Chapter

Bioaccessibility, Bioavailability, Antioxidant Activities and Health Beneficial Properties of Some Selected Spices

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Abstract

Herbs and spices have been used as therapeutic agents in traditional medicine due to the presence of bioactive compounds including flavonoids, polyphenols, alkaloids, carotenoids, organosulfur compounds, glucosinolates etc. As a result, they are associated with various functional properties such as digestive stimulant, antioxidant, anti-inflammatory anticancer, anti-diabetic, cardioprotective, neuroprotective, and antimicrobial activities. However, the bioefficacy of different spices are affected by the bioavailabilties of their bioactive compounds and depends on various factors such bioaccessibility, molecular structures, composition of food matrices, and metabolizing enzymes. In this chapter we discuss on major phytochemical compounds of some selected spices including turmeric, garlic, ginger, onion, cinnamon, chili pepper, and black pepper including their bio accessibilities, bioavailabilities and their health beneficial effects. The knowledge of bioaccessibility and bioavailability of spices bioactive compounds will give a better understanding towards the development of strategies to optimize the positive health benefits of spices.

Keywords: spices, phytochemicals, polyphenols, nutrients, bioavailability, bioactive compounds, antioxidant activities, anti-inflammatory activities, anticancer properties

1. Introduction

Herbs and spices from leaves, seeds, bark, roots, rhizomes, or buds of aromatic plants have long been used for ages in food and medicine. Although herbs and spices are used to enhance flavor, taste, and color of foods, they also supply basic nutrients, promote health, and prevent from the risk of development of chronic diseases [1–5]. There are numerous groups of bioactive compounds present in herbs and spices due to which they are gaining continuous interest over time from scientific and health perspectives [3–7]. Several phytochemicals comprising carotenoids, phenolic compounds (flavonoids, flavonol, flavanols, anthocyanins, proanthocynains, and phenolic acids), phytosterols, phytostanols, tocotrienols,

organosulfur compounds, alkaloids, dietary fibers, prebiotics, protein, amino acids, and minerals contribute to the potential health benefits [3, 4, 7]. In general, the spices phytochemicals are safe to humans and recognized as GRAS (Generally Recognized As Safe) by USFDA (United State Food and Drug Administration) except some cases with age, and medical conditions. The spices are consumed as fresh, processed, or cooked where it could undergo physical and chemical transformation from the original sources and could affect their levels of content and efficacy [4–7]. Numerous research reports supported the potential role of spices phytochemicals in reducing and curing form diseases such as coronary heart disease, hypercholesterolemia, high blood pressure, diabetes, inflammation, cancers, arthritis, microbial, viral, and parasitic infections [4–10]. Extensive *in vitro* and *in vivo* studies and clinical trial investigations confirmed the correlations of molecular structures of these phytochemicals and their biochemical activities [4–10]. However, most of their mechanisms of actions are still not completely understood to underscore their corresponding health benefits. One of the major pathways of these protective roles of phytochemicals are associated with their antioxidant activities by reducing activities of reactive oxidants which cause oxidative stress related chronic diseases like cancer, diabetes, cardiovascular diseases and other pathogenic conditions [8, 9]. In order to exert the biological benefits of spices chemical compounds it needs to bioavailable which depends various factors like nature and composition of food matrices and health status of human being [11, 12]. However, one of the major challenges of most of the spice phytochemicals is poor oral bioavailability. Several strategies such as nanoparticles, polymers, and liposomes inclusion have been adopted to improve the bioavailabilities of phytochemicals. Moreover, in most of the cases the health benefits of spices are attributed to the isolated and/or synergistic biological activities of phytochemicals present in the spices [13, 14]. Novel formulations and supplements have been developed using the extracts of spice phytochemicals for multiple health benefits following synergistic effect. This chapter gives and overview of bioactive compounds and their potential health benefits such as antioxidant activities, anti-inflammatory activities, antidiabetic, and anticancer activities by some selective spices such as turmeric, garlic, ginger, onion, chili, cinnamon, and black peppers.

2. Bioactive compounds and health benefits of spices

2.1 Turmeric (*Curcuma longa* L)

2.1.1 Bioactive compounds

Turmeric is an orange-yellow-colored rhizomes which has been used as spice and health care additives since the ancient times. Turmeric is rich in polyphenolic compounds. Curcumin is the major polyphenolic compounds in turmeric followed by demethoxycurcumin and bisdemethoxycurcumin. Some other bioactive compounds found in the rhizome of turmeric are α-turmerone, and β-turmerone [15, 16]. Moreover, turmeric contains volatile compounds like camphor, eucalyptol, β-pinene phenyl propionoids, monoterpenes, sesquiterpenes, α-pinene, camphene, α-phellandrene, 3-carene, β-cymene, β-elemene, α-santalene, caryophyllene, α-farnesene, zingiberene, β-cedrene, α-bisabolol, and β-sesquiphellandrene [15, 16].

2.1.2 Antioxidant activities

Various research studies indicated that turmeric possesses moderate to strong antioxidant activities due to the presence of curcuminoids. The antioxidant potential of curcuminoids arises from its structural composition with functional groups including the β-diketo group and phenyl rings containing varying amounts of hydroxyl and methoxy substituents [15, 16]. Due to its potential antioxidant activities curcumins have been reported to have significant role in maintaining oxidative stress mediated pathological conditions [15–17]. It also protects biomembranes against peroxidative damage via scavenging of free radical activities involved in the peroxidation [15–17]. For very long-time number research is carried out to oversee the mechanism of antioxidant activities of curcumin. Jovanovic et al. reported that the central methylenic group of curcumin can donate H- rather than from the phenolic group [18]. However, some other studies proposed that phenolic group of curcumin better H donor to act as strong free radical scavenger [19, 20]. In addition to the free radical scavenging pathways curcuminoids displayed antioxidant activities stimulating the activities of antioxidant enzymes such as glutathione peroxidase, superoxide dismutase, and catalase [15, 16, 21]. Moreover, curcumin displayed antioxidant activities by preventing the inhibition of Nrf2, NFκB translocation and IκB degradation which are involved in regulating antioxidant activity [15–17].

2.1.3 Anti-inflammatory activities

Numerous *in vitro* and *in vivo* research studies on anti-inflammatory activity of curcumin derivatives reported that curcumin exhibited anti-inflammatory activities by interacting with various biomolecules related to inflammation such as cyclooxygenase 2, phospholipase, lipoxygenase, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, monocyte chemoattractant protein-1 (MCP-1), interferon-inducible protein, tumor necrosis factor (TNF), and interleukin-12 (IL-12) [15, 16, 21, 22]. Curcumin suppresses the regulation of proinflammatory interleukins (IL-1, −2, −6, −8, and − 12), cytokines (tumor necrosis factor-alpha (TNF-α), monocyte chemoattractant protein-1) by causing down-regulation of janus kinase and signal transducer and activator of transcription (JAK/STAT) signaling pathway which can contribute to the anti-inflammatory activity in the brain [15, 16, 21–23].

2.1.4 Anticancer activities

Curcumins have been shown to prevent carcinogenesis by affecting many phases of cancer including development, transformation, invasion, angiogenesis, and metastasis [15, 24]. It is effective for decreasing or preventing various cancer types such as colon, pancreas, breast, prostates, and lung cancers [15, 24–28]. Curcumin has been reported to suppress the growth of tumor cells via cell proliferation pathway (cyclin D1, c-myc), cell survival pathway (Bcl-2, Bcl-xL, cFLIP, XIAP, and cIAP1), caspase activation pathway (caspase -8, -3, and -9), tumor suppressor pathway (p53, p21), death receptor pathway (DR4, DR5), protein kinase pathway, adenosine monophosphate-activated protein kinase (AMPK) pathway [27–30].

2.1.5 Antidiabetic effect

Curcumin exhibited antidiabetic activities by decreasing hepatic glucose production, suppressing inflammatory response stemming from hyperglycemia, increasing

GLUT2, GLUT3, and GLUT4 gene expression, increasing glucose intake of cells, and activating AMPK [31]. It could decrease blood glucose decreasing insulin resistance. Curcumin also played significant role to control of hyperglycemia by downregulating alpha-glucosidase and alpha-amylase activity [32]. After being treated diabetic rats with curcumin the glucose tolerance and insulin sensitivity of diabetic rats were enhanced [33].

2.1.6 Gastrointestinal effect

Research study showed that abdominal pain or irritation and Irritable Bowel Syndrome (IBS) are reduced by the administration of *C. longa* extract [34]. Curcumin could ameliorate the gastric damage, recover from gastric mucosal injury, reduce the leucocyte adherences, intracellular adherence molecule1, and tumor necrosis factor (TNF)-α formation in nonsteroidal anti-inflammatory drugs (NSAIDs)-induced gastropathy in rats [28].

2.1.7 Cardiovascular health

Administration of curcuminoids regulate triglycerides, cholesterol, and other lipids in the bloodstream which are the risk factors for cardiovascular disorders [15, 35, 36]. In an animal model study mice fed with the turmeric added diet possessed 20% less blockage of the arteries in comparison with that mouse fed with the American diet [37]. In another investigation, rabbits fed with turmeric enriched diet to treat the atherosclerosis disease. It has been reported that the cholesterol, and triglycerides levels have been reduced in the turmeric treated rabbits [38]. Turmeric contains antioxidants that inhibit damage to cholesterol and thus provided a protective activity against atherosclerosis [38].

2.2 Garlic (*Allium sativum* L.)

2.2.1 Bioactive compounds

Garlic is composed of various bioactive compounds covering polysaccharides, organosulfur compounds, saponins, and phenolic compounds [39–42]. Among them the major bioactive compound of garlic are organosulfur compounds, such as diallyl thiosulfonate (allicin), diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), E/Z-ajoene, S-allyl-cysteine (SAC), and S-allyl-cysteine sulfoxide (alliin) which are responsible for numerous health benefits [43]. Several phenolic compounds such as resorcylic acid, pyrogallol, gallic acid, rutin, protocatechuic acid, as well as quercetin are significant bioactive compounds contribute to biochemical properties [39–43].

2.2.2 Antioxidant activity

Various in vitro studies revealed that garlic extract exhibited antioxidant activities in DPPH, ABTS, FRAP, H_2O_2 scavenging assay, and Fe^{2+} chelating assays [42–44]. It was reported that storage of garlic for long days accumulated higher level of antioxidant than the fresh ones and shows higher antioxidant activities. However, the postharvest conditions and storage time garlic affect the extent of their antioxidant activities. Usually, fresh garlic had a stronger antioxidant activity than cooked and

fermented garlic [45]. Other than radical scavenging activities earlier studies of garlic extract showed that antioxidant activities of garlic compounds resulted the expression of some antioxidant enzymes, such as heme oxygenase-1 (HO-1), stimulating the activities of antioxidant enzyme activities, and the regulation of the Nrf2-ARE pathway [46]. Earlier studies indicated that garlic saponins scavenge intracellular reactive oxygen species (ROS) and also protect DNA damage induced by H_2O_2.

2.2.3 Anti-inflammatory activities

Garlic offers anti-inflammatory benefits because of the presence of various diallyl disulfide compound that controls the effects of pro-inflammatory cytokines [47, 48]. Garlic has great potential to treat inflammatory diseases including arthritis in humans [49]. *In vitro* and *in vivo* experiments studies reported that garlic could inhibit inflammation mainly by inhibiting inflammatory mediators, such as NO, TNF-α, and IL-1 [47].

2.2.4 Anticancer activities

Several research studies indicated that garlic organosulfur compounds displayed anticancer activities via the inhibiting the cell proliferation and inducing apoptosis of cancer cells both in human culture as well as animal models [50]. Garlic active constituents could protect against diverse cancers, such as colorectal, lung, gastric, and bladder cancers [51–53]. These compounds showed anticancer activities by suppressing cell growth and proliferation and exhibited an anti-proliferative effect on human cancer cell lines, such as liver (HepG2), colon (Caco2), prostate (PC-3), and breast (MCF-7) cancer cells [39]. Moreover, the anticancer properties of garlic occur via the regulation of carcinogen metabolism, induction of apoptosis, suppression of angiogenesis, and inhibition of invasion and migration [39, 44].

2.2.5 Antidiabetic activity

Garlic supplements were effective in the management of type 2 diabetes mellitus. Garlic has been shown to reduce pancreatic cell injury, oxidative stress, and pathological changes in streptomycin-induced type 1 diabetic rats. Results from the meta-analysis performed on 768 patients with type 2 diabetes mellitus in nine randomized controlled trials showed that garlic supplements significantly reduced fructosamine and glycosylated hemoglobin [54]. Fermented garlic products had certain positive effects on obesity by inhibiting lipogenesis and regulating lipid metabolism [55].

2.2.6 Antimicrobial activities

Several research study reported that garlic extract showed antibacterial activities by inhibiting the growth of *Staphylococcus aureus*, *Escherichia coli*, and *Bacillus subtilis* [56]. Garlic extract compounds also showed antifungal activities by inhibiting the growth of fungus *Penicillium funiculosum* [57]. In a clinical trial, the treatment of raw garlic inhibited *Helicobacter pylori* in the stomach of patients with *H. pylori* infection [58].

2.2.7 Cardiovascular protection

Multiple research studies indicated that consumption of garlic and its compounds effectively reduced blood pressure, total cholesterol, low-density lipoprotein

cholesterol, and cardiovascular complexities [59]. Garlic derived compounds reduced oxidative stress, increased the regulation of endothelial nitric oxide (NO), and stimulated the production of the vascular gasotransmitter hydrogen sulfide (H_2S), and inhibited the angiotensin converting enzyme [39, 60]. These could affect to induce smooth muscle cell relaxation, vasodilation, and lower hypertension.

2.3 Ginger (*Zingiber officinale* Rosc)

2.3.1 Bioactive compounds

Major bioactive compounds of gingers comprise of phenolic and terpene compounds [61]. Among the phenolic compounds gingerols, shogaols, and paradols are found to be major ones. In fresh ginger gingerols are available in different forms such as 6-gingerol, 8-gingerol, and 10-gingerol [62, 63]. Ginger is dried and stored for long time after harvesting for commercial purpose. During long time storage gingerols are transformed into corresponding shogaols and shogaols transformed into paradols [64]. Ginger contains several phenolic and terpenoids compounds such as quercetin, zingerone, gingerenone-A, 6-dehydrogingerdione, β-bisabolene, α-curcumene, zingiberene, β-farnesene, and β-sesquiphellandrene, which are major part of ginger essential oils [62]. Also, polysaccharides, lipids, organic acids, and raw fibers are other important compounds available in ginger.

2.3.2 Antioxidant activity

Several *in vitro* studies on antioxidant activities of ginger have been investigated using (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH), and 2,2- azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assays [64]. Number of *in vitro* antioxidant activity assays have also been investigated by using various cell models and provided underlying mechanisms of antioxidant action [62, 64]. For example, ginger extract showed antioxidant effects in human chondrocyte cells, with oxidative stress mediated by interleukin-1β (IL-1β) [65]. It stimulated the expression of several antioxidant enzymes and reduced the generation of ROS and lipid peroxidation [62]. Additionally, ginger extract could reduce the production of ROS in human fibrosarcoma cells with H_2O_2-induced oxidative stress [66]. Ginger and its bioactive compounds (such as 6-shogaol) exhibited antioxidant activity via the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway [67]. 6-shogaol increased intracellular glutathione/glutathione disulfide (GSH/GSSG) and upregulated Nrf2 target gene expression in human colon cancer cells [68].

2.3.3 Anticancer activities

Ginger possessed promising potential for inhibiting the proliferation of multiple cancer cells, such as cancers of the colon, liver, lung, and cervix [62, 69, 70]. Treatment of the human colorectal cancers such as HCT-116, H-1299, and LoVo cells with 6-gingerol and 10-gingerol reduced the cell viability and induced apoptosis in a dose-dependent manner [71, 72]. Ginger extract was responsible for the activating transcription factor 3 (ATF3)-mediated apoptosis induction in human colorectal cancer cells [73]. 6-shogaol and 10-shogaol displayed anti-cancer potentials against human promyelocytic leukemia of HL-60 cells [51]. The anticancer effects of 6-gingerol, 10-gingerol, 6-shogaol, and 10-shogaol acted as prominent bioactive

compounds for anticancer activities that used multiple molecular targets such as NF-κB, TNF-α, PI3K, Caspase-3 [62, 69–72].

2.3.4 Antidiabetic activity

Ginger has been examined for blood glucose lowering effect and improvement in metabolic disorders in diabetic animals and humans. Streptozotocin (STZ) is considered as a diabetogenic agent due to its ability to selectively destroy the β-cells of the pancreatic islets. When STZ rat were administered by ginger extract their blood glucose levels were decreased and the body weights was improved [52]. Oral administration of aqueous ginger extract increased the serum insulin levels and insulin sensitivity in the alloxan-induced and insulin-resistant diabetic rats [53]. Wei et al. demonstrated that 6-shogaol, 6-paradol, and 8-paradol showed antidiabetic activities by improving glucose utilization in both the adipocytes and muscle cells in high-fat diet (HFD) fed rats [74].

2.3.5 Gastrointestinal activity

After oral administration of 6-gingerol in rats it showed high tissue partitioning and distribution in the brain, heart, lung, spleen, liver, kidney, stomach, and small intestinal tissue. However, the highest concentration were detected in the gastrointestinal tract [75]. That is why ginger is commonly used to treating gastrointestinal diseases since ancient times and 6-gingerol and its analogues compounds are reported to be responsible for the gastro-intestinal pharmacological activity [62].

2.4 Onion (*Allium cepa* L.)

2.4.1 Bioactive compounds

Quercetin and its glucoside are major compounds found in onions [76]. Other secondary metabolites are saponins, flavonoids, and phytosterols, polysaccharides, organosulfur compounds-onionin A and cysteine sulfoxides and various phenolic compounds [76, 77]. Anthocyanins are also found in onion. Onion contains three types of alkyl cysteine sulfoxides (ACSO), 1 trans- (±S-1-propenyl-L-cysteine sulfOxide (PECSO), 2(±S-methyl-L-cysteine sulfoxide (MCSO), and 3(±S-propyl-L-cysteine sulfoxide (PCS) [76, 78].

2.4.2 Antioxidant activity

Onion is one of the great sources of natural antioxidant comprising quercetin, kaempferol, and anthocyinns, and some other polyphenolic compounds [76, 77]. Numerous in vitro studies adopting DPPH, ABTS, ORAC and TEAC assay suggested the strong antioxidant potential of onion [78]. Several human trial and other animal model studies demonstrated that the antioxidant role against oxidative stress and lipid peroxidation in various body organs [79, 80]. Due to their antioxidant activities onion and its extract compounds reduced risk of neurodegenerative disorders [81]. Onion decreased lipid peroxidation and enhanced activities of antioxidant enzymes such as SOD, (superoxide dismutase), CAT (catalase), GSH (glutathione), GPx(glutathione peroxidase), TrxR (Thioredoxin reductase), SDH, GST and GR [80].

2.4.3 Anti-inflammatory activity

Presence of polyphenolic compounds in onion such as tannin, flavonoids, anthocyanin, saponin contributed to anti-inflammatory activities [76, 81]. Onion exhibited anti-inflammatory activities due to presence of high level of quercetin and some organosulfur compounds [76, 81]. Quercetin exhibited anti-inflammatory activities by reducing the production of inflammatory cytokines such as IL-1, IL-4, and TNF-α and inhibited the proliferation and activity of lymphocytes [82, 83]. Moreover Umoh et al. showed that quercetin enriched red onion decreased inflammation by inhibition of NF-κB, MARK and STAT-1 [83]. Organosulfur compounds such as thiosulfinates and cepaenes exhibited anti-inflammatory properties by inhibiting the actions of COX and LOX enzymes in arachidonic acid metabolic pathways [84].

2.4.4 Anticancer activities

Earlier research studies indicated that moderate consumption of onions may have a role in the prevention of a wide range of different cancers, including colorectal, breast, lung, stomach, liver, brain, renal, bladder, ovarian, esophagus, and laryngeal cancer [61, 85–87]. Several epidemiological studies reported that due to the high level of flavonoids in onion it protect from developing lung cancers [85]. Numerous research studies demonstrated that the organosulfur compounds in onions are responsible for their anticarcinogenic properties in cell experiments, animals and human trials [86]. Another class of anticarcinogenic compounds of highly abundant is organoselenium compounds [76].

2.4.5 Antimicrobial activity

It has been evident form the earlier research that onion extract possesses antibacterial and antifungal properties [87–90]. *In vitro* studies indicated that aqueous extract of onion inhibited growth of *E. coli*, *Serratia marcescens, Steptococcus species, Acetobacillus odontolyticus, Pseudomonas aeruginosa and Salmonella Typhosa, Streptococcus mutans, Streptococcus sobrinus, Porphyromonas gingivalis and Prevotella intermedia* [87–92]. A petroleum ether extract of onion inhibited the in vitro growth of *Clotridium paraputrificum and S. aureus* [76].

2.4.6 Anti-diabetic activity

Several research studies reported that onion and its extract are strongly associated with managing diabetes and reducing diabetic complications [93–95]. Several animal model studies also reported that onions play significant role in lowering blood sugar levels in fasting diabetic rats [94]. Quercetin from onion inhibited the action of digestive enzymes α-glucosidase and induce hypoglycemia [96]. It also reduced insulin resistance by increasing adiponectin which is responsible for carbohydrate digestion [96]. Quercetin also protected pancreatic islets against oxidative damage by acting through phosphorylation of extracellular signal-regulated kinase (ERK) [97]. Quercetin showed a significant increase in protection against DNA damage from hydrogen peroxide on human diabetic lymphocytes [98]. Sulfur containing compounds such as S-methly cysteine sulpoxide and S-allyl cysteine sulpoxide controlled the blood glucose and lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG CoA reductase and increase the level of

insulin in blood [99]. Earlier study indicated that administration of onion extract to human reduced LDL-C, waist circumference, and total cholesterol in blood [100–102].

2.5 Chili (*Capsicum annuum* L.)

2.5.1 Bioactive compounds

Capsaicinoids, an acid amide of vanillylamine with C9-C12 branched fatty acid chain is the major compound of chili that confers the characteristic pungency [103]. Other major isomers of capsacins are dihydrocapsaicin, nordihydrocapsaicin, homocapsaicin, and homodihydrocapsaicin [103–105]. Other bioactive valuable bioactive compounds such as polyphenols (phenolic acids, apigenin, luteolin, quercetin, catechins, anthocyanins and proanthocyanidins), steroids, saponins, anthroquinones, carotenoids, terpenoids and alkaloids are highly abundant in chili peppers [103–106].

2.5.2 Antioxidant activity

As chili pepper contains high level of vitamin C, E, anthocyanin, and phenolic compounds it showed strong antioxidant activities *in vitro, in vivo,* and clinical studies [103–107]. From earlier research studies it was demonstrated a positive correlation between phenolic content and antioxidant potential with strong radical scavenging activities in ABTS, DPPH, and FRAP assays [103]. Various *in vivo* studies indicated antioxidant activities by mitigating oxidative stress in various tissues or organs [104–106].

2.5.3 Anti-inflammatory activity

It has been shown that capsaicin could reduce inflammations in different animal models and human trials. Capsacin has been reported to have anti-inflammatory activities by inhibiting the NO, IL-6, and TNF-α in LPS-induced in RAW 264.7 cells [107, 108]. Capsaicin reduced the inflammatory responses by inhibiting the pro-inflammatory cytokines such as interleukin 1β (IL-1β) and tumor nuclear factor-kappa (NF-κ) [109]. Capsaicin could be used as analgesic since it could induce inflammatory effects in adipose tissues [110].

2.5.4 Anticancer properties

Chili phytochemicals has been reported to trigger apoptosis of various cancerous cell lines including skin cancer, colon cancer, bladder cancer, breast cancer, prostate cancer and lung cancer in human and some other experimental animal models [111–120]. Capsaicin exhibited inhibitory effects against cancer initiation, promotion, progression, and metastasis. It has been found that capsaicin could inhibit nuclear factor-kappa (NF-κ) activation in prostate cancer cells. In some cases, capsaicin could alter the expression of several genes involved in cancer growth process. For example, capsaicin down-regulated Bcl-2 (B-cell lymphoma 2) expression during the growth of skin cancer in mouse [113, 115]. Capsaicin induced p53 phosphorylation at the Ser-15 residue and activated the apoptosis of cancer cells [119]. In vitro studies revealed that capsaicin could inhibit the growth of blood cancer by inhibiting human T-cell leukemia virus type 1 [120].

2.5.5 Antimicrobial activity

It has been demonstrated that capsaicinoids and other phenolic compounds inhibited growth of microorganism like bacteria, yeasts, and fungi [121]. Capsaicin could inactivate the virus binding proteins and prevent their replication [121]. Previous reports supported that capsaicin showed strong antimicrobial activities against *Streptococcus pyogenes, E. coli, S. aureus, Proteus mirabilis, Proteus vulgaris, P. aeruginosa, Enterobacter aerogenes and S. mutans*. Bell pepper extract inhibited the *Listeria monocytogenes, Salmonella typhimurium, S. aureus,* and *Bacillus cereus* including few foodborne bacteria *Salmonella typgimurium* [122].

2.5.6 Anti-diabetic activity

Chili pepper imparted antidiabetic activity by their potential inhibition capacities of α-amylase and α-glucosidase activities which has a significant effect in carbohydrate metabolism [123]. It has been reported that consumption of chili pepper reduces the glucose absorption in the intestine and controls post-prandial rise of glucose [124]. Administration of capsaicin to rats lowered blood glucose levels and increased blood insulin level [125].

2.5.7 Cardiovascular activity

Capsaicin promoted vascular health by increasing nitric oxide (NO) production and reducing inflammatory responses. It also reduced low-density lipoprotein (LDL) levels, increased high-density lipoprotein (HDL) levels, and reduced oxidative stress levels in various tissues [126]. Capsaicin could lower low-density lipoprotein cholesterol (LDL-C), plasma cholesterol, and inhibits LPS-induced IL-1β, IL-6 and TNF-α production in a time- and dose-dependent [127–129].

2.6 Cinnamon bark (*Cinnamomum cassia*)

2.6.1 Bioactive compounds

The major phytochemical in cinnamon bark is cinnamaldehyde. Some other bioactive compounds of essential oils in cinnamon bark are cinnamic acid, coumarin, cinnamyl alcohol, and 2-methoxycinnamaldehyde [130]. Cinnamon bark also contain terpenoids such as oxygenated sesquiterpenes, oxygenated monoterpenes, sesquiterpene hydrocarbon [130–132]. In addition to essential oils and terpenoids cinnamon bark consist of guaiacol, benzenepropanal, cis-cinnamaldehyde, bornyl acetate, acetophenone, geranyl acetate, tetradecanal. Oxygenated monoterpenes are eucalyptol, linalool, borneol, L-α-terpineol, benzaldehyde, anethole, and eugenol. Some of the sesquiterpene hydrocarbons are α-cubebene, copaene, β-caryophyllene, α-muurolene, trans-α-bergamotene, α-humulene, α-amorphene, 1 s-cis-calamenene, calarene, cedrene, and β-cadinene [130–132].

2.6.2 Antioxidant activity

Cinnamon is considered as one of the most important flavored spices with strong antioxidant activity [133]. Different extraction method has been applied to investigate the antioxidant activities of cinnamon bark extract. For example Yang et al. [134]

investigated the antioxidant activity of ethanol and aqueous extracts of cassia bark to evaluate its antioxidant activity by the DPPH and ABTS radical scavenging activity. Both extracts reported to possess strong antioxidant activities however ethanolic extract possessed higher than the aqueous extract [134]. The polyphenolic extracts of cinnamon bark reduced oxidative stress in a dose-dependent manner through inhibition of 5-lipooxygenase enzyme [135].

2.6.3 Anti-inflammatory activities

Numerous research studies reported that cinnamon essential oil possess anti-inflammatory activities and have been used in soothing and numbing for joint aches and pain [136, 137]. On human dermal fibroblast system, a model of chronic inflammation and fibrosis, cinnamon (*Cinnamomum zeylanicum*) bark essential oil (CBEO) significantly inhibited the production of several inflammatory biomarkers such as vascular cell adhesion molecule-1, intercellular cell adhesion molecule-1, monocyte chemoattractant protein-1, interferon gamma induced protein 10 [138]. Cinnamon extract also showed significant reduction in both IL-6 and TNF-α level on Lipopolysaccharide (LPS)-induced Interlukin-6 (IL-6) and Tumor Necrosis Factor-α (TNF-α) which indicates anti-inflammatory effect [136–138].

2.6.4 Antidiabetic effect

Available *in vitro* and *in vivo* evidence demonstrated that cinnamon confers health benefits in relation to hypoglycaemic activity [139, 140]. Consumption of cinnamon bark reported to have antidiabetic activities as it showed improvements in fasting blood glucose and lipid profile after consumption [139]. *In vivo* studies on cinnamon extract showed that it could improve insulin action via enhancing glucose uptake [141]. The cinnamon bark extract could reduce the blood glucose level by decreasing the carbohydrate absorption in the small intestine [142]. Another *in vivo* study demonstrated that administration of cassia bark extracts the intestinal glycosidase activity was reduced, whereas the serum insulin level and HDL-cholesterol level are increased [142]. Compiling the human studies of 2003–2018 concerning the glycemic profiles of individuals with type II diabetes mellitus showed that fasting blood glucose reduced from 12.9 to 52.2 mg/dL and HbA1c from 0.27 to 0.83%, after moderate consumption of cinnamon extract [143]. Some meta-analysis also indicated that cinnamon powder intake decreased fasting blood glucose and HbA1c [144]. Methylhydroxychalcone polymer (MHCP) in cinnamon bark reported as effective mimetic of insulin which could activate glycogen synthase and inhibit actions of glycogen synthase kinase-3b as well as insulin receptor phosphorylation homologous [145].

2.6.5 Cardiovascular health

Previous research studies reported that cinnamon could reduce the risk of cardiovascular diseases and its complications such as cardiac ischemia, cardiac hypertrophy, and myocardial infarction [130]. Cinnamaldehyde and cinnamic acid are among the main cinnamon compounds with protective effects on cardiovascular diseases through different molecular mechanisms [130]. Cinnamaldehyde played crucial role in the cardiovascular system like vasorelaxation and reduction in blood pressure [146]. Cinnamaldehyde could protect human umbilical vein endothelial cells from the oxidative stress via stimulation of the nuclear factor erythroid

2-related factor signaling pathway [147]. Cinnamaldehyde prevents the progression of hypertension in insulin deficiency and insulin resistance due to its insulinotropic properties [148]. Using Wistar rats of induced metabolic syndrome it was found that cinnamon altered the body composition in association with improved insulin sensitivity [149].

2.7 Black pepper (*Piper nigrum*)

2.7.1 Bioactive compounds

Black pepper is composed of carbohydrate, proteins, fibers, fats, minerals, and aromatic phytochemicals. Among the phytochemicals piperine is the major bioactive compound that gives the pungent flavor to black pepper [150]. Other volatile flavor compounds in black pepper are terpenes, α- and β-pinene, myrcene, α-phellandrene, limonene, linalool, methyl propanal, methylbutanal, butyric acid, methylpyrazine and methoxypyrazines [150–153].

2.7.2 Antioxidant activity

It is evident from earlier research investigations that piperine from black pepper exhibited antioxidant potential and reduce lipid peroxidation [150, 151]. and *in vitro* study demonstrated that the antioxidant potential of piperine could be resulted by trapping superoxide and hydroxyl free radicals, retarding lipid peroxidation, and inhibiting human lipoxygenase activities [151]. Piperine acted as potent antioxidant by reducing thiobarbituric acid-reactive substances and maintaining superoxide dismutase, catalase, glutathione peroxidase, glutathione- S-transferase, and glutathione levels [153].

2.7.3 Anti-inflammatory activities

Number research studies demonstrated analgesic and anti-inflammatory activity of piperine and black pepper extracts using various animal model and clinical studies [154]. Piperine also acted as useful gastrointestinal anti-inflammatory agent. Moreover, it showed anti-inflammatory effects on interleukin 1β (IL-1β)-stimulated fibroblast-like synoviocytes [155]. Piperine effectively treated asthma by inhibiting airway inflammation due to suppression of cytokines (IL-4, IL-5, IL-13) and enhanced TGF-β gene expression in the lungs in a murine model system [156].

2.7.4 Antidiabetic activity

Various animal model and human trial studies reported hypoglycemic effect of piperine. Administration of peiperine to hyperglycemic rats reported that it could reduce lipid peroxidation, hyperglycemic activities, and showed antioxidant activities. With Alloxan-induced diabetic rats it was reported piperine could reduce the blood glucose level [157]. Also, it was reported to enhance the serum cholesterol, serum liver cholesterol concentration, and hepatic cholesterol-7α-hydroxylase level after administration of piperine. Several research studies demonstrated that piperine could be used as bioavailability enhancer for other phytochemicals to receive better health beneficial properties. For examples, co-administration of curcumin with piperine was found to decrease the levels of total cholesterol (TC), triglyceride (TG) and

low-density lipoprotein cholesterol in the serum and liver in higher extent compared with administration of curcumin alone [158].

2.7.5 Cardiovascular health

Piperine played critical role on cardiovascular disease by mediating oxidation status, lipid metabolism, and inflammation [150]. Piperine inhibited development of lipid droplet, oxidized low density lipoprotein uptake in macrophages, retarded lipid peroxidation, induce cholesterol efflux from macrophages [159]. It has been reported to show antihypertensive, antithrombosis effect, and protect arterial stenosis through retarding vascular smooth muscle cell proliferation [150].

3. Bioaccebilities and bioavailabilities of bioactive compounds

In order to receive optimum health benefits from the bioactive compounds of foods, they have to be released from the food matrix and be bioaccessible in the gastrointestinal tract, then undergo metabolism and reach the target tissue of action. Finally, this phenomenon determines the bioavailability of the biomolecules before showing its bioefficacy [11]. Bioavailability is a complex process that involves several different phases like liberation, absorption, distribution, metabolism, and elimination. There are several factors that could affect bioavailability of bioactive compounds such as nature of food matrices, molecular structures, metabolizing enzymes, type of food processing and cooking methods [160]. Improvement in the bioavailability of food component could enhance bioefficacy of bioactive compounds. Several technologies have been developed to improve the bioavailability such as structural modifications, colloidal systems, entrapped in liposome, inclusion complexation, nanoencapsulation polymer encapsulation, and emulsion [161].

As aforementioned curcumin has many potential health benefits such as anti-inflammatory, antioxidant, anticancer, antiviral, and neurotrophic activity. However, due to its insolubility in water, the poor intestinal absorption, structural instability limits the potential therapeutic and nutritional benefits [24]. Therefore, efforts have been directed to develop curcumin formulations with greater bioavailability and systemic tissue distribution [162]. Among them modification of curcumin's chemical structure, conjugation of curcumin with lipid molecules, nanoparticle encapsulated curcumin, additive matrices with piperine are some of major approaches [162]. In a study polylactic-co-glycolic acid (PLGA) and PLGA-polyethylene glycol (PEG) (PLGA-PEG) blend nanoparticles containing curcumin in rats and it was found that compared to the curcumin aqueous suspension, the PLGA and PLGA-PEG nanoparticles increased the curcumin bioavailability by 15.6- and 55.4-fold, respectively [163]. Yu et al. [164] developed a food grade curcuminoid organogel using Span 20 and medium chain triacylglycerols with high bioaccessibility and high loading of curcumin. Among the biological active components of garlic, sulfur compounds especially allicin have antioxidant, anticancer and antibacterial functions and thus are considered as the main pharmacological active components in garlic. However, it was demonstrated it suffers from instability, low aqueous solubility, strong gastrointestinal irritation and low bioavailability. To circumvent this issue nanotechnology and other embedding technology have been used. The bioactive compounds extracted from garlic were incorporated into biodegradable and biocompatible nanoparticles such as liposomes, nano-emulsions, solid lipid nanoparticles (SLN),

micelles, nano-spheres and nano-capsules, protein-based nanoparticles, biopolymeric particles, and phyto-phospholipid complexes [165]. These techniques could enhance their stability, aqueous solubility, bioavailability, target specificity and circulation time. Garlic oil nanoemulsion generated with ultrasonic emulsification could improve efficacy and reduce toxicity in treating or preventing dyslipidemia [166]. Garlic Essential Oil (GEO) have been nanoencapsulated with chitosan and persian gum as wall materials which improved stability and dispersibility [167]. GEO have been embedded in liposomes formed by lecithin (LT) and β-sitosterol (β-S) and improved the bioavailability upto 51%. [168]. [6]-gingerol is the key component of ginger that provides several health benefits. However due to its poor solubility in water coupled it results in low bioavailability. Several strategies such as gingerol incorporated nanoparticles, micelles, emulsions, solid dispersion, liposomes have been prepared to improve the bioavailability. The formulation of [6]-gingerol like proliposomes prepared through modified thin-film dispersion method, which were physicochemically stable with narrow size distribution and improved bioavailability and antitumor activity [169]. Another formulation was prepared by using solid dispersion of ginger extract with hydrophilic polymer, hydroxypropyl cellulose that improved 5 fold higher gingerol bioavailability [170, 171]. Quercetin, the major compound of onion also suffers low availability due to its poor solubility [172]. Several formulations been prepared to improve the poor solubility of quercetin. For example, β-cyclodextrin inclusion complex of quercetin, nano-system quercetin prepared using Eudragit®E and polyvinyl alcohol (PVA), solid lipid nanoparticles of quercetin using soybean lecithin, Tween 80, and PEG 400 increased the poor solubility and good dispersion of quercetin [173–176]. Similarly, capsaicin the major bioactive compounds of pepper suffer some limitations for the short half-life, low bioavailability, burning sensation and skin irritation etc. Several strategies have been applied to improve the delivery of capsaicin such as emerging micro and nanotechnologies to encapsulate capsaicin to liposomes eg: phosphatidylcholine (PC) liposomes, microemulsion, solid-lipid nanoparticle, polymeric carriers such as micelle (eg capsaicin with polyvinylpyrrolidone (PVP)/sodium cholate/phospholipid mixed micellar system, dendrimers (dendrimers formed from oleoyl chloride, Polyethylene glycol (PEG) 400, and triethylamine, and polymersome), Inorganic carriers (metal nanoparticles egcapsaicin-capped silver nanoparticles, carbon spheres) [177–180].

4. Conclusions

Herb and spices are receiving continued interest in food industry because of their numerous health benefits from providing nutrition and maintaining healthy lives. Due to the presence several group of phytochemicals comprising diverse group of phytochemicals including polyphenols, carotenoids, alkaloids, terpenoids, phytosterols, glucosinolates, and many others it protects from chronic diseases like inflammation, diabetes, cancer, Alzheimers, cardiovascular diseases, dementia, and obesities. *In vtro*, *in vivo*, cell culture, and clinical research studies have uncovered the role of these phytochemicals in most of the heath beneficial properties. However, in most of the cases the detail mechanisms are not completely understood. Moreover, depending on the nature of food ingredients and processing of food, nature of eating style greatly affects the bioavailability of active components of spices which in turn affect its bioefficacy. Significant studies indicated the existence of positive health effects from the isolated compounds, e.g. curcumin, quercetin, allicin, gingerol, piperine

etc. In some cases, the isolated compounds may not work effectively but combination of one phytochemical with others in food matrices leads to the synergistic effects in biological properties. Thus, combinations of selective phytochemicals may exert multiple functions in the human body after consumption. Using emerging technology of formulation sciences would lead to the development of novel formulations and nutrient supplements to improve the bioefficacy and synergistic effect of spices phytochemicals after consumption.

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