Immunomodulatory perspectives of potential biological spices with special reference to cancer and diabetes

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ABSTRACT

In millennia, nutritionists are motivated to explore innovative approaches against lifestyle-related syndromes for improving public health and life span. Spices are the promising and cost-effective choice for consumer owing to their high antioxidant potential, that is, ability to entrap free radicals at cellular level to alleviate various metabolic syndromes. Besides that, spices are not only popular in developed countries, but also attaining consideration in developing world due to extensive biological activity and safe status. In this regard, contemporary nutrition regime has gained researchers’ attention on spices to mitigate various metabolic syndromes. Moreover, the promising bioactive moieties – that is, curcumin and curcuminoids (turmeric); limonene (cardamom), allicin, allyl isothiocyanate (garlic), cinnamic aldehyde, 2-hydroxycinnamaldehyde, and eugenol (cinnamon); gingerol, zingiberone, zingiberene (ginger), dipropyle disulfides, and quercetin (onion); piperidine piperine, limonene, α- and β-pinene (black pepper); crocetin, crocin, and safranal (saffron) – have been identified as chemopreventing agents against various malignancies.

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Introduction

The role of nutrition in appropriate functionality of the immune system is well established since ancient times (Saeed et al., 2016). Spices have gained enormous popularity on nutraceutical and functional value as mentioned in previous histories. In addition to increasing the aroma and savor of foods, herbs and spices are widely utilized as preventive and curative agents in degenerative diseases (Komalavalli, Nithya, Muthukumarasamy, & Mohan, 2013). Herbal medicines are now being used for the treatment of various diseases, including cancer and diabetes in many countries (Ghazanfari et al., 2013). Approximately 180 spice-derived bioactive components have been reported as effective against various...
These spices showed impressive biological responses and curing role against a wide range of disorders such as cancer, diabetes, and cardiovascular diseases (Komalavalli, Nithya, Muthukumarasamy, & Mohan, 2014). These are potential sources of biochemical compounds such as polyphenols, flavonoids, quinines, polypeptides, terpenoids, alkaloids, or their oxygen-substituted byproducts and acted like as antioxidants. These are cherished mixtures of terpenoids (such as geraniol, linalool, menthol, α-terpineol, borneol, citronnillol, and thujanol) and phenols (including carvacrol, thymol, guaiacol, and eugenol and aromatic aldehydes) (Raina & Negi, 2012). Spices suppress the oxidative rancidity, slow down the development of off-flavor and retardation of microbial growth in food-containing products such as snack foods and meat products (Houghton, 2015).

1. Turmeric

Turmeric (Curcuma longa Zingiberaceae) is the potential source of at least 235 compounds, primarily phenolic compounds and terpenoids such as diarylpentanoids, diaryleptanoids, sesquiterpenes, monoterpenes, triterpenoids, diterpenes, sterols, and alkaloids. It is a mixture of three curcuminoids, 71.5% curcumin (curcumin I), 19.4% demethoxycurcumin (curcumin II), and 9.1% bisdemethoxycurcumin (curcumin III) (Kim, Zamel, Bai, & Liu, 2013). Schneider, Gordon, Edwards, and Luis (2015) determined that turmeric suppressed the activation of NF-κB induced by phorbol myristate acetate (PMA), TNF-α, or H2O2 through delaying the phosphorylation of IKKα. Likewise, it also suppresses the tissue plasminogen activator (TPA)-induced NF-κB activation through weakening consequent translocation of the p65 subunit and the degradation of IκBα in HL-60 cells. It lowers the TPA-encouraged activation of NF-κB through direct intermission of the binding of NF-κB to its agreement DNA sequences (Sun, Liu, Wu, Feng, & Meng, 2015). In addition, curcumin also blocks IκBα degradation, cytokine-encouraged NF-κB DNA-binding activity, IKK activity in HT-29, RelA atomic translocation, IκB serine 32 phosphorylation, Caco-2, and EC-6 cells (Gonçalves et al., 2015). The previous explorations of Abdel-Daim and Abdou (2015) determined that high administration of curcumin inhibited the BCG-convinced IL-8 production and LPS (lipopolysaccharide)-mediated TLR2 mRNA induction on mouse splenic macrophages in human monocytes and gingival fibroblasts through overwhelming NF-κB initiation. Additionally, it also powerfully inhibits propagation of HT-29 and HCT-15 human colon tumor cell lines (Kocaadam & Sanlier, 2015).

Curcumin has chemopreventive potential against diabetic secondary complications, that is, wound healing, retinopathy, reduction of advanced glycation, and diabetic nephropathy-renal lesions end products. Curcumin exhibits anti-inflammatory potential in cancer-necrosis-factor-α-treated HaCaT cells through reserve of nuclear factor-κB and mitogen-stimulated protein kinase (Cho, Lee, & Kim, 2007). In diabetic rats, it enhances the activation of peroxisome proliferator-activated receptor (PPAR)-γ and increases the antioxidant level of pancreatic β-cells (Murugan & Pari, 2006). Curcumin shows the protective effect in diabetes rats due to the inhibition of vascular endothelial growth factor (VEGF) and NF-κB signaling, pro-inflammatory cytokines (IL-1b), and increasing activity of chaperone molecules. Similarly, Jang et al. (2008) determined that curcumin normalized the lipid blood profile along with attenuation in insulin resistance, and reduction in leptin
levels in hamsters-fed high-fat rats. Furthermore, turmeric lowered blood sugar glucose level, reduced TNF-α levels, and improved the insulin sensitivity in male Sprague Dawley rats. It also improved glucose tolerance, amplified adipose tissue adiponectin making, lowered insulin conflict, and pro-inflammatory cytokines with IL-1β, TNF-α, and partial white adipose tissue macrophage permeation in obese, leptin-deficient ob/ob C57 BL/6J rats (Weisberg et al., 2003). Wickenberg, Ingemansson, and Hlebowicz (2010) assessed that the supplementation of 6 g/day turmeric improved the postprandial serum insulin levels in mice, whilst lowered the plasma glucose levels.

2. Garlic

Garlic (Allium sativum L.) is the most widely studied and oldest cultivated plant and has been used in food-based products for over 4000 years. The word ‘garlic’ was derived from the Anglo-saxon ‘gar-leac’ or spike plant (Sheoran et al., 2017). It comprises more than 200 biochemical compounds and additional key compounds are allicin, alliiin, cyroalliiin, dialyl disulfide (DADS), and ajoene, β-phellandrene, geraniol, citral, α-phellandrene, linalool, and enzymes (allinase, myrosinase, and peroxidase) (Karangiya et al., 2016). Throughout metabolism, garlic is transformed into various metabolites such as allyl-mercaptan, N-acetyl-S-allyl cysteine, dialyl sulfoxide, dialyl sulfide, dialyl-sulfone, dialyl disulfide, and allylmethyl sulfide. About pharmacological role, garlic has prospective to prevent the cells from the different cancer phases through neutralizing free radicals, improving glutathione contents, increasing the actions of antioxidant enzymes, that is, S-transferase, glutathione, catalase, suppression of cytochrome p450E1, avoiding the chromosomal damage, and DNA repair mechanisms (Kim, 2016). As an anti-carcinogenic agent, garlic and its organosulfur compounds (OSCs) prevent the cell proliferation through blocking cell cycle process, inhibition of DNA adduct formation, bringing apoptosis, upregulation of antioxidant defenses, inflection of carcinogen metabolism, and DNA repair systems (Percival, 2016). These dietary bioactive OSCs modulate the cancer cascades and act as latent chemopreventive and chemotherapeutic agents (Tsubura, Lai, Kuwata, Uehara, & Yoshizawa, 2011). The garlic and its oil-soluble compounds such as DADS downfall the carcinogen activation, cause arrest at G2/M stage of cell cycle, enhance phase 2 detoxifying processes, increase acetylation of histones, encourage mitochondrial apoptotic pathway, effect gap-junctional intercellular communication, connection in signal transduction, modulation of cellular redox state, post-translational alteration, and participate in the growth of multidrug resistance. They also inhibit the propagation of tumor cells in vitro through the induction of apoptosis (Iciek, Kwiecień, & Włodek, 2009; Melino, Sabelli, & Paci, 2011).

Similarly, garlic extract also depresses the blood sugar level and inhibits superoxide formation and lipid per-oxidation in rats. S-allyl cysteine is a potent antioxidant which blocked the AGEs synthesis that augmented the insulin release effect and hepatic metabolism (Khan et al., 2012). Allicin controls the blood sugar level in serum and modifies the activities of hemoglobin coenzyme-A reductase and liver hexokinase glucose-6-phosphatase. Likewise, supplementation of allicin to rabbits crucially enhanced the liver glycogen and free amino acids contents that overwhelms the triglycerides level, liver serum proteins, and fasting blood sugar (FBS) when compared to high sucrose-fed diet mice (Tripathi, Bhoyar, & Baheti, 2011).
3. Ginger

Ginger (*Zingiber officinale*) belongs to the family Zingiberaceae and is the source of gingerol (5-hydroxy-1-(4-hydroxy-3-methoxy phenyl) decan-3-one. It is also a promising source of essential volatile oils, including 30–70% alpha-zingiberene, 15–20% beta-sesquiphellandrene, 10–15% beta-bisabolene, curcumene, betaphellandrene, camphene, zingiberene, cineole, geranyl acetate, terpineol, terpenes, geraniol, borneol, linalool, alpha-farnesene, and limonene (Kumar, Manasa, Rahman, & Sudhakar, 2012). Gingerol overpowers the production of reactive oxygen species brought by ferric chloride FeCl3-ascorbatesystem and also hinders the oxidation activity of xanthine. It also increases the concentration of catalase and SOD in the tissues, whilst the level of oxidized glutathione lowers (Manju & Nalini, 2005).

The previous results of Hsu et al. (2010) demonstrated that 6-dehydrogingerdione prevented breast cancer through activating caspase, upregulating p21 level and downregulating cyclin A, cyclin B1, Cdc25C, Cdc2, and hence arrested cells at G2/M phase and caused apoptosis. Apparently, ginger works as an anticancer agent overblocking NF-κB activation by the inhibition of TNF-α pro-inflammatory cytokine (Kim, Chun, Kundu, & Surh, 2004). Likewise, 6-paradol and 6-gingerol possess a solid anti-inflammatory action and inhibit the TNF-α production in TPA-treated female ICR rats (Shishodia & Aggarwal, 2006). The gingerols and zerumbone have been known as strong inhibitors for pro-inflammatory cytokine TNF and NF-κB. It blocks the different steps of NF-κB signaling pathway, including translocation of NF-κB into the nucleus, DNA obligatory of dimers with the basal transcriptional equipment, and activates the NF-κB signaling cascade (Habib et al., 2008).

Akhani, Vishwakarma, and Goyal (2004) determined that ginger juice exhibits hypoglycemic activities in both usual and streptozotocin (STZ)-induced diabetic mice, through its inhibitory effect on serotonin-induced hyperglycemic and hypoinsulinemia. On the other end, the management of ginger extract to STZ-induced diabetic mice caused substantial decreases in plasma malondialdehyde concentration and significant increases in total antioxidant capacity as well as erythrocyte antioxidant enzyme activities (GSH-Px and SOD) (Afshari et al., 2007).

4. Cinnamon

Cinnamon (*Cinnamomum zeylanicum*) is the source of cinnamaldehyde and trans-cinnamaldehyde essential oils, which showed various health-endorsing properties (Yeh et al., 2013). It is a source of several bioactive components, that is, cinnamaldehyde, cinnamic acid, cinnamate, and several essential oils, including trans-cinnamaldehyde, cinnamy1 acetate, eugenol, 1-borneol, b-caryophyllene, caryophyllene oxide, E-nerolidol, L-borneyl acetate, α-terpineol, α-cubebeene, α-thujene, and terpinolene. Cinnamon and its polyphenols extract repressed the proliferation of cancer cells lines and encouraged cell death of tumor cells through inhibiting AP1 and NF-kB activity and their target genes i.e. Bcl-xL, Bcl-2, and upregulating pro-apoptotic molecules (Kwon et al., 2010). It also lowers the stages of HIF-1α and COX-2 in melanoma cell outlines and in the melanoma mouse model. Cinnamon expressively decreases the growth rate of SiHa cells in a dose conditional manner and limits the development of cervical cancer cells in rats (Singh et al., 2009). It downregulates the appearance of Her-2 in SiHa cells and this appearance is linked with the decrease in the expression of MMP-2 protein. The administration
of cinnamon significantly inhibited the azoxymethane (AOM) encouraged colon carcinogenesis in mice (Liao et al., 2015).

It also improved the insulin receptor (IR) function through the enzyme that bases insulin to bind to cells and suppressing the enzyme (IR phosphatase), important to phosphorylation of the IR that is linked with enhanced insulin sensitivity. The methylhydroxychalcone polymer (MHCP) in cinnamon has the ability to act as insulin mimetic in 3T3-L1 adipocytes (Jarvill-taylor, Anderson, & Graves, 2001). The MHCP downregulated glycogen synthase kinase-3β (GSK-3β) activity and stimulated the autophosphorylation of the IR, glycogen synthesis, glycogen synthase (GS) activity, and upregulated glucose endorsement in 3T3-L1 adipocytes. Anderson et al. (2004) assessed the in vitro insulin-potentiating activity of procyanidin type-A polymers (monomers) of cinnamon in epididymal fat cells (Shiao, Lee, Lin, & Wang, 1994). Similarly, cinnamon also reduces the sugar level through increasing glucose transport (Kannappan, Jayaraman, Rajasekar, Ravichandran, & Anuradha, 2006; Kim, Hynu, & Choung, 2006)

5. Clove

Clove is a prominent source of essential oils such as caryophyllene, eugenol, alpha-terpinyl acetate, alpha-humulene, methyl eugenol, eugenyl, naphthalene, actyl eugenol, heptanone, sesquiterpenes, chavicol, vanillian, and methyl salicylate pinene (Sengupta, Ghosh, & Bhattacharjee, 2005). Kim et al. (2005) determined the chemopreventive role of eugenol in peel tumor of rats. The orally administrated eugenol controlled the proliferation of carcinogenesis at the premalignant stage. It also downregulates the H-ras, c-Myc, and Bcl2 countenance along with the upregulated Bax, p53, and active caspase-3 expression in the skin lesions of the rats. Similarly, eugenol treatment recovers the cellular GSH and activities of various enzymes such as GR, CAT, GPX, GST, and XO level. It also enhances the p21 and p53 WAF1 stages in the 7,12-dimethylbenz (α) anthracene (DMBA)-treated rats. It also overwhelms the COX-2 and iNOS countenance and levels of pro-inflammatory cytokines (TNF-α, IL-6, PGE-2), and ODC activity in mice. Eugenol has an inhibitory effect on the NF-kB, upstream signing molecule that controls the look of above-mentioned genes. The concentration of clove oil at 300 μl/ml presented extreme cell death and apoptotic cell demise in TE-13 cells within 1 day whilst DU-145 cells showed slight cell death (Dwivedi, Shrivastava, Hussain, Ganguly, & Bharadwaj, 2011). Furthermore, eugenol protects the decrease of glutathione and antioxidant enzymes caused by TPA (Kaur, Athar, & Alam, 2010). Gupta, Garg, Uniyal, and Kumari (2008) showed that orally administrated clove protects the living organism from damage caused by free radicals, lipid per-oxidation, and DNA strand breaking, as well as protein damage.

During cellular metabolism, production of reactive oxygen species and environmental factors injured the cell membranes that caused diabetes (Hartnett et al., 2000). STZ-induced diabetic rats increase the oxidative stress, oxidized LDL-cholesterol, and other lipoproteins problems (Jafarnejad, Bathaie, Nakhjavani, & Hassan, 2008).

6. Basil

The Basil (Ocimum sanctum) belongs to family Labiatae. It is a rich source of essential oil which contains octane, α-thujene, ethyl 2-methyl butyrate, α-pinene, (Z)-3-hexanol,
myrecene, β-pinene, limocene, ethyl benzene, allo-oc-imene, terpiniolene, α-cubebene, butyl-benzene, eugenol, linalool, carvacrol, borneol, methyl eugenol, iedol, humulene oxide, germacrene-D, τ-cadinol, α-guaiol, (EZ)-famesol, α-bisabolol, elemol, cissesquisainene hydrate, selin-11-en-4-α-ol, tetradecanal, and 14-hydroxy-α-humulene. These oils have antioxidant potential due to their redox properties that quench singlet and triplet oxygen, and absorb and neutralize free radicals (Asami, Hong, Barrett, & Mitchell, 2003). The application of basil downregulates the expression of genes that endorses the propagation, migration, and assault of tumor cells and also downregulates the FAK, activated ERK-1/2, and p65 (subunit of NF-κB). The aqueous extract of basil considerably overcomes the growth of orthotopically transplanted cancer cells. It upregulates the genes that induce apoptosis (BAD), and metastasis (E-cadherin) and downregulate such genes that endorse chemo/radiation resistance, and survival (Bcl-2 and Bcl-xL) (Shimizu et al., 2013). Basil possesses the anticancer mechanisms through lowering nitric oxide (NO), decreasing the incidence of 3-methyl dimethyl amino azobenzene, and benzo (a) pyrine-induced neoplasia and inducing hematomas in mice (Kim et al., 2010). The alcoholic extract of basil plant enhances the activities of cytochrome b5, glutathione S-transferase, cytochrome p450, and aryl hydrocarbon hydroxylase that detoxify the carcinogens and mutagens (Govind & Madhuri, 2006). The basil plant has potential to lower the incidence of 3-methyl-4-dimethylaminoazobenzene-induced hepatomas of mice and benzo (a) pyrine-induced neoplasia of forestomach in rats. Likewise, the ethanolic extract of basil leaves overcomes the oxidative stress and DMBA-persuaded genotoxicity through sinking the amount of lipid and protein corrosion, moderating xenobiotic metabolizing enzymes, and upregulating antioxidant emplacements. Similarly, Manikandan, Letchoumy, Prathiba, and Nagini (2007) resolve the anticancer potential of basil beside N-methyl-N′-nitro-N-nitrosoguanidine-persuaded gastric carcinogenesis, cell propagation, apoptosis, and angiogenesis in a rogue forestomach carcinogenesis model.

7. Cumin

Cumin (Nigella sativa L.) belongs to family Ranunculaceae and is an excellent source of thymoquinone (TQ), thymol, and dithymoquinone compounds. These compounds are operative against cardiovascular diseases, different types of human cancers, diabetes complications, kidney disease, asthma, etc. (Lutterodt et al., 2010). TQ shows anticancer effect against human myeloblastic leukemia HL-60 prison cell. It also induces apoptosis linked with DNA ripping and a reduction in mitochondrial membrane probable in 518A2 melanoma and HL-60 cells. TQ inhibits the MCF-7 breast tumor cells lines in mice (Farah & Begum, 2003). It has 88% inhibitory effect on human hepatoma HepG2 cells. Similarly, it increases the glutathione transferase and quinone reductase contents and TQ. The oral managements of cumin (0.05–0.1 g/kg BW) meaningfully lowered the DNA synthesis, H2O2 generation, and incidence of tumors. It suppressed the proliferation, DNA synthesis, and viability of cancerous cells (C4-B, LNCaP, PC-3, and DU145).

In antidiabetic effects, cumin considerably enhanced the area beneath the glucose acceptance curve and hyperglycemic peak in rabbits. The methanolic extract of cumin seeds lowers the blood glucose and overcomes the creatinine, blood urea nitrogen, glycosylated hemoglobin, and better-quality serum glycogen and insulin contents in STZ and alloxan diabetic rats (Jagtap & Patil, 2010). The management of cumin lowered the
hyperglycemia and glucosuria attended by an enhancement in body weight, blood urea, and compact evacuation of urea and creatinine for eight weeks in STZ-diabetic rats. Cuminaldehyde also inhibited the aldose reductase and alphaglucosidase enzymes activities (Lee, 2005). The earlier studies of Aruna, Rukkumani, Varma, and Menon (2005) showed that orally administrated cumin reduced the body weight, tissue cholesterol, triglycerides, free fatty acids (FFAs), and phospholipids level. Cumin lowered alkaline phosphatase (ALP), aspartate transaminase (AST), and \( \gamma \)-glutamyl transferase (GGT) activities and reduced the tissue levels of triglycerides, cholesterol, and phospholipids and prohibited the changes in the arrangement of fatty acids in the plasma of mice. In a study conducted by Tabasi et al. (2015), they demonstrated that *N. sativa* exerts pro-apoptotic and anti-proliferative effects on human kidney adenocarcinoma cells in a concentration- and time-dependent manner.

8. Rosemary

*Rosemary* (*Rosmarinus officinalis* L.) is being used as a food flavoring agent due to its powerful antimicrobial, anticancer, antidiabetic activities, and also as a chemopreventive agent (Wang, Wu, Zu, & Fu, 2008). It constitutes a wide variety of bioactive phytochemicals such as, carnosic acid, carnosol, 7-methyl-epirosmanol, rosmanol, rosmadial, isorosmanol, rosmaridiphenol, caffeic acid, and rosmariquinone. Approximately 90% of the antioxidant activity of rosemary is attributable to the presence of carnosol and camosic acid (Saber & Hawazen, 2012). These bioactive compounds such as carnosic acid and rosmarinic acid hinder the proliferation of MCF-7 (human breast adenocarcinoma), DU145 (human prostate carcinoma), NCI-H82 (human, small cell lung carcinoma), K-562 (human chronic myeloid leukemia), Hep-3B (human (black) liver carcinoma), MDA-MB-231 (human breast adenocarcinoma, and PC-3 (human prostate adenocarcinoma) cancer cell lines (Yesil-Celiktas, Sevimli, Bedir, & Vardar-Sukan, 2010). Rosemary extracts lower the NF-\( \kappa \)B activation, TNF-\( \alpha \)-induced ROS generation, and then enhanced the TNF-\( \alpha \) persuaded apoptosis (Moon, Kim, Lee, Choi, & Kim, 2010). Kim et al. (2011) determined that ursolic acid suppresses different stages of cancer such as tumorigenesis, tumor promotion, and angiogenesis. Ursolic acid induces apoptosis in human breast tumor cell line, MDA-MB-231, and lowers the cell proliferation rate. The oral supplementation of rosemary leaf extract lowers the glucose level, total cholesterol, triglycerides, and low-density lipoprotein (LDL)-cholesterol and enhances the high-density lipoprotein (HDL)-cholesterol. As a hypolipidemic agent, it is also tortuous in exclusion of the lipids from the body (Deví & Sharma, 2004). The supreme important phenolic mixtures such as caffeic, ferulic acids, ellagic, rosmarinic acid, sesamol, and vanillin suppress the atherosclerosis. Additionally, rosemary compounds have cardio protective abilities to guard LDL from oxidative alteration in mice (Nofer et al., 2002)

9. Oregano

The oregano (*Origanum vulgare*) consists of oleanolic acid, flavonoids, ursolic acid, caffeic, terpinene, hydroquinones, \( p \)-cymene, carvacrol, lisothespermic, thymol, and rosmarinic acids, and tannins. Talpur, Echard, Ingram, Bagchi, and Preuss (2005) investigated that oregano extract improves glucose concentration through growing insulin sensitivity.
It exerts the anti-hyperglycemic role owing to the interference on stimulation of glucose application or captivation of dietary starches in small intestine or by peripheral tissues. Likewise, Ortiz-Andrade et al. (2007) presented the anti-hyperglycemic activity of oregano phenolic glucosides due to inhibition of tubular glucose re-absorption and a decrease in the intestinal absorption of glucose. Similarly, Vinay et al. (2010) indicated that supplementation of aqueous extract of oregano leaves significantly lowered the glycosylated hemoglobin (HbA1C) (high level of HbAlc indicates Diabetes Mellitus (DM)) in rats. Moreover, Broadhurst, Polansky, and Anderson (2000) evaluated that oregano extracts showed the hypoglycemic effect through civilizing glucose and insulin metabolism. The administration of oregano showed a substantial increment in muscle and liver glycogen level in diabetic rats (Vinay et al., 2010). The management of aqueous extract of oregano leaves lessen the concentration of blood glucose in STZ-induced diabetic mice without affecting basal plasma insulin absorptions (Lemhadri, Zeggwagh, Maghrani, Jouad, & Eddouks, 2004).

10. Fenugreek

Fenugreek (Trigonella foenum graecum L.) is used in diverse thrifs around the world for antidiabetic, reducing cholesterol level, anticancer, antimicrobial, manufacture food products such as stew with rice, flavor cheese, and syrup. It shows many health approving properties such as emollient, tonic, demulcent, carminative, astringent emmenagogue, diuretic, restorative, expectorant, vermifugal, and aphrodisiac. The pharmacological and biological activities of fenugreek are due to the presence of N compounds, steroids, polyphenolic compounds, the flavonoids luteolin, apigenin, isovitexin, quercetin, vitexin, orientin, amino acids, and volatile constituents. The fenugreek seeds halt the DMBA-induced mammary hyperplasia observed in DMBA-persuaded breast cancer in mice (Raju, Patlolla, Swamy, & Rao, 2004). Likewise, the ethanolic extract of fenugreek exhibited anti-neoplastic consequence on the growth of MCF-7 cells through declining the mitochondrial membrane potential, persuading early apoptotic changes via flicking of phosphatidylserine, humiliating cellular DNA into fragments, and lowering cell viability (Corbiere et al., 2003). Fenugreek and its bioactive components exhibit anticancer role through several functional and molecular targets. They encourage apoptosis in multiple tumor cell lines such as osteosarcoma, human colon, breast, leukemia, and liver (Corbiere et al., 2003; Raju et al., 2004). They block the immigration and invasion through decreasing NO and prostaglandin production by inhibiting iNOS and COX-2 in an osteosarcoma cell line, and lowering matrix metalloproteinase expression in human prostate cancer PC-3 cells, respectively (Liu et al., 2005; Srinivasan et al., 2009). Additionally, they block the initiation of I-κB kinase, AKT, NF-KB, and inhibit the production of pro-inflammatory cytokines like TNF-α, IL-1, and IL-6 by cancer cells (Chen, Shih, Huang, Cheng, & Means, 2011; Varjas et al., 2011).

11. Coriander

The coriander (Coriandrum sativum) belongs to Apiose family and is comprised of linalool (60–80%), γ-terpinene (1–8%), terpinen-4-ol (trace–3%), hydrocarbons; ρ-cymene (trace–3.5%), ketones (7–9%), and esters (Ganesan, Phaiphan, Murugan, & Baharin, 2013). It is also a good source of mahanimbicine, mahanine, and mahanimbine and has
| Spices      | Botanical name          | Composition                                                                                                                                                                                                 | References                                                                                     |
|-------------|-------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Turmeric    | Curcuma longa           | Diarylpentanoids, diarylheptanoids, sesquiterpenes, monoterpenes, triterpenoids, diterpenes, sterols, and alkaloid 71.5% curcumin (curcumin I), 19.4% demethoxycurcumin (curcumin II), and 9.1% bisdemethoxycurcumin (curcumin III) | Henrotin et al. (2010) and Pfeiffer, Höhle, Solyom, and Metzler (2003)                                |
| Garlic      | Allium sativum L.       | Allicin, allii, cycoallin, DADS, and ajoene, β-phellandrene, geraniol, citral, α-phellandrene, linalool and enzymes (allinase, myrosinase, and peroxidase) flavonoids, vitamins (A, B1, C), and minerals such as potassium, phosphorous, manganese, selenium, sulfur, magnesium, calcium, sodium, iron, germanium, and trace iodine | Bungu, Van de Venter, and Frost (2008), Cerella, Dicato, Jacob, and Diederich (2011)                |
| Ginger      | Zingiber officinale     | Carbohydrates 60–70%, water 9–12%, protein 9%, ash 8%, fatty oil 3–6%, crude fiber 3–8%, and volatile oil 2–3% 30–70% alpha-zingiberene, 15–20% beta-sesquiphellandrene, 10–15% beta-bisabolene, curcumene, betaphellandrene, camphene, zingiberene, cineole, geranyl acetate, terphineol, terpenes, geraniol, borneol, linalool, alpha-farmesene, and limonene | Kumar et al. (2012)                                                                             |
| Cinnamon    | Cinnamomum zeylanicum   | Cinnamaldehyde, cinnamatic acid, cinnamate, and several essential oils including trans-cinnamaldehyde, cinnamyl acetate, eugenol, l-borneol, b-caryophyllene, caryophyllene oxide, E-nerolidol, l-bornyl acetate, α-terpineol, α-cubebeene, α-thujiene, and terpinolene | Kwon et al. (2010)                                                                             |
| Clove       |                         | Caryophyllene, eugenol, alpha-terpinyl acetate, alpha-humulene, methyl eugenol, eugenyl, naphthalene, acyl eugenol, heptanone, sesquiterpenes, chavicol, vanillan, and methyl salicylate pinene | Banerjee and Das (2005), Das et al. (2004), and Sengupta et al. (2005)                           |
| Basil       | Ocimum sanctum          | Octane, α-thujiene, ethyl 2-methyl butyrate, α-pinene, (Z)-3-hexanol, myrecene, β-pinene, limocene, ethyl benzene, allo-c-imene, terpinolene, α-cubebeene, butyl-benzene, eugenol, linalool, carvacrol, borneol, methyl eugenol, iodol, humulene oxide, germacrene-D, τ-cadinol, α-quaial, (EZ)-famesol, α-bisbolol, elemol, cissesquisainene hydrate, selin-11-en-4-ol, tetradecanal, and 14-hydroxy-α-humulene | Kothari, Bhattacharya, and Ramesh (2004), Mondello et al. (2002), and Vina and Murillo (2003) |
| Rosemary    | Rosmarinus officinalis L.| Carnosic acid, carnosol, 7-methyl-epirosmanol, rosmanol, rosmadial, isorosmanol, rosmariquinone, caffeic acid, and rosmariquinine | Saber and Hawazen (2012)                                                                         |
| Oregano     | Origanum vulgare        | Oleanolic acid, flavonoids, ursolic acid, caffeic, terpinene, hydroquinones, p-cymene, carvacrol, linalool, thymol, and rosemarinic acids, and tannins.                                                        | Bozin, Mimica-Duki, Simin, and Anackov (2006), Giordani et al. (2010), and Tampieri et al. (2005) |
| Fenugreek   | Trigonella foenum graecum L. | Steroids, polyphenolic compounds, the flavonoids luteolin, apigenin, isovitexin, quercetin, vitexin, orientin, amino acids, and volatile constituents constituents (1–8%), terpinen-4-ol (trace–3%), hydrocarbons; p-cymene (trace–3.5%), ketones (7–9%) and esters | Mehrfarin et al. (2010)                                                                         |
| Coriander   | Coriandrum sativum      | γ-terpine (1–8%), terpinen-4-ol (trace–3%), hydrocarbons; p-cymene (trace–3.5%), ketones (7–9%) and esters                                                                                             | Ganesan et al. (2013)                                                                           |
| Cardamom    | Elettaria cardamomum (L.) | 1,8-cineole (21–41%), α-terpinyl acetate (21–35%), α-terpine (6.2–11.5%), sabinene + β-pinene (0.3–2.4%), limonene (1.7–3.7%), linalool (0.4–8.7%), borneol (0.1–1.2%), nerol (0.6–1.6%), linalyl acetate (1.6–2.4%), neryl acetate (0.8–1.2%), geraniol (1.1–3.7%), farnesol (up to 12.5%), isosafrole (3.8%) and nerolidol (0.2–6.7%) | Georgiev and Stoyanova (2006) and Misharina et al. (2009)                                        |
| Thymus      | Thymus serpyllum L.     | Thymol, carvacrol, linalool, α-terpine and 1,8-cineole. In Estonia, the major components comprise E-nerolidol, caryophyllene oxide, myrcene, (E)-β-caryophyllene, and germacrene-D | Raa, Paaver, Arak, and Orav (2004) and Seung-Joo et al. (2005)                                  |
Table 2. Anticancer perspectives of spices.

| Sr. no. | Spices | Mechanisms | References |
|--------|--------|------------|------------|
| 1 | Turmeric | Suppressed the activation of NF-κB induced by PMA, TNF-α, or H₂O₂ | Singh and Aggarwal (1995) |
| | | Abrogated LPS persuaded mitogen-activated protein kinase (MAPK) initiation and the translocation of NF-κB p65 Downregulated TNF-α-induced NF-κB initiation | Kim et al. (2005) and Lee (2005) |
| | | Arrested the NF-κB obligatory activity in A549 cells Mediated TRAIL-induced apoptosis Suppressed the NF-κB-dependent countenance of IL-6 downstream, deprivation of IκBα upstream and subsequent NF-κB DNA-binding activity in WI-38 VA13 cell Inhibited Ap-1 and NF-κB initiation | Lee and Surh (2004) and Wang et al. (2004) |
| | | Lowered the TPA-encouraged activation of NF-κB through direct intermission of the binding of NF-κB to its agreement DNA sequences | Han, Keum, Seo, and Surh (2002) |
| | | Blocked IκBα degradation, cytokine- encouraged NF-κB DNA-binding activity, IKK activity in HT-29, RelA atomic translocation, IκBα serine 32 phosphorylation, Caco-2, and EC-6 cells | Renard, Delaive, Van, Remacle, and Raes (2001) |
| | | Inhibited the BCG-convincing IL-8 production and LPS-mediated TLR2 mRNA induction | Kato et al. (2004) |
| | | Inhibited the activity of NF-κB in primary ATL cells and HTLV-1 infected T-cell lines | Jung et al. (2006) |
| | | Inhibited the activation of activator protein-1 (AP-1) by hindering phosphorylation of IκB | Surh, Han, Keum, Seo, and Lee (2000) |
| | | Reduced the activity of cytochrome P450 and COX-2 Downlegalized endogenous bcl-2 and baxxL proteins in DU145 cells | Leu and Maa (2002) and Dorai, Cao, Dorai, Buttyan, and Katz (2001) |
| | | Declined the expression of cyclooxygenase-2 (COX-2) and also blocked the phosphorylation of cytosolic phospholipase (cPLA(2)) Reserved catalytic activities of 5-lipoxygenase (LOX). Inhibited propagation of HT-29 and HCT-15 human colon tumor cell lines | Ravindran, Prasad, and Aggarwal (2009) |
| 2 | Garlic | Prevented from the cell proliferation through blocking cell cycle progress, inhibition of DNA adduct formation, bringing apoptosis Modulated the cancer cascades and acts as latent chemopreventive and chemotherapeutic agents Arrested G2/M stage of cell cycle Enhanced phase 2 detoxifying processes Increased acetylation of histones Modulated cellular redox state, post-translational alteration, and participate in the growth of multidrug resistance Inhibited the propagation of tumor cells in vitro through the induction of apoptosis Hindered the oxidation activity of xanthine Increased the concentration of catalase and SOD Inhibited the colon carcinogenesis induced through aprocarcinogen, DMH Activated caspase Upregulated the p21 level Downregulated cyclin A, cyclin B1, Cdc25C, Cdc2 Arrested cells at G2/M phase and caused apoptosis Suppressed cell proliferation, NF-κB activation Captured cell cycle at G1 phase through down variable cyclin D1 Elevated expression of TNF-α and NF-κB Deactivated NF-κB by the inhibition of the pro-inflammatory TNF-α Inhibited TNF-α production in TPA-treated female ICR rats | Nagini (2008) and Tsubura et al. (2011) and Iciek et al. (2009) and Melino et al. (2011) |
| | | | Hsu et al. (2010) and Ippoushi, Azuma, Ito, Horie, and Higashio (2003) and Kim et al. (2005) and Okidgo and Mmeka (2006) |
| | | | Park, Chun, Lee, Lee, and Surh (1998) |

(Continued)
| Sr. no. | Spices | Mechanisms | References |
|--------|--------|------------|------------|
| 3      | Cinnamon | Modulated angiogenesis and cytotoxic activity of CD8+ T cells Induced the apoptosis in a cancer cells lines Reduced the levels and activities of AP1 and NF-κB and their target genes such as Bcl-2 and Bcl-xL | Kwon et al. (2010) |
|        |        | Decreased the growth rate of SiHa cells | Schoene, Kelly, Polansky, and Anderson (2005) and Singh et al. (2009) |
|        |        | Downregulated the appearance of Her-2 in SiHa cells Decrease in the expression of MMP-2 protein Increased the intracellular Ca^{2+} concentration Induced apoptosis | Krum and Mattson (1999) and Meijerman, Beijnen, and Schellens (2006) |
|        |        | Repressed the thioredoxin reductase and activated the Nrf2. | Cabello et al. (2009) |
|        |        | Inhibited the azoxymethane encouraged colon carcinogenesis Lowered the interest of alamine in the rat intestine. | Bhattacharjee, Rana, and Sengupta (2007) |
|        |        | Repressed the proliferation of cancer cells lines and encouraged cell death of tumor cells Inhibited AP1 and NF-κB activity and their target genes i.e. Bcl-xL, Bcl-2, and upregulated pro-apoptotic molecules | Kwon et al. (2010) |
|        |        | Lowered the stages of HIF-1α and COX-2 in melanoma cell outlines and in the melanoma mouse model | Gasparini and Xu (2003) and Pugh (2003) |
|        |        | Lowered the Cox-2 and HIF-1α appearance in the cancer tissues | Gasparini and Xu (2003) and Tomozawa et al. (2000) |
| 4      | Clove | Downregulated the H-ras, c-Myc, and Bcl2 countenance along with upregulated the Bax, p53, and active caspase-3 expression in the skin lesions of the rats Recovered the cellular GSH and various enzymes like activities of GR, CAT, GPX, GST, and XO level. It also enhances the p21 and p53 WAF1 stages Overwhelms the COX-2 and iNOS countenance and levels of pro-inflammatory cytokines (TNF-α, IL-6, PGE-2), and ODC activity in mice. Protected from free radicals, lipid per-oxidation, DNA strand breaking, and protein damage. Furthermore, eugenol protects the decrease of GSH and antioxidant enzymes caused by TPA Induced extreme cell death and apoptotic cell demise in TE-13 cells within 1 day whilst DU-145 cells showed slight cell death | Gupta et al. (2008) Kaur et al. (2010) Dwivedi et al. (2011) |
| 5      | Basil | Downregulated the expression of genes that endorses the propagation, migration and assault of tumor cells Downcontrol the FAK, activated ERK-1/2, and p65 (subunit of NF-κB) Downregulated such genes that endorse chemo/radiation resistance, and survival (Bcl-2 and Bcl-xL) Lowered NO amount, 3-methyl dimethyl amino azobenzene, and benzo (a) pyrine-induced neoplasia and inducing hematomas Prevented from the social laryngeal epithelial carcinoma cell line (HEp-2), human cervical tumor cell line (HeLa), and NIH 3T3 mouse embryonic fibroblasts | Shimizu et al. (2013) Kim et al. (1998) Kathirvel and Ravi (2011) |

(Continued)
| Sr. no. | Spices | Mechanisms                                                                 | References |
|--------|--------|-----------------------------------------------------------------------------|------------|
| Lowered 20-methylcholanthrene persuaded tumor incidence and tumor volume. | Prakash and Gupta (2000) |
| Downregulated VEGF and Bcl-2 expression induced gastric cancer bearing rates | Manikandan et al. (2007) and Prashar et al. (1998) |
| Enhanced the activities of cytochrome b5, glutathione S-transferase, cytochrome p450, and aryl hydrocarbon hydroxylase that detoxify the carcinogens and mutagens | Govind and Madhuri (2006) |
| Induced hepatomas of mice and benzo(a)pyrene-induced neoplasia of forestomach | Devi (2001) |
| Cumin | Induced apoptosis linked with DNA ripping and a reduction in mitochondrial membrane probable in 518A2 melanoma and HL-60 cells. | Farah and Begum (2003) |
| Encouraged apoptosis and reserved proliferation in pancreatic ductal adenocarcinoma cells | Chehl, Chipitsyna, Gong, Yeo, and Arafat (2009) |
| Downregulated the consequence of TQ on MUC4 in pancreatic tumor cells Showed 88% inhibitory effect on human hepatoma HepG2 cells Enhanced glutathione transferase and quinone reductase contents | Khan and Sultana (2005) |
| Preventive effect against ferric nitroltriacetate (FeNTA)-induced renal oxidative stress, renal carcinogenesis, and hyper-proliferative response | Ashour et al. (2014), Hassan, Ahmed, Galeb, El-Taweel, and Abu-Bedair (2008), and Roepke et al. (2007) |
| Induced the p53 sovereign apoptosis through using p53-null human osteosarcoma cells in rats. | Sethi et al. (2008) |
| Suppressed the NF-κB activation through inhibition of the activation of IκB alpha-kinase, IκB alpha degradation, IκB alpha phosphorylation, p65 fissionable translocation, the NF-κB reliant on gene expression, and p65 phosphorylation. It inhibits the through binding of recombinant p65 and nuclear p65 to the DNA, and this binding was inverted by DTT. It did not suppress p65 binding to DNA when cells were transfected with the p65 plasmid comprising cysteine remainder 38 mutated to serine | |
| Downregulated the countenance of proliferative (cyclooxygenase-2, c-Myc, and cyclin D1), NF-κB-regulated antiapoptotic (IAP1, IAP2, Bcl-xL, XIAP Bcl-2, and survivin), and angiogenic (vascular endothelial growing factor and atmosphere metalloproteinase-9) gene yields | |
| Rosemary | Hindered the proliferation of MCF-7 (human breast adenocarcinoma), DU145 (human prostate carcinoma), NCI-H82 (human, small cell lung carcinoma), K-562 (human chronic myeloid leukemia), Hep-3B (human (black) liver carcinoma), and MDA-MB-231 (human breast adenocarcinoma and PC-3 (human prostate adenocarcinoma) cancer cell lines | Yesil-Celiktas et al. (2010) |
| Lowered the NF-κB activation, TNF-α-induced ROS generation, and then enhanced the TNF-α-persuaded apoptosis | Moon et al. (2010) |
| Induced the apoptotic cell death in lymphoblastic leukemia carnosol and lowered the tumor proliferation | Dörrie, Gerauer, Wachter, and Zunino (2001) |
| Reduced the cell expiry in the pre-B ALL lines REH, and SEM, RS4;11 | Zunino and Storms (2009) |

(Continued)
| Sr. no. | Spices      | Mechanisms                                                                 | References                          |
|--------|-------------|-----------------------------------------------------------------------------|-------------------------------------|
| 8      | Oregano     | Enhanced the serum level of CYT-C in colorectal cancer-induced rats          | Chen et al. (2011)                  |
|        |             | Enhanced the expression of Fas and FasL that leads to cleavage and activation | Kim et al. (2011)                   |
|        |             | of procaspase-8 and tBid and then mobilization of Bax from cytosol into      |                                     |
|        |             | mitochondria                                                                |                                     |
|        |             | Induced apoptosis in human breast tumor cell line, MDA-MB-231 and lowers     | Jiang and Wang (2004)               |
|        |             | the cell proliferation rate                                                  |                                     |
|        |             | Induced apoptotic molecules associated to either extrinsic or inherent       |                                     |
|        |             | apoptosis signal pathway in MDA-MB-231 cells                                 |                                     |
|        |             | Induced Bcl-2 downregulation and Bax upregulation then proclamation of       | Stevenson et al. (2011)             |
|        |             | cytochrome C to the cytosol from mitochondria                               |                                     |
| 9      | Fenugreek   | Suppressed the growth of human hepatocellular carcinoma cell line HepG-2     | Yin et al. (2012)                   |
|        |             | through inducing apoptosis.                                                  |                                     |
|        |             | Exhibited cytotoxic activity alongside non-small cell lung cancer (NSCLC-N6) | Chinou, Liolios, Moreau, and Roussakis (2007) |
|        |             | and murine leukemia (P388) cell lines.                                        |                                     |
|        |             | Showed cytotoxicity in human lung carcinoma cell line A-549, lymphocytic    | Chinou et al. (2007) and Yin et al. (2012) |
|        |             | leukemia cell lines P-388 and L-1210                                          |                                     |
|        |             | Induced cell growth arrest and cell death in a dose and time reliant in     | Isebella, Rosaria, Maria, and Luciana (2009) |
|        |             | colon adenocarcinoma (CaCO2) cells                                           |                                     |
|        |             | Protected the DNA from variety damaging agents and hinder the proliferation  | Shaban, Seyed, and Ali (2009)       |
|        |             | of cancer cells                                                              |                                     |
|        |             | Exhibited the significant proliferative activity beside human breast tumor  | Tatjana, Aleksandra, Zorica, and Milka (2010) |
|        |             | cell lines (MDR-MB-453), and (MDA-MB-361)                                    |                                     |
| 10     | Coriander   | Exhibited anti-neoplastic consequence on the growth of MCF-7 cells           | Corbiere et al. (2003)              |
|        |             | through declining the mitochondrial membrane potential, persuading early    |                                     |
|        |             | apoptotic changes via flicking of phosphatidylserine, humiliating cellular  |                                     |
|        |             | DNA into fragments, and lowering cell viability                              |                                     |
|        |             | Induced apoptosis in the HT-29 human colon tumor cell line                   | Raju et al. (2004)                  |
|        |             | Upregulated the expression of caspase-3 and inhibited the bcl-2              |                                     |
|        |             | Induced chemoprotection in osteosarcoma cells, HT-29 cells, and DMBA-          | Liu et al. (2005)                   |
|        |             | persuaded cancer in AKR/J H-2k rats involve consequent overthwart of          |                                     |
|        |             | arachidonic acid metabolism pathway Downregulated the cyclooxygenase-2 and   |                                     |
|        |             | enhanced the mRNA appearance of p53 and p21 and stimulated nuclear          |                                     |
|        |             | factor kappa B (NF-κB) chief to apoptosis                                    |                                     |
| 11     | Saffron     | Significantly lowered the cell viability as attention and duration of exposure| Mousavi, Tavakkol-Afshari, Brook, and Jafari-Anarkooli (2009) |
|        |             | amplified (IC50 of 400 ± 18.5 μg/mL after 48 hours) in MCF-7 cells          |                                     |
|        |             | Prolonged progression of papilloma growth and decreased squamous cell         | Nair, Kurumboor, and Hasegawa (1995) |
|        |             | carcinoma Decreased soft tissue sarcoma in treated mice                     |                                     |
|        |             | Inhibited nucleic acids synthesis in carcinoma development                   |                                     |
|        |             | Exhibited almost 95.6% reduction of solid tumor                             | Bakshi et al. (2009)                |
| 12     | Cardamon   | Lowered the liver Cytochrome P450 content and overwhelms the chemical       | Bhattacharjee et al. (2007)         |
|        |             | carcinogenesis in Swiss                                                     |                                     |
anticancer effect on the human cell lines like human cervical HeLa, human breast MCF-7, and murine leukemia cell lines (Thilahgavani, Perumal, Mohd, & Abdul, 2011). Coriander seeds lower the absorption of cholesterol and cholesterol to phospholipid ratio and significantly enhanced the phospholipid level in the spice managed group as compared to 1,2-dimethyl hydrazine (DMH)-persuaded colon cancer in rats. The utilization of coriander reduced the blood glucose level in mice owing to improvement in glucose uptake and metabolism with inspiration of insulin secretion by muscle. The utilization of coriander seeds caused hypoglycemia effect as well as also protect from cardiovascular diseases caused by hyperlipidemia in the metabolic syndrome, and T2DM (Abderrahmane, Soumia, Zafar, & Badiaam, 2011).

12. Saffron

Saffron is a conspicuous source of crocetin that disturbs the growth of cancer cells lines through multiple mechanisms such as suppressing nucleic acid synthesis, inducing apoptosis, hindering growth factor signaling pathways, and attractive anti-oxidative system (Samarghandian, Boskabady, & Davoodi, 2010). The saffron ethanolic extract depresses the cell feasibility in malignant cells in absorption and time-dependent manner (Abdullaev & Espinosa-Aguirre, 2004). It also inhibits the chemically induced skin carcinogenesis such as carcinogen bio-activation and tumor proliferation. The after and before supplementation of saffron enhance the GPx, GST, superoxide dismutase, and catalase in liver rats (Das, Chakrabarty, & Das, 2004).

Saffron and its bioactive ingredients crocus inhibit the cell development in neoplastic cells to a greater extent than in normal cells (Bakshi et al., 2009). Saffron extract containing dimethyl-crocetin was evaluated against human leukemia and murine tumor cell lines where saffron extract reduced ascites tumor growth and augmented the life expectancy of mice up to 45–120%. Furthermore, the extract also inhibits nucleic acids’ synthesis.
Table 3. Antidiabetic perspectives of spices.

| Sr. no. | Spices | Mechanisms | References |
|---------|--------|------------|------------|
| 1       | Turmeric | Inhibited the nitric oxide synthase (NOS) overexpression and NF-κB activation | Weber et al. (2006) |
|         |         | Exhibited anti-inflammatory potential in cancer necrosis factor alpha-treated HaCaT cells through reserve of nuclear factor-κB and mitogen-stimulated protein kinase | Cho et al. (2007) |
|         |         | Reduced diabetes problems such as nephrologic, ophthalmologic, and cardiovascular | Suryanarayana et al. (2005) |
|         |         | Decreased renal lesions in STZ encouraged diabetes mice | Khajehdehi et al. (2012) |
|         |         | Lowered plasma lipid peroxides, enlarged antioxidant α-tocopherol and coenzyme Q levels | Quiles et al. (2002) |
|         |         | Improved the postprandial serum insulin levels | Wickenberg et al. (2010) |
|         |         | Exhibited inhibition on macrophage inflammatory protein-1a, tumor necrosis factor-a by PMA, membrane cofactor protein-1 and IL-1b, alveolar macrophages and the production of interleukin (IL)-8 | Iqbal, Okazaki, and Okada (2003) |
|         |         | Inhibited VEGF, and NF-κB signaling, pro-inflammatory cytokines (IL-1b) and increasing activity of chaperone molecules | Murugan and Pari (2006) |
|         |         | Inhibited the glucose level enhancement in hyperglycemic KK-A(y) mice | Kuroda et al. (2005) |
|         |         | Stimulated the human adipocyte diversity in a dose-dependent manner and shown human PPAR-γ ligand-binding activity in a GAL4-PPAR-gamma whimsy assay | |
|         |         | Reduced the glucose level, FFAs, glycosylated hemoglobin, triglyceride, total cholesterol, and lipid per-oxidation levels | Arun and Nalini (2002) |
|         |         | Enhanced the hepatic glycolokinase activity and plasma insulin points in CS7BL/Ks-db/db diabetic rats | |
|         |         | Attenuated insulin resistance, and reduction in leptin levels | Jang et al. (2008) |
|         |         | Lowered blood sugar glucose level, reduces TNF-α levels, and improved the insulin sensitivity | Weisberg et al. (2003) |
| 2       | Garlic  | Improved the hepatic glycogen equal and permitted amino acid content and dropped the glucose and triglyceride concentration | Khan et al. (2012) |
|         |         | Inhibited superoxide formation and lipid per-oxidation | |
|         |         | Blocked the AGEs synthesis | Tripathi et al. (2011) |
|         |         | Enhanced the liver glycogen and free amino acids contents that overwhelms the triglycerides level, liver serum proteins, and FBS | Noor, Bansal, and Vijayalakshmi (2013) |
|         |         | Triggered many enzymes including lecithin–cholesterol acyltransferase (LCAT), glucose-6-phosphatase, and hexokinase, 3-hydroxy-3-methylglutaryl (HMG) CoA reductase | |
|         |         | Lessened the levels of anti-islet cell antibodies ICA, elevated pan innate cells marker (CD11b), the elevated pan B cell marker (CD19), and elevated pan T-cell marker (CD90) | Osman, Adnan, Salmah, and Alashkham (2012) |

(Continued)
| Sr. no. | Spices    | Mechanisms                                                                 | References                                                                 |
|---------|-----------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|
| 3       | Ginger    | Released bound insulin or improved insulin sensitivity and high pancreatic excretion of insulin from β-cells | Liu, Wong, Li, Hse, and Sheen (2006).                                      |
|         |           | Modulated the NADPH oxidase                                                 | Yang et al. (2013)                                                        |
| 4       | Cinnamon  | Released bound insulin or improved insulin sensitivity and high pancreatic excretion of insulin from β-cells | Liu, Wong, Li, Hse, and Sheen (2006).                                      |
|         |           | Decreased TBARS level                                                      | Afshari et al. (2007) and Cho et al. (2002)                                |
| 5       | Clove     | Reduced plasma glucose level                                                | Kannappan et al. (2006)                                                  |
| 6       | Basil     | Reduced plasma glucose level                                                | Kannappan et al. (2006)                                                  |
| 7       | Cumin     | Reduced plasma glucose level                                                | Kannappan et al. (2006)                                                  |

(Continued)
| Sr. no. | Spices   | Mechanisms                                                                                   | References                                                                 |
|------|----------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
|      |          | lived protein) Lowered the area beneath the glucose lenience curve Inhibited the aldose reductase and alaphaglucosidase enzymes activities | Aruna et al. (2005)                                                          |
|      |          | Repressed alcohol and thermally oxidized oil induced hyperlipidemia Lowered ALP, AST, and γ- GGT activities Lowered the activity of phospholipase A and C | Ani and Akhilenre r (2008) and Fujita, Yamagami, and Ohshima (2001) and paper folder |
|      |          | Inhibited α-glucosidase, this enzyme Decreased serum glucose level                            | Fujita, Yamagami, and Ohshima (2001)                                         |
|      |          | Hindered α-glucosidase, and Aldose reductase Decreased absorption of glucose from intestine through reduction glucose transport processes Avoided rises of insulin level in the body |  |
| 8    | Rosemary | Suppressed the LDL oxidation in a dose-reliant manner Lowered high blood sugar level          | Fuhrman, Volkova, Rosenblat, and Aviram (2000) and Naidu and Thippeswamy (2002) |
|      |          | Improved glucose concentration through growing insulin sensitivity                            | Talpur et al. (2005)                                                         |
|      |          | Inhibited tubular glucose re-absorption and a decrease in the intestinal absorption of glucose| Maghrani, Lemhadri, Jouad, Michel, and Eddouks (2003), Ortiz-Andrade et al. (2007), and Takeda et al. (2008) |
|      |          | Significantly lowered the neck and neck of glycosylated hemoglobin (HbA1C) (high level of HbAlc indicates DM) Stimulated the insulin level from the remainder pancreatic β-cells | Vinay et al. (2010)                                                          |
|      |          | Enhanced the pancreatic amylase Prolonged the carbohydrate digestion time                      | Valiathan (1998)                                                             |
|      |          | Exhibited robust inhibitory activity against porcine pancreatic amylase (PPA) in vitro trial of rats Inhibited the PPA activity | McCue, Vattem, and Shetty (2004)                                             |
|      |          | Lessened the concentration of blood glucose in STZ-induced diabetic mice without affecting basal plasma insulin absorptions | Lemhadri et al. (2004)                                                      |
| 9    | Oregano  | Showed the insulin tropic activity, improved the glucose-persuaded insulin issue               | Sauvaire et al. (1998)                                                      |
|      |          | Enhanced the number of IRS, and decreases the area beneath the plasma glucose curve in human studies | Raghuram, Sharma, Sivakumar, and Sahay (1994)                                 |
|      |          | Showed the anti-hyperglycemia action through overwhelming the accomplishments of alpha-amylase, and rouse the glucose reliant on insulin excretion from pancreatic beta cells | Ethan, Grace, and Michael (2003)                                            |
| 10   | Fenugreek| Showed the insulin tropic activity, improved the glucose-persuaded insulin issue               | Sauvaire et al. (1998)                                                      |
|      |          | Enhanced the number of IRS, and decreases the area beneath the plasma glucose curve in human studies | Raghuram, Sharma, Sivakumar, and Sahay (1994)                                 |
|      |          | Showed the anti-hyperglycemia action through overwhelming the accomplishments of alpha-amylase, and rouse the glucose reliant on insulin excretion from pancreatic beta cells | Ethan, Grace, and Michael (2003)                                            |
| 11   | Coriander| Lowered the absorptions of cholesterol and cholesterol to phospholipid ratio and significantly enhanced the phospholipid level | Chithra and Leelamma (2000)                                                  |
|      |          | Reduced the blood glucose level in mice owing to improvement in glucose uptake and metabolism Elevated the levels of insulin resistant, insulin, TG, TC, and LDL-cholesterol | Gray and Flatt (1999)                                                        |
|      |          | Lowered the cholesterol biosynthesis through suppression of 3-hydroxy-3-methylglutaryl coenzyme-A reductase (cholesterol biosynthesis enzyme) Increased in LCAT activity Improved the poverty of cholesterol to fecal bile acids and impartial sterols Suppressed the lipogenic enzymes or inhibited hormone-sensitive tissue lipases Activated LCAT and tissues lipases | Another group of researchers: Aissaoui, Zizi, Israili, and Lyoussi (2011), Chithra and Leelamma (1997), Dhanapakiam, Joseph, Ramaswamy, Moonthi, and Kumar (2007) , and Pari and Venkateswaran (2003) |
|      |          | Encouraged glucose consumption by peripheral tissues including muscle and adipose tissue or by enhanced insulin signaling Increased hepatic | The groups of different scientists : Gallagher, Flatt, Duffy, and Abdel-Wahab (2003), |

(Continued)
in carcinoma development and thus concluded that dimethyl-crocetin interrupts interaction of DNA. In an in vitro trial, Abdullaev (2002) examined cytotoxic activity of saffron extract in colony forming assay and showed anti-mutagenic behavior. Furthermore, saffron extract showed a dose-dependent inhibition in HeLa cells. Crocin shows dose-dependent activity through lowering the cell viability in diffusion-limited aggregation cells (Bakshi et al., 2009).

13. Cardamom

Cardamon (*Elettaria cardamomum* L.) belongs to Zingiberaceae family and has 1,8-cineole (21–41%), α-terpinyl acetate (21–35%), α-terpineol (6.2–11.5%), sabinen + β-pinene (0.3–2.4%), limonene (1.7–3.7%), linalool (0.4–8.7%), borneol (0.1–1.2%), nerol (0.6–1.6%), linalyl acetate (1.6–2.4%), neryl acetate (0.8–1.2%), geraniol (1.1–3.7%), farnesol (up to 12.5%), isosafrole (3.8%), and nerolidol (0.2–6.7%) (Misharina, Terenina, & Krikunova, 2009). The cardamom showed preventive role in AOM-persuaded colonic aberrant crypt foci in Swiss Albino mice. It modulates the status of proliferation, modification of cyclooxygenase-2 (COX-2) expression, and inducible nitric oxide synthase (iNOS) (Sengupta et al., 2005). It also overwhelms the acid-soluble sulfhydryl level and hepatic carcinogen absorbing enzymes (aryl hydrocarbon hydroxylase, cytochrome P450, and glutathione S-transferase). The essential oils of cardamom meaningfully elevated the acid-soluble sulfhydryl and glutathione S-transferase activity in rats when compared to placebo.

14. Thyme

The thymus (*Thymus serpyllum* L.) belongs to family Labiateae and is usually used for various functions such as anti-septic, anthelmintic, carminative, expectorant, sedative,
and tonic. Carvacrol, thymol, and borneol are principal constituents found in thyme (Jaafari et al., 2007). The major ingredients of thyme are thymol, carvacrol, linalool, α-terpineneol, and 1,8-cineole (Seung-Joo, Katumi, Takayuki, & Kwang-Geun, 2005).

Carvacrol has vital in vitro antitumor effect beside tumor cell lines such as Hep-2, B-16, and A-549 (Karkabounas, Kostoula, & Daskalou, 2006). Horvathova, Turcaniova, and Slamenaova (2007) described the anti-proliferative activity of carvacrol with IC 50 of 90 μM and 67 μM for 24 h and 48 h of cell incubation, respectively. The earlier results of Zeytinoglu, Incesu, and Baser (2003) determined that carvacrol suppressed the growth of myoblast cells through activating mutated N-ras oncogene. In K-562 cells, carvacrol and thymol considerably lowered the level of DNA damage due to their strong antioxidant potential. They also suppressed the mutagenicity induced by 4-nitro-ophenylendiamine (Tables 1–3).

**Conclusion**

Spices are acknowledged to have several advantageous physiological possessions, including the anticancer and antidiabetic influence. Plentiful studies are carried out in past few decades which confirms anti-inflammatory, digestive stimulatory, hypolipidemic, antidiabetic, antioxidant, and anti-mutagenic actions of a range of spices. The research over spices is still having a wide span of exploration and probability to evaluate the spice therapy as substitute and complementary in various lifestyle-related disorders.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

**Notes on contributors**

**Dr. Muhammad Imran**’s field of interest is food science and technology, food nutrition and functional and nutraceutical compounds. Recovery of bioactive compounds for food and biomedical applications, identification/development of dietary antiangiogenic functional foods/nutraceuticals are his primary areas of interest.

**Dr. Muhammad Nadeem**’s research focuses on the physiologic effects of bioactive food components to reduce risk factors for cardiovascular and obesity-related chronic diseases.

**Dr. Farhan Saeed**’s research focuses on the interaction of dietary constituents (macronutrients and nonnutritional components) with processes/risk factors for chronic human diseases (i.e. coronary vascular disease and cancer).

**Dr. Ali Imran**’s research themes include infant and young child feeding (breast feeding and complementary feeding), relationships between infection and nutrition, and control of specific micronutrient deficiencies, with particular focus on vitamin A, zinc, and iron.

**Dr. Moazzam Rafiq Khan**’s research interests are nutraceutical functions of phytochemicals; Sensory/nutritional qualities of fruit and vegetable products. He is also working on fruits and vegetable processing technologies.

**Dr. Muhammad Asif Khan**’s research interests include study of the health effects of the dietary fermentable fiber, resistant starch, which includes molecular effects and the effect on the microbiota. This includes the study of the whole grain and non-whole grain forms of resistant starch and the effects of different dietary levels of fat on fermentation of resistant starch.
Dr. Sheraz Ahmed focuses his research on Food Microbiology and Food Safety, Control/elimination of Listeria monocytogenes, E. coli O157:H7, Shigella, Salmonella, Campylobacter, Vibrio, Bacillus cereus, Hepatitis A, and Norovirus in food and water.

Dr. Abdur Rauf’s field of specialization is Medicinal Chemistry; Pharmacology, Green synthesis of nanoparticles and molecular docking of bioactive compounds.

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