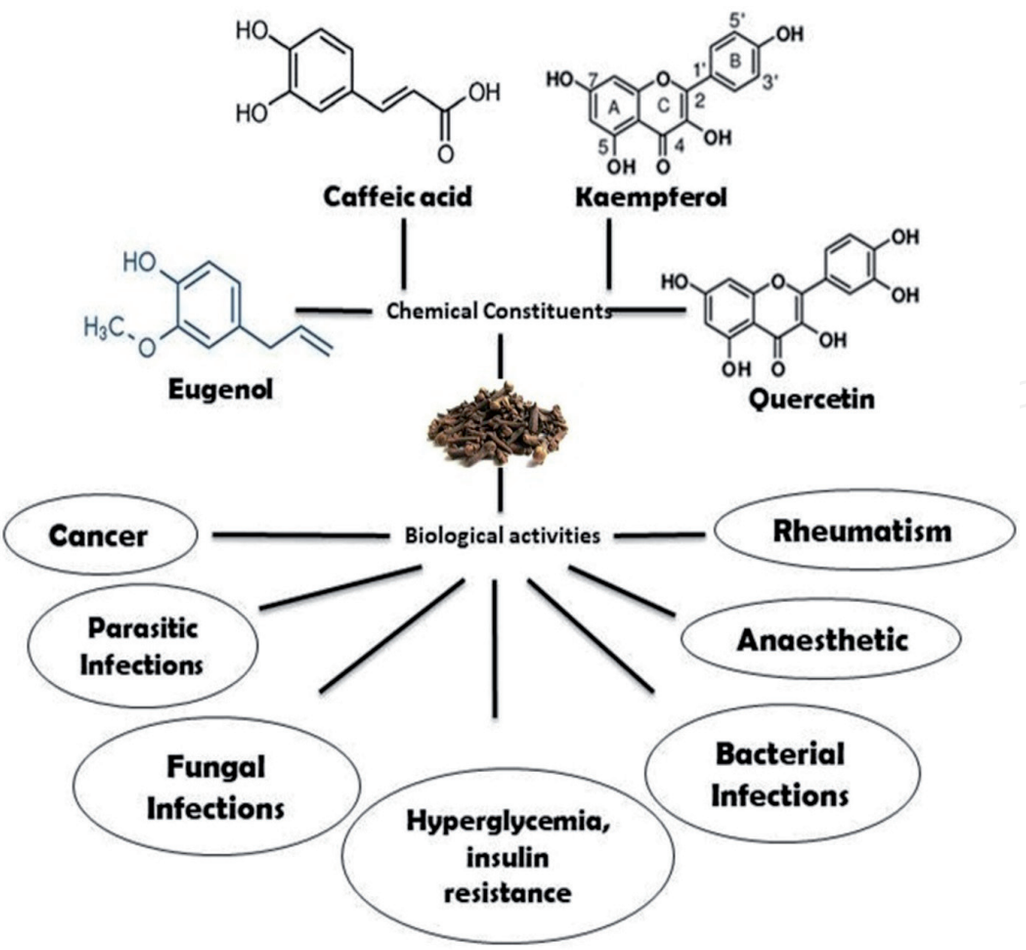

Figure 4.
Chemical constituents and biological properties of Clove.

respectively) [99]. Hypoglycemic effects of clove have also been identified. Methanol extract of clove activated AMP-activated protein kinase (AMPK) pathway, a regulator of cellular energy homeostasis thereby regulating glucose metabolism [100]. A recent report has pointed out that it relieves insulin resistance [101].

Consumption of clove is safe, and it offers numerous benefits, however, studies have shown that clove oil increases clotting time [102] which might increases the risk of bleeding in case of bleeding disorders.

6. Cardamom

Cardamom [*Elettaria cardamomum* (L.) Maton, also known as "Queen of Spices"] is an aromatic spice commonly used as a flavoring agent. This perennial herb belongs to Zingiberaceae family. It is native to Western Ghats of Southern India and widely cultivated in countries such as Sri Lanka, North America, Guatemala, New Guinea, and Thailand. Essential oil of cardamom constitutes α- terpinyl acetate, 1,8-cineole, linalool, limonene, eugenol, safrole (**Figure 5a**) [103, 104].

Cardamom is a valuable in relieving against ischemic heart disease. It showed protective effects against cardiac dysfunction associated with oxidative stress. A dose of 100 and 200 mg/kg of cardamom extract showed cardioprotective effects in albino rats who were induced with myocardial infarction due to isoproterenol [105]. Further, cardamom-oil maintained cholesterol homeostasis by potentially reducing cholesterol levels in hypercholesterolemic conditions and restoring atherogenicity index [106]. In addition, a dose of 1.5 g of cardamom powder for 12 weeks (two times a day) decreased the blood pressure in hypertensive individuals by 19 mmHg in systolic and 12 mmHg in diastolic BP [107].

Cardamom is an effective immunomodulatory agent due to its anti-inflammatory effects. It is capable of downregulating pro-inflammatory cytokines (**Figure 5b**) [108]; suppressing T helper (TH)1 cytokine release and enhancing

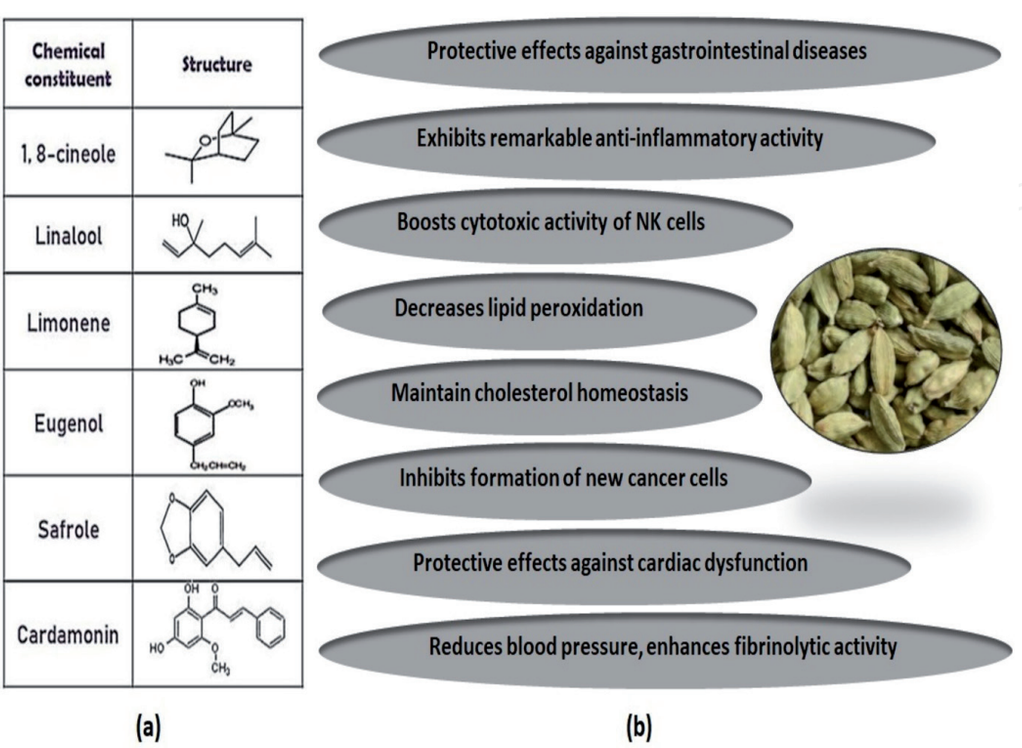

Figure 5.
(a) Chemical constituents of Cardamom; (b) Biological properties of Cardamom.

T helper (TH)2 cytokine release [109]. Methanol and petroleum ether extract of cardamom reduced 70% and 50% lesions in ethanol-induced ulcer mice model at 500 mg/kg and 100 mg/kg respectively exhibiting gastroprotective effects [110]. A constituent of cardamom, cardamonin inhibited the formation of new cancer stem cells in case of breast cancer by effectively suppressing the up-regulation of IL-8 and, MCP-1 cytokines and activation of NF-κB pathway [111]. Antibacterial effects of cardamom has also been demonstrated [108, 112].

Recently, its efficacy against toxic effects of uranium has been reported. Uranium increases sodium and calcium ion levels, decreases and phosphate ion levels, inhibits Na+/K+ ATPase increasing the influx of into the neurons, and thereby damaging central nervous system. Aqueous extracts of cardamom (250 mg/kg) significantly increased the levels of phosphate and potassium ions and decreased the levels of calcium and sodium ions in albino rats administered with uranyl acetate dehydrate (40 mg/kg) [113]. Furthermore, protective effects against neurological disorders have also been reported as oral administration with 100 and 200 mg/kg of cardamom oil improved behavioral patterns, inhibited amyloid-β expression, declined in oxidative stress and inhibited of acetylcholinesterase in Wister rats [114, 115].

7. Red chili

Out of the wide variety of species under genus *Capsicum* like frutescens, pubscens, baccatum etc., dried fruits of *Capsicum annum* L. are the most commonly used spice of Solanaceae family. Commonly known as red chili, lal mirch, this plant is native to Central and South America and is cultivated in many parts of the world such as India, China. Biochemical analysis of red chili led to the identification of capsaicinoids (capsaicin, dihydrocapsaincin) (**Figure 6**), antioxidant vitamins (ascorbic acid, vitamin E), carotenoids (β - carotene, β cryptoxanthine) and several organic acids and minerals [116, 117]. Red chili has a phenolic substance, capsaicin responsible for its pungent smell and irritant properties. Capsaicin excites nociceptors that induce pain along with rise in temperature giving a sensation of heat (pungency). As spicy is not one of the five basic tastes viz. sweet, sour, bitter, umami and salty, heat produced by capsaicin is considered as taste of red chili.

Capsaicin also exhibits anti-inflammatory properties [118]. It showed protective effects against gastric mucosal injury (ethanol-induced) in rats [119].

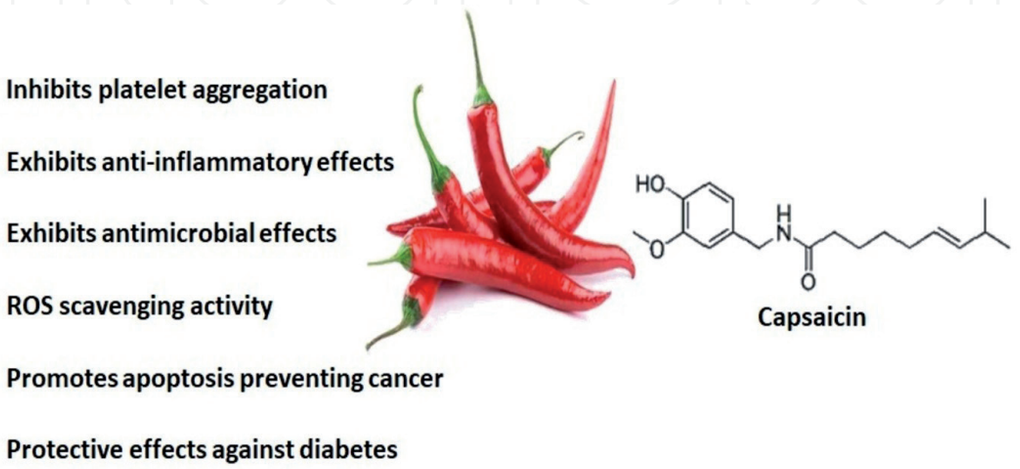

Figure 6.
Biological properties and chemical constituent of Red Chili.

Capsaicin treatment ameliorated lipid peroxidation, inhibited myeloperoxidase activity in gastric lesions (ethanol induced) in rats [120].

Dried red chili powder (1% w/v) showed inhibitory effects against *Listeria monocytogenes* [121]. Tropical application of capsaicin (0.075%) reduced fat accumulation in mesenteric and epididymal adipose tissue by increasing expression of adipokines [122]. It was also found that a dose of 200 mg/kg of capsaicin decreases plasma triglyceride levels and fasting glucose in obese mouse model kept on high fat diet [123].

Earlier studies suggested the risk of oral cavity [124] and stomach [125] cancer on consumption of red chili, however, recent reports suggested that consumption of red chili is safe and does not increase risks of cancer [126]. Numerous reports have suggested protective effects of capsaicin against cancer. Capsaicin showed inhibitory effects on the growth of human KB cancer cells by promoting apoptosis at a concentration of 200–250 μM [127]. Further, capsaicin led to the formation of reactive oxidative species through mitochondria (at a dose of 150 μM) causing loss in mitochondrial membrane potential in BxPC-3 and AsPC-1, human pancreatic cancer cell lines [128]; inhibited activation of NF-kB and AP-1, transcription factors responsible for cellular proliferation and malignant formation, in mice model [129]. In addition, capsaicin inhibited growth of MCF breast cancer cell lines by causing cell cycle arrest at S phase and induced poly(ADP-ribose) polymerase-1 (PARP-1) cleavage (apoptosis is marked by the cleavage of PARP-1) by activating caspase-7 which is involved in apoptosis (**Figure 6**) [130]. Capsaicin and cisplatin, in a synergistic manner, arrested the growth of SNU-668, human gastric cell line at G1/S phase [131].

8. Black cumin

Seeds of *Nigella sativa* L., an annual flowering plant of Ranunculaceae family, have been of extensive use as a spice. Commonly known as black cumin, it is native to South and Southwest Asia and has diverse medicinal applications. Phytochemical analysis of black cumin seeds has showed presence of thymoquinone (TQ), para-cymene, and carvone, linoleic acid, oleic acid, palmitic acid, and stearic acid (**Figure** 7) [132].

Black cumin has been reported to exhibit anti-inflammatory properties. Intra-peritoneal injection black cumin essential oil reduced inhibited carrageenan-induced paw oedema in rats thereby relieving inflammation [133]. Aqueous extracts of black cumin up-regulated the secretion of T-helper 2 cells and suppressed the secretion of pro-inflammatory cytokines viz. IL-6, TNFα, and NO [109]. Furthermore, black El-Mahmoudy et al., isolated TQ from essential oil of black cumin seeds and showed that TQ reduced nitrite accumulation and decreased inducible nitric oxide synthase levels (responsible for NO production) in rat peritoneal macrophages suggesting anti-inflammatory and cytoprotective effects of black cumin [134]. Methanol extract of seeds of black cumin (1 mg/ml) protected erythrocytes against protein degradation and loss of deformability induced due to peroxide [135] and has proved to stimulate innate humoral immune responses [136]. Proteins purified from black cumin exhibit potent antioxidant activities [137]. Furthermore, neuroprotective effects of black cumin have also been reported [138].

In addition, black cumin exhibits anti-bacterial, anti-viral, anti-helminthic effects. Black cumin seed oil (BSO) showed protective effects against murine cytomegalovirus (MCMV) that targets liver and spleen. Treatment with BSO showed approximately 38% and 20% decrease in viral load in liver and spleen

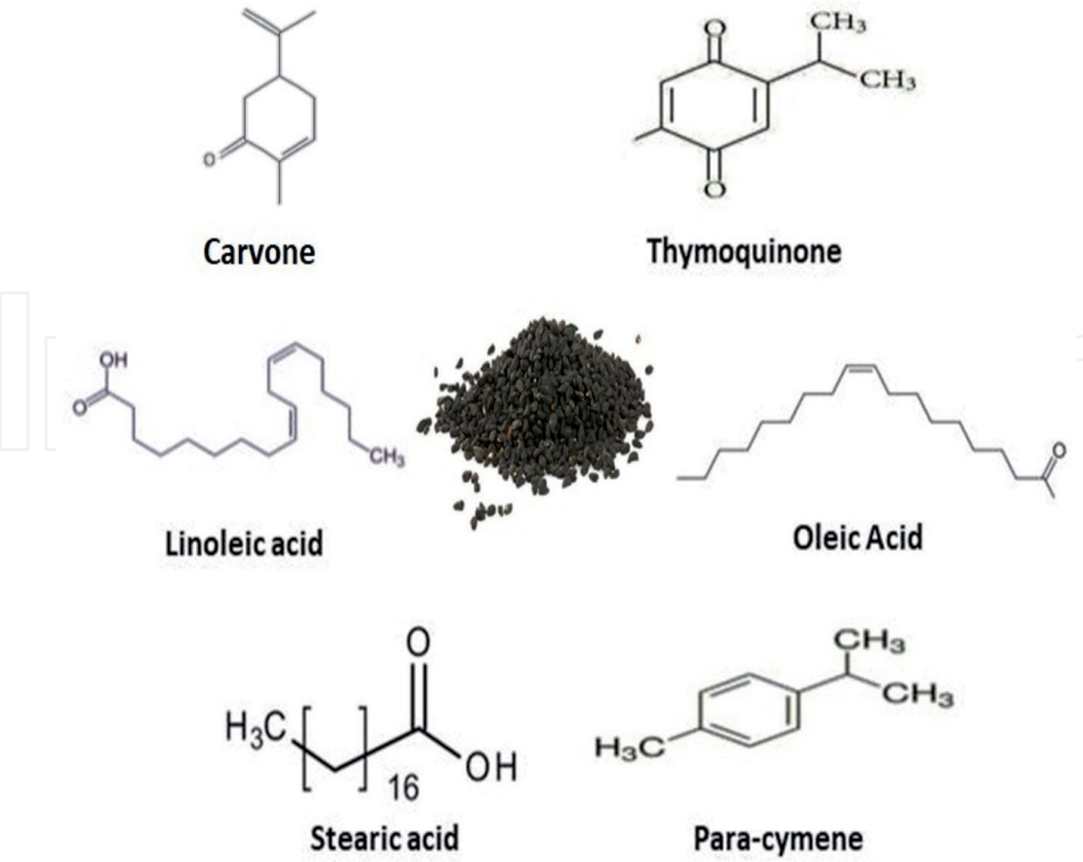

Figure 7.
Chemical constituents of Black Cumin.

respectively in MCMV infected mice [139]. Decrease in the number of *S. mansoni* worms in liver and eggs in both liver and intestine of mice has been observed after treatment with black cumin oil at a dose of 2.5 ml/kg and 5 ml/kg [140]. TQ has proved to be an effective bactericidal agent as it inhibited growth of *Staphylococcus aureus* (BIC_{50} = 22 μg/ml) [141], *Salmonella typhii* [142] *Streptococcus mutans* [143]. Further, black cumin inhibited the *P. yoelii* parasitemia by 94% [144].

Black cumin has protective effects against diabetes. Black cumin seeds (BCS) led to the decrease in elevated levels of glucose with increase in GSH levels and further inhibited liver damage induced by lipid peroxidation in diabetic rabbits [145]. In addition, improvement of glucose homeostasis in patients with type 2 diabetes on administration of black cumin (2 g/day for 3 months) with hypoglycemic drugs have also been reported [146].

Furthermore, aqueous extracts of black cumin significantly up-regulated cytotoxic activity of natural killer cells against YAC-1 tumor cells [109]. Oral administration of TQ at a dose of 0.01% suppressed benzo(a)pyrene induced forestomach tumor in mice by 70% [147] exhibiting anti-tumor effects.

Minor toxicological effects have also been reported, however, numerous studies demonstrated diverse therapeutic effects of black cumin and TQ and have supported its safe consumption [132].

9. Conclusion

Spices are rich source of bioactive components with innumerable beneficial attributes that have been verified and accepted by modern world in the past few decades. These are nowadays considered as a crucial & natural component of our

daily diet. Consumption of spices aids in combating diseases when they are at their peak, for instance, best remedy for stomach infections are fennel seeds; turmeric is the tonic for fever-related diseases. Antimicrobial activities of spices make them valuable in hot climates as they prevent food spoilage. Although they lower the risk of various diseases such as diabetes, cancer, etc., there are some contradictions about their use. Despite all the pleiotropic effects offered by the spices, further evaluation about their mechanism of action is mandated to validate their clinical effects and their amount of consumption.

Conflict of interest

The authors declare no conflict of interest.

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