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BIOACTIVE POTENTIAL OF THE SPICE BLEND 'BENGALI GARAM MASALA': AN OVERVIEW

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ABSTRACT

Spices are used all over the world as flavouring and colouring agents or as food additives. They have been used traditionally as a part of the daily diet, as a home-made remedy to various ailments and as purgative, carminative, diuretic etc. The active biomolecules obtained from the spices are responsible for their medicinal properties. Bengali garam masala, consisting of green cardamom, clove and cinnamon is a quintessential spice blend and an integral part of the daily cuisine in Bengal. Blending of these three spices in Bengali garam masala also provide a number of health beneficiary effects due to the presence of wide varieties of bioactive molecules having therapeutic potentials. This review highlights the properties of the three main ingredients used in Bengali garam masala. It delves into the active phytochemicals obtained from these compounds and their contribution in the pharmacological properties of the crude extract. It also investigates the synergistic action of the three, blended to give the garam masala mixture.

Keywords: cardamom, cinnamon, clove, garam masala, spice, bioactive potential

INTRODUCTION

According to the ESA (European Spice Association) definition, herbs and spices, traditionally added to food, are edible parts of plants having aromatic, flavouring and visual properties. The word spice comes from the French word "espice" meaning

"sort/kind" **[1]**. Though spices and herbs are used synonymously, they are different in at least two respects. Any part of the plant, i.e., root, bark, fruit, seed etc. may be used as spice while herbs usually comprise of the stem, leaves or flowers of the plant. Also, spices, sometimes grounded into fine powder, are used for colouring, flavouring or preserving food items while herbs are mainly used for flavouring or as garnish **[1]**. Spices are important industrially and are used for making soaps, perfume, dyes and incenses **[1]**. Apart from the above mentioned uses, consumption or topical application of both spices and herbs provide immense health benefits **[1]** and are used as tonic, anti-spasmodic, anti-helminthic, stomachic, and carminative **[2]**.

In the old world, spices (mainly pepper and cinnamon) demanded more attention than gems and jewels and were the actual source of wealth **[1]**. Spice merchants of Alexandria, Cairo, and Venice were held in great esteem and monopolized the business. Mixing and addition of spices to food were a closely guarded secret and humans were bartered in exchange of spices. Even prophet Muhammad used the trade as a platform to spread the message of God and baby Jesus was given two spices, frankincense and myrrh, as gifts from the three great men **[3]**. In the Middle ages (late 14^{th}- early 15^{th} century), Portuguese and Spanish people began to look for new trade routes in search of spices and in the process discovered new countries; Marco Polo discovered China, Columbus discovered present day America and Ferdinand Magellan travelled the world. During this time, cinnamon, clove, nutmeg and pepper promised immense riches **[3]**. In recent times, spices are of common usage all over the world; knowledge about its usage has spread from one culture to another. Also, the traditional information of their medicinal properties is being scientifically validated and the active principles isolated by the pharmaceutical industry for therapeutic uses.

India, being a megadiversity country, houses a wide variety of spices namely chilli, mustard, cardamom to name a few. The use of various spices renders a rich taste to the Indian cuisine making it famous all over the world. India, with 8.8% of the share, ranks number three in spice trade of the world **[1]**. The rich aroma, fine taste and texture of the Indian spices command high prices in the global market **[1]**. India is the largest consumer of spices in the world. It also exports chilli, coriander, cumin, fennel, pepper and turmeric to China, Germany, Malaysia, United Arab Emirates and United States **[1]**.

Besides the traditional use as a flavouring agent, spices also play a key role in the history of medicine. Their abilities in healing myriad ailments added supernatural

implications to their powers **[3]**. In India, the history of spices dates back 5000 years to Ayurveda where a number of spices have been outlined for their remedial properties, either by itself or in combination. Curative properties of spices in Rigveda and Atharvaveda are most probably the earliest documentation of the medicinal use of spices **[4, 5]**. Besides adding variation and concealing disagreeable odour, traditionally, they were used to aid digestion, lowering of body temperature and increase in perspiration rate, as antiseptic, anti-inflammatory, anti-oxidant and carminative agents **[1]**. Phenolic acids, flavonoids, phenolic diterpenes, volatile oils and other phenolic compounds isolated from spices are the underlying molecules responsible for the medicinal properties of spices **[6-14]**.

Garam masala, a spice blend is widely used in Indian cuisine. It consists of a mixture of three or more spices, either coarsely grounded or finely powdered, whose ingredients vary according to the different cultures in the different regions of India **[15]**. To enhance the flavour it is mainly toasted in oven at a low temperature and added near the end of cooking. In the eastern part of India, mainly in West Bengal, three basic ingredients are used in garam masala, namely clove (*Syzygium sp*), cinnamon (*Cinnamomum sp*) and cardamom (*Elettaria sp*) each of which have notable health benefits **[4]**. Cardamom helps in treating genitourinary disorders and is a mood elevator. Cinnamon has cardioprotective and neuroprotective abilities whereas clove is a potent anti-inflammatory, antioxidant and anti-cancer agent **[16, 17, 18]**. As with other spices, various phenolic compounds such as flavonoids, natural oils etc. are responsible for their healing activity **(Table 1)**. Combining the three spices would therefore increase the health benefits as the number of bioactive molecules with remedial potential would be more in the mixture than either of the individual spice. Inarguably, garam masala helps in reduction of body weight, increases metabolism by altering cytochrome-b5 and cytochrome-p450 levels in the liver **[5]**. An attempt has been made in this review to discuss the pharmacological properties of the individual spices that constitute Bengali garam masala and also the spice blend as a whole. It also attempts to highlight the underlying phytochemicals responsible for their medicinal properties.

MATERIALS AND METHODS

The components of garam masala, used mainly in West Bengal, were confirmed from an online database after consultation with a few knowledgeable people using the same in cooking. The properties of each of the components and the spice blend were then identified using Pubmed, Science

Direct, Google Scholar, etc. The bioactive molecules and mechanisms of action were also searched using the database mentioned above.

RESULTS AND DISCUSSION

The 'Bengali garam masala' blend is a mixture of green cardamom, cinnamon and clove in equitable proportions. Cardamom belongs to the ginger family; cinnamon belongs to the same family as that of bay leaves while clove is classified in Myrtaceae family. The three spices are highly different in their origin yet blends together to give a rich and unique taste to food. Also, each of the spices has an array of health benefits. The additive and synergistic effect of the blend also has different bio functions. The myriad properties of the garam masala are mainly attributed to the polyphenolic and other components of each of the spices **(Table 1)**. The properties of each of the spices and mixture are discussed in detail.

Table 1: Bengali Garam masala and its biochemical components [19, 20, 21]

Sl. No.	Scientific Name	Common Name /Local Name	Family	Plant parts used	Important Biochemical components
1.	*Elettaria cardamomum*	Cardamom/ 'Elach'	Zingiberaceae	Plump seed pods containing oil-rich seeds.	Limonene, 1,8-cineole, Terpinolene, Myrcene, Caffeic acid, Quercetin, Kaempferol, Luteolin, Pelargonidin
2.	*Cinnamomum verum*	Cinnamon / 'Darchini'	Lauraceae	Bark of the Cinnamomum tree.	Eugenol, Limonene, Terpineol, Catechins, Proanthocyanidins, Tannins, Linalool, Safrole, Pinene, Methyleugenol, Benzaldehyde
3.	*Syzygium aromaticum*	Clove/ 'Labanga'	Myrtaceae	Dry bud of flower	Eugenol, Isoeugenol, Acetyleugenol, Sesquiterpene, Pinene, Vanillin, Gallic acid, Flavonoids, Phenolic acids

Green Cardamom

Cardamom, belonging to the ginger family Zingiberaceae, is popularly known as "Elaichi" in India. It is referred to as the queen of spices which originated in Bhutan, India and Nepal **[4, 22]**. Two genera of cardamom are used as spices namely *Amomum* sp. (brown cardamom or "badi elaichi") and *Elettaria* sp. (green cardamom or "chhoti elaichi") **[3]**. Green cardamom is a shrub consisting of a large stem giving off long, narrow pointed leaves; plump pods containing seeds rich in oil. The pods are plucked and either sold as green cardamom or as white after treatment with sulphur dioxide **[3]**. Cardamom is used in curries,

breads, pastries and even in Turkish coffee **[3]**. Traditionally, it has been used in Ayurveda and Chinese medicine as an appetizer, carminative, digestive, treatment of cough and cold and as an aphrodisiac **[4, 23]**. It is also used for the treatment of teeth and gum infections, inflammation of eye, throat problems, genito-urinary disorders, gastro-intestinal disorders, gall bladder stones etc. **[4, 8, 9, 22, 24-28]**. Health benefits of cardamom as reported by several investigations include the following:

Anti-microbial property:

Noumi *et al*. (2018) reported that the essential oil of green cardamom is effective against 25 bacterial species and 7 fungal species. Gram positive bacteria are more effectively inhibited than the gram negative ones. The inhibition zones ranges from 6 to 41.33mm for bacteria and 14.33 to 21.67mm for fungi as examined by disc diffusion assay **[29]**.Cardamom essential oil was also tested for their activity against *B. cereus, C. albicans, L. monocytogenes, P. aeruginosa, S. aureus, S. mutans, S. thyphimurium* by disc diffusion assay. It is found that *C. albicans* and *S. mutans* are the most sensitive; others are intermediate in their sensitivity and *P. aeruginosa* resistant to the oil **[30]**. Cardamom fruit and seed extract can inhibit periodontal bacteria, *Aggregatibacter actinomycete-mcomitans, Fusobacterium nucleatum, Porphyromonas gingivalis*, and *Prevotella intermedia*; *P. gingivalis* and *A. actinomycetemcomitans* being most and least sensitive respectively **[31]**.

Anti-diabetic and Cardioprotective property:

Elettaria cardamomum is able to modulate the glycemic indexes. Serum concentration of insulin, glycated haemoglobin (HbA1c), triglyceride (TG), homeostasis model assessment (HOMA-IR) are decreased where as sirtuin-1 (SIRT1) is increased in obese patients (N=38) treated with cardamom compared in comparison to control (N=37) **[32]**. Overweight pre-diabetic women, when fed with 3g of cardamom for 2 months, total cholesterol and low density lipoprotein (LDL) levels decreased but insulin sensitivity increased **[33]**.

Anti-inflammatory and Analgesic property:

Cardamom oil obtained by steam distillation of crushed fruits inhibits carrageenin induced paw edema in male albino rats. It also prevents writhing induced by *p*-benzoquinone exhibiting its potent analgesic activity [34]. Hexane extract of cardamom inhibits carrageenin induced paw edema in male Wistar rats at 50-100 mg/kg b.w. It also successfully inhibits NO production in serum; COX-2 enzyme in peripheral blood mononuclear cells (PBMC); COX-2, TNF-α and IL-6

protein in tissue homogenates from rat paw **[35]**. Cardamom fruit and seed extract inhibits IL-1β, TNF-α and IL-8. The reduction in inflammatory mediators is possibly due to the dose dependent inhibition of NF-κB pathway in U937 cells stimulated with lipopolysaccharide (LPS) **[31]**. Aqueous extract of cardamom (50 and 100 µg/ml) causes an increase in IL-10 and IL-4 in a dose dependent manner in presence of Concanavalin A (Con A). It (1-100 µg/ml) also inhibits LPS and IFN-ɤ induced TNF-α and IL-6 production in splenocytes obtained from BALB/c mice, thus up-regulating Th2 and down-regulating Th1 in its attempt to bring down inflammation. Another important inflammatory mediator like NO is also reduced **[36]**.

Anti-oxidant property:

In vitro studies have demonstrated that hexane extract of *E. repens* inhibits free radical generation, increases metal chelating activity, reduces ferri to ferrocyanide, and thus increases the total anti-oxidant activity. It also prevents protein oxidation as seen with bovine serum albumin (BSA), protect plasmid DNA from degradation and inhibit lipid peroxidation in liver induced by 2,2'-azobis-2-methyl-propanimidamide dihydrochloride (AAPH) and paw homogenates induced by carrageenin. It also increases the level of superoxide dismutase (SOD), catalase and glutathione (GSH) in paw homogenates **[35]**. Nair *et al*. (1998) reported that capsules from cardamom can neutralize free radicals due to the presence of kaempferol, luteolins and quercitin **[37]**.

Neuroprotection in memory and cognition:

Obesity and brain specific insulin resistance may be one of the reasons of Alzheimer's disease. This may be due to abnormal GSK3β activation, causing accumulation of amyloid beta (Aβ). Petroleum ether extract of cardamom can alter Alzheimer like conditions in rats where type-2 diabetes mellitus has been induced. It increases cognitive functions in rats as measured by passive avoidance test and water maze test. It also decreases hippocampal levels of acetylcholinesterase, caspase 3 activity, reduces accumulation of Aβ and p-tau in brain and increases expression of glutamate receptor. It also inhibits IL-1β, TNF-α, hippocampal lipid peroxidation. It upregulates the activity of anti-oxidant enzymes like superoxide dismutase (SOD) and glutathione (GSH) but downregulates glycogen synthase kinase-3beta (GSK-3β) activity in the hippocampus **[38]**. 1,8 cineole extract from cardamom seeds (50 and 100 µM) seeds inhibits Aβ42 oligomerization and iron induced cell death in SH-ST5Y cells; it is more effective than pure 1,8 cineole **[39]**.

Anti-cancer property:

Aqueous extract of cardamom (1-100 µg/ml) though by itself is not toxic to YAC-1 tumour cells, stimulates natural killer (NK) cells against YAC-1 cells in a dose dependent manner [36]. Oral administration of aqueous extract of cardamom (500 mg/kg b.w.) inhibits tumour multiplicity and burden (fore-stomach papilloma) in benzopyrene induced Swiss albino mice, increases antioxidant enzymes like glutathione transferase (GST), glutathione peroxidise (GPx), SOD, catalase, and inhibits lipid peroxidation **[40]**.

Gastro protective activity:

The petroleum ether soluble fraction (50 mg/kg b.w.) is more potent in reducing ethanol induced gastric lesions than the insoluble fraction (450 mg/b.w.) obtained from the methanolic extract of cardamom. The essential oil obtained from the soluble petroleum ether fraction (73.3% at 50 mg/kg) is even more effective than the parent (50% at 50 mg/kg) compound in reducing gastric ulcers. Similar results have been obtained with aspirin induced gastric ulcers but in such cases petroleum ether soluble fraction is more effective than the essential oil **[41]**.

Cinnamon

Cinnamon is actually the bark of the evergreen tree *Cinnamomum* (*Cinnamomum verum, C. cassia* or *C. zeylanicum*) belonging to family Lauraceae **[3, 22]**. It is indigenous to South America, Carribean Islands and South East Asia (India, Sri Lanka, Bangladesh and Nepal) **[22, 24]**. The word cinnamon comes from the Greek word "kinnamomon" and its genus name *Cinnamon* is derived from its native place "Ceylon", present day Sri Lanka. The spice is actually the inner bark of the tree which is carefully harvested during the rainy season from the trees ageing 25 years or more. Bark from *C. verum* is known as true cinnamon. It is soft compared to the others and crumbles easily. Bark of *C. cassia* is harder and difficult to grind. Apart from garam masala, it is used in several other spice blends such as pumpkin pie mix or barbecue rubs to name a few. Besides using as a spice, it is also used in making candies, potpourris etc. for its unique aroma **[3]**. Traditionally it has been used for indurations and tumours of liver, abdomen, breast and uterus **[42]**. It is also used as antiseptic, astringent, carminative, fungicidal, digestive, antidiabetic, neuroprotective etc. **[43-48]**. The natural oils and other derivatives namely, cinnamate, cinnamic acid and cinnamaldehyde **(Table 1)** seem responsible for their protective and immunity boosting properties **[17, 22]**, the details of which are discussed below:

Anti-microbial property:

Several literatures published during last few years have indicated that cinnamon oil (*C. zeylanicum* and *C. cassia*) is effective against a wide range of microbes. Its potential role as an anti-microbial agent have been demonstrated in different groups of pathogenic bacteria such as *Bacillus subtilis, Clostridium difficile*, *Enterobactor aerogens*, *Escherichia coli, Hemophilus influenzae, Helicobacter pylori, Klebsiella pneumoniae, Mycobacterium tuberculosis, Pseudomonas aeruginosa, Salmonella thyphi*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Yersinia enterocolitica*. Cinnamon is also effective against wide variety of fungus that includes seven species of *Aspergillus*, five species of *Candida* and three species of *Microsporum.* Anti-fungal activity has also been studied against *Crytococcus neoformans, Epidermophyton floccosum, Hisioplasma capsulatum, Mucor plumbeus, Penicillium roqueforti* and in yeast namely *Candida lipolytica, Debaryomyces hansenii, Saccharomyces cerevisiae, Torulopsis utilis,* and *Zygosaccharomyces rouxii*. Moreover, it has been claimed in these investigations that the cinnamon oil is more potent a microbial agent than clove or neem oil **[17, 49-52]**. The essential oil of *C. zeylanicum* is found to be effective against human rota virus and the protozoa *Cryptosporidium parvum* **[49, 53]**. Cinnamaldehyde isolated from cinnamon is a potent antimicrobial agent. It possibly inhibits microbial activity by blocking membrane function, cell wall formation and affecting the activities of different enzymes **[54]**.

Anti-diabetic property:

Cinnamon at doses of 5, 10 and 20 mg/kg body weight gives protection to pancreatic beta cells and enhances insulin secretion. It reduces cholesterol in addition to blood glucose levels. Methylhydroxychalcone polymer, hydroxycinnamic acid derivatives, catechin, campherol, quercitin, rutin etc. isolated from cinnamon are responsible for its anti-diabetic activity **[55-59]**. Ethanolic extracts of four types of cinnamon, *Cinnamomum cassia, C. burmanii, C. loureirii, and C. zeylanicum*, were tested for their alpha amylase and alpha glucosidase activity. Cinnamon inhibits alpha amylase activity with *C. cassia* showing the highest activity. All the extracts show a better performance in inhibiting alpha glucosidase with *C. burmanii* having the highest activity. All three except *C. loureirii* also reduce oral starch digestion **[60]**. Furthermore, *C. zeylanicum* also helps in lowering HbA1c, low density lipoproteins (LDL) and blood glucose along with increase in high density lipoproteins (HDL) and circulating insulin. Cinnamtannin-B1 obtained from *C. zeylanicum* reduces diabetes by reducing absorption of intestinal glucose, increasing

cellular uptake of glucose, stimulating release of insulin and modulating biochemical pathways by upregulating glucose metabolism, glycogen synthesis and downregulating gluconeogenesis **[61]**. Polyphenols, eugenols, cinnamic acid and cinnamaldehyde are responsible for the various anti-diabetic properties of cinnamon **[62]**.

Anti-inflammatory property:

Trans-cinnamaldehyde and p-cymene inhibit LPS induced IL-8 in THP-1 monocytes. It also inhibits NF-κB and activator protein (AP-1) in HEK-TLR2 and HEK-TLR 4 cells. Trans-cinnamaldehyde significantly reduces inducible reporter gene secreted embryonic alkaline phosphatase (SEAP) in HEK-TLR2 and HEK-TLR 4 cells **[63]**. Trans-cinnamaldehyde (25-100μM) inhibits LPS induced NO, COX-2 and inducible nitric oxide synthase (iNOS) in RAW264.7 cells. It also inhibits TNF-α, IL-1β and IL-6 in the murine macrophage cell line. The anti-inflammatory effect is mediated by inhibiting the ERK, JNK and p38 mitogen activated protein (MAP) kinase signalling pathways as measured by anti-phospho-ERK, JNK and p38 antibodies **[64]**. 2-hydroxycinnamaldehyde acts as an inhibitor in the NF-κB signalling pathway **[65]**. Cinnamon is also effective in treating arthritis by inhibiting the mediators of pain and inflammation **[66]**.

Hepatoprotective property:

Administration of ethanol extract of *C. zeylanicum* (0.01 -0.1 g/kg body weight) to male Wistar rats for 28 days prevents carbon tetrachloride (CCl_4) induced toxicity as marked by a decrease in serum aspartate transaminase (AST), alkaline phosphatase (ALP) and alanine transaminase (ALT) and increase in SOD, catalase and total protein. Histopathological studies also confirm that cinnamon reduces damage induced by CCl_4 in liver tissues though hydropic and vacuolar degeneration and lymphocyte infiltration at the periphery of central vein is observed **[67]**. The aqueous extract also possess hepatoprotective effects but the ethanolic extract is better compared between the two **[68]**.

Anti-cancer property:

Cinnamon is an effective anti-cancer agent. It inhibits the growth of various cancer cell lines like U937, Wurzburg, Jurkat, cervical cancer cell line etc. It up-regulates perforin and granzyme levels, various growth factors like vascular endothelial growth factor-alpha (VEGF-α), fibroblast growth factor (FGF), epithelial growth factor (EGF), transforming growth factor beta (TGF-β), monocyte chemo-attractant protein and a number of pro-inflammatory mediators like IFN-ɤ, TNF-α [69, 70, 71]. On the other hand, it down-regulates hypoxia inducible factor-1 alpha (HIF-1α) and COX-2 thus preventing angiogenesis

[72]. Essential oil inhibits epidermal growth factor receptor, matrix metalloproteinase-1 and plasminogen activator inhibitor-1 (PAI-1) in human dermal fibroblast **[71]**. Eugenol, cinnamaldehyde obtained from cinnamon are also effective against various cell lines; eugenol can be considered potent of the two as it is effective against HeLa cells, colon cancer cells, HT-29 and HC-T15, promyelocytic leukemia cell line, HL-60, prostate cancer cell line, PC-3 etc **[73-77]**. Eugenol also inhibits dimethylbenz-[a]anthracene (DMBA) croton oil induced carcinogenesis beside reducing 12-O-tetradecanoylphorbol-13-acetate (TPA) induced iNOS, COX-2, PGE-2, TNF-α and IL-6 **[78, 79]**. Cinnamon mediates its anti-cancer activity by encouraging apoptosis. Cinnamon and eugenol increase caspase 3, 8, 9, p53, $p21^{WAF1,}$ Bax, Bid, and inhibits Bcl-Xl, Bcl-2 and survivin proteins **[75, 79, 80]**.

Apart from the above mentioned health benefits exhibited by cinnamon, essential oil of *C. zeylanicum* obtained from its leaves and bark is also used as mosquito repellent and to kill the eggs and females of human head louse *Pediculus humanus capitis* **[81, 82]**.

Clove

Clove is the flower bud of *Syzygium* sp., belonging to the family Myrtaceae. They are native of the Spice Islands named Maluku of Indonesia **[3, 22]**. The flower bud is picked when bright red and sold as spice after drying to give its distinct aroma and taste **[3]**. Clove is named from the French word "clou" meaning "nail" due to its shape which resembles an irregular nail **[3, 23, 83]**. Due to their unique fragrance, they are burned as incense or smoked in cigarettes. In the 16^{th}-17^{th} century, the British, Dutch, Portuguese and Spanish fought between themselves for the supremacy of the Spice Islands; such was the demand of cloves. The West refers to clove as sweet spice whereas in East it is used for more zesty preparations **[3]**. The medicinal property of cloves was documented in Ayurveda, Chinese medicine and Western herbalism. It is a well known as a painkiller for toothaches since ages [23, 84]. Traditionally, it is also used as an analgesic, anaesthetic, anti-microbial, antiperspirant, antiseptic, antihelminthic, carminative, deodorant, digestive, stimulant and against diarrhoea and burns **[16, 22, 85-88]**. Eugenol and flavonoids are the active principles responsible for the various pharmacological properties of cloves **(Table 1)**. The activities of the crude extracts and various active principles of clove are detailed below:

Anti-microbial Property:

Clove oil and eugenol is effective against both gram negative bacteria like

Escherichia coli, Clostridium difficile, Pseudomonas aeruginosa, Salmonella enteritidis and gram positive bacteria like *Bacillus cereus, Staphylococcus aureus, Streptococcus pneumoniae.* Moreover, both have antifungal effects on *Aspergillus flavus, Penicillium expansum, Saccharomyces cerevisiae*. 1,2,3-triazole eugenol glucosides derived from eugenol is effective against *Micrococcus luteus* and *Salmonella thyphimurium*. Eugenil acetate is effective against *Acinetobacter*. It also acts as a promising anti-fungal agent. Polyhydroxybutyrate-eugenol is effective against *B. cereus, E. coli*, *S. aureus* bacteria and *Aspergillus flavus*, *A. niger, Penicillium, Rhizopus* **[89]**. Eugenol affects the fluidity and permeability of the fungal cell membrane thus disrupting the growth of fungi **[90]**. The anti-microbial activity of eugenol is dependent on its ability to disrupt cell membrane causing leakage of ions and damaging DNA.

Anti-diabetic Property:

Powder of clove bud (20 and 40 g/kg b.w.) reduces blood glucose levels, carbohydrate metabolising enzyme α-glucosidase in pancreatic tissue and angiotensin-1 converting enzyme in Wistar rats on high fat diet where type-2 diabetes was induced by streptozotocin **[91]**. Oleanolic and maslinic acid derived from clove reduce intake of food, blood glucose and ghrelin level in diabetic rats induced by streptozotocin **[92]**.

Anti-cancer property:

Clove is a potent anticancer agent and is effective against various types of cancers like breast cancer, cervical cancer, colon cancer, liver cancer, ovarian cancer, pancreatic cancer, prosprate cancer and oesophageal cancer **[93]**. Ethanolic extract of clove inhibited breast cancer and colon cancer by arresting cell cycle in the S phase and inducing apoptosis **[94, 95]**. It inhibited the growth of HT-29, BEL-7402, SKOV-3, PANC-1, DU-145, TE-13 representing colon, liver, ovarian, pancreatic, prostate and oesophagean cancer cell lines respectively **[94, 95, 96]**. Eugenol decreases the viability of HeLa cell lines in a dose dependent manner. In HeLa cells and cervical cancer cells it induces apoptosis by stimulating caspase3, Bax and PARP but no change in Bcl2 protein has been observed **[97]**.

Hepatoprotective and Nephroprotective property:

In diabetic rats fed with clove bud powder, liver function enzymes like aspartate transaminase (AST) and alanine transaminase (ALT) were reduced along with reduction in malondialdehyde content **[91]**. The decreased levels of antioxidant enzymes, catalase, SOD, GSH and ascorbic acid increased after treatment with clove **[91]**. Cold pressed clove oil at 100 and 200

mg/kg body weight reduces CCl_4 mediated toxicity in Wistar rats. It attenuates levels of AST, ALT and alkaline phosphatase (ALP) along with serum concentrations of bilirubin. It also decreases the total lipid, total cholesterol, triglycerides, LDL, VLDL and lipid peroxidation. HDL level and GSH show increase with treatment. Remarkable improvement is observed in necrosis and degenerated liver tissues after treatment though mild degenerative changes subsisted at 100 mg/kg b.w and congestion of the central blood vessel and sinusoids at 200 mg/kg b.w has been noticed. With respect to kidney, urea, uric acid and creatinine levels decrease and total protein, especially albumin and globulin levels increase after treatment with clove oil **[98]**.

Anti-inflammatory and Analgesic property:

Aqueous extract of clove inhibits LPS induced lung inflammation by reducing ROS generation in human neutrophils, myeloperoxidase activity in azurophilic granules, metalloproteinase 2, 9 and also reducing the neutrophil recruitment in lung tissues **[99]**. 3-acetyloleanolic acid, derived from clove is the best in pain relief as measured by tail flick test; oleanolic acid and its other derivatives exhibit similar results in reducing pain. In formalin induced pain test, 3-acetyloleanolic acid again gives the best results. But trifluoroacetyl derivatives are observed to be better than oleanolic acid. Oleanolic acid and all its derivatives significantly reduce albumin induced inflammation of hind paw in Wistar rats **[100]**.

Neuroprotective property:

Clove may be considered as a potent neuroprotective agent as many reports on its ability to prevent neural disorders are available. Some of them are elucidated below:

Alzheimer's disease: SIRT1 is an important molecule in reducing oxidative stress which in turn, is responsible for Alzheimer's disease. Ethanol extract of clove decreases extracellular and intracellular free radical generation and increases antioxidant enzymes like GSH, SOD and catalase in SH-SY5Y cells where neurotoxicity is induced using amyloid beta. It also prevents cell death induced by amyloid beta toxicity. The extract up-regulates SIRT1 and decreases ɤ-secretase protein thus helping to improve Alzheimer's like condition **[101]**.

Schizophrenia: Maslinic acid, obtained from clove at 30 mg/kg downregulates MK-801, an N-methyl-D7aspartate (NMDA) receptor antagonist induced hyperactivity in ICR mice. It improves sensorimotor gating activity by decreasing the amplitude of acoustic startle, increases social ability and recognition and prevents any adverse effects in the motor system indicated by the absence of cataleptic

behaviour. It reduces the phosphorylation of protein kinase-B, GSK-3β, CREB and ERK thus affecting Akt/GSK-3β and CREB/ERK signalling pathway **[102]**.

Epilepsy: Administration of eugenol protects hippocampal neurons of brain from excitotoxic, ischemic, and oxidative injury, both *in vivo* and *in vitro* conditions. The protection is due to the ability of eugenol to disperse granule cell by suppressing activation of mammalian target of rapamycin complex 1 (mTORC1) in mouse model of epilepsy induced by kainic acid **[103]**.

Bengali Garam Masala: The spice blend

A very few investigations are available that deal with the evaluation of the bioactive potential of the common Indian spice blend – garam masala as a whole. Studies reveal the beneficial properties of the spice blend especially as an antioxidant and as anti-microbial agent.

Anti-oxidant property:

The spice blend shows promising activities as an anti-oxidant. Several anti-oxidant assays have been performed. DPPH radical scavenging assay helps to determine the scavenging potential of antioxidant extracts based on their capabilities as hydrogen donor in tandem with electron transfer. The results of DPPH assay of garam masala has been found almost equivalent to its components except for cardamom. Lower activity of cardamom may be due to lesser extraction of non-polar bioactives which play an important role in DPPH assay. In FRAP assay, garam masala scores well over its ingredients in regard to the reducing capacity. It can be assumed that electron transfer mechanism is predominant for the spice blend as it is evident from FRAP assay. This may be due to the presence of polar polyphenols in the spice blend and it is also evident from the study that polar phenolics are the predominant antioxidants present in the aqueous extract of garam masala. But on the contrary, garam masala shows comparatively low level of hydroxyl radical scavenging activity than its components and cinnamon has the highest capability **[4]**.

Antimicrobial property:

Agar well diffusion method is used to study the anti-microbial activity of garam masala against some common food borne pathogen such as *Bacillus cereus, Escherichia coli, Staphylococcus aureus and Klebsiella pneumoniae.* 1:1:1 w/w ratio of the three components of garam masala is taken and aqueous mixture of different concentrations has been prepared. Significant inhibition has been achieved at 200 µg/ml concentration of the spice mix for both the gram-positive and gram-negative bacteria. Cinnamon may be the major contributing factor for its antimicrobial activity as it shows the best antibacterial activity amongst the three **[4]**. Moreover,

combination of clove and cinnamon oil is effective against both Gram-positive organisms *(Bacillus cereus, Enterococcus faecalis, Listeria monocytogenes,* and *Staphylococcus aureus*), and Gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Salmonella choleraesuis,* and *Yersinia enterocolitica)* **[104]**.

CONCLUSION

Spices have made their way into our daily diet since ancient times. They render a strong flavour to food even when used in minimal quantities. This is beneficial because they increase the flavour of food without increasing the calories. They also add small amounts of minerals and micronutrients to diet including calcium, iron, magnesium etc. **[24]**. Optimal use of Bengali garam masala in daily cooking is a good source of anti-oxidants and has antimicrobial properties. Each of the individual components is beneficial for human health and prevents inflammation, cancer, neurological disorders etc. Among the three, cinnamon and clove have been extensively studied including isolation of active components followed by mechanism involved. In comparison, fewer studies has been found on cardamom and mainly executed with the crude extract. The preliminary study on the pharmacological properties of spice blend, especially the Bengali variety, yielded very little information. Extensive studies need to be done in future to evaluate the immense bioactive potential of the blend in improving human health.

CONFLICT OF INTEREST: There is no conflict of interest.

REFERENCES

[1] Dubey. Indian Spices and their Medicinal Value, Indian Journal of Pharmaceutical Education and Research, Vol. 51(3), 2017 (Special Issue), S330-S332

[2] Garg G, Sharma S, Dua A *et.al.* Antibacterial potential of polyphenol rich methanol extract of Cardamom (*Amomum subulatum*), Journal of Innovative Biology, Vol. 3 (1), 2016, 271-275.

[3] Bilderback L. The complete idiot's guide to spices and herbs, Alpha Publications, A member of Penguin Group (USA) Inc. , 2007, 3-5

[4] Basu T, Bhattacharyya S, Maitra S *et.al.* Evaluation of antioxidant and antimicrobial activities of Garam Masala, an Indian spice blend, and its' components *in vitro*, Scholars Research Library: Der Pharmacia Lettre, 8 (20), 2016, 110-116.

[5] Kocchar KP, Dietary spices in health and diseases, Indian J of Physiol Pharmacol, 52 (4) 2008, 327-354.

[6] Shan B, Yizhong Z, Sun CM *et.al.* Antioxidant capacity of 26 spice extracts and characterization of their

phenolic constituents, J Agric Food Chem, 53, 2005, 7749-7759.

[7] Aruoma OI, Spencer JPE, Rossi R *et.al.* An evaluation of the antioxidant and antiviral action of extracts of rosemary and provencal herbs, Food Chem.Toxicol.34, 1996, 449-456.

[8] Cuvelier ME, Berset C, Richard H. Antioxidant constituents in sage (*Salvia officinalis*). J. Agric. Food Chem., 42, 1994, 665-669.

[9] Melo ED, Mancini J, Guerra NB. Characterization of antioxidant compounds in aqueous coriander extract (*Coriandrum sativum* L.). Lebensm.-Wiss. Technol.-Food Sci. Technol. 38, 2005, 15-19.

[10] Aruoma OI, Halliwell B, Aeschbach R *et.al.* Antioxidant and prooxidant properties of active rosemary constituents-Carnosol and carnosic acid. Xenobiotica, 22, 1992, 257-268.

[11] Frankel EN, Huang SW, Aeschbach R *et.al.* Antioxidant activity of a rosemary extract and its constituents, carnosic acid, carnosol, and rosmarinic acid, in bulk oil and oil-in-water emulsion. J. Agric. Food Chem. 44, 1996, 131-135.

[12] Lamaison JL, Petitjeanfreytet C, Carnat A. Medicinal Lamiaceae with antioxidative activity, potential sources of rosmarinic acid. Pharm. Acta Helv. 66,1991,185-188.

[13] Grayer RJ, Bryan SE, Veitch NC *et.al.* External flavones in sweet basil, *Ocimum basilicum*, and related taxa, Phytochemistry, 43, 1996, 1041-1047.

[14] Schwarz K, Ternes W. Antioxidative constituents of *Rosmarinus officinalis* and *Salvia officinalis*. 2. Isolation of carnosic acid and formation of other phenolic diterpenes. Z. Lebensm. Unters. Forsch. 195, 1992, 99-103.

[15] Vasavada MN, Dwivedi S and Cornforth D. Evaluation of Garam Masala spices and phosphates as antioxidants in cooked ground beef, Journal of Food Science, 71(5), 2006, C292-C297.

[16] Parle M and Khanna D. Clove: A champion spice, International Journal of Research in Ayurveda & Pharmacy, 2(1), 2011, 47-54.

[17] Rao PV and Gan SH. Cinnamon: A multifaceted medicinal plant, Evid-based Complement & Alternat Med, 2014, 642942

[18] Husain N and Pandey B. Ethno-medicinal use and pharmacological actions of some of the domestically used Indian spices- A review, Indo American Journal of Pharmaceutical Research, 5(12), 2015, 3892-3895.

[19] Bhattacharjee S, Se ngupta A. Spices in cancer prevention—An overview, Internet J. Nutr. Wellness, 2008, 7, 1–16.

[20] Kaefer, CM, Milner JA. The role of herbs and spices in cancer prevention, J. Nutr. Biochem., 19, 2008, 347–354.

[21] Allwyn Sundar Raj A, Aaron S, Seinenbalg SS, *et.al.* Review on

recent trends in isolation of antioxidants from spices and its biological effects of essential oils, J. Eng. Res. Appl., 4, 2014, 75–84.

[22] Muthumani A and Jensirani M. Health benefits of spices, KISANWORLD, 2017, 50-53.

[23] Paper H. Ajaikumar B, Kunnumakkara CK, Dey S. *et.al.* Traditional Uses of Spices: An overview in molecular targets and therapeutic uses of spices: modern uses for ancient medicine; Edited by Bharat B. Aggarwal and Ajaikumar B. Kunnumakkara published by World Scientific Publishing Co. Pte. Ltd., 2009, 3

[24] Sachan A Kr, Kumar S, Kumari K et.al. Medicinal uses of spices used in our traditional culture: Worldwide, Journal of Medicinal Plants Studies 6(3), 2018, 116-122.

[25] Duke JA, Bogenschutz-Godwin MJ, de Cellier J *et.al. Elettaria cardamomum* (L.) Maton (Zingiberaceae) Cardamon, Malabar or Mysore cardamon, in CRC Handbook of Medicinal Spices, CRC Press, Washington DC, 2003, 120-138.

[26] Kapoor LD. In Handbook of Ayurvedic medicinal plants, CRC Press Inc., Boca Raton, 1990, 172.

[27] Ballabh B, Chaurasia OP, Ahmed Z, *et.al.* Traditional medicinal plants of cold desert Ladakh-used against kidney and urinary disorders, J. Ethnopharmacol. **118**(2), 2008, 331–339.

[28] Jafri MA, Farah JK and Singh S. Evaluation of the gastric antiulcerogenic effect of large cardamom (fruits of *Amomum subulatum* Roxb). J. Ethnopharmacol. 75(2–3), 2001, 89–94.

[29] Noumi E, Snoussi M, Alreshidi MM, *et al.* Chemical and biological evaluation of essential oils from cardamom species, Molecules, 23(11), 2018, 2818.

[30] Abdullah AA, Butt MS, Shahid M, *et.al.* Evaluating the antimicrobial potential of green cardamom essential oil focusing on quorum sensing inhibition of *Chromobacterium violaceum*, J Food Sci Technol, 54(8) 2017, 2306-2315.

[31] Souissi M, Azelmat J, Chaieb K, *et.al.* Antibacterial and anti-inflammatory activities of cardamom (*Elettaria cardamomum*) extracts: Potential therapeutic benefits for periodontal infections, Anaerobe, 61, 2020, 102089.

[32] Aghasi M, Koohdani F, Qorbani M, *et al.* Beneficial effects of green cardamom on serum SIRT1, glycemic indices and triglyceride levels in patients with type 2 diabetes mellitus: a randomized double-blind placebo controlled clinical trial, J Sci Food Agric, 99(8), 2019, 3933-3940.

[33] Fatemeh Y, Siassi F, Rahimi A, *et al.* The effect of cardamom

supplementation on serum lipids, glycemic indices and blood pressure in overweight and obese pre-diabetic women: a randomized controlled trial, J Diabetes Metab Disord, 16, 2017, 40.

[34] Al-Zuhair H, El-Sayeh B, Ameen HA, *et.al.* Pharmacological studies of cardamom oil in animals, Pharmacol Res, 34(1-2), 1996, 79-82.

[35] Kandikattu HK, Rachitha P, Jayashree GV, *et al.* Anti-inflammatory and anti-oxidant effects of Cardamom (*Elettaria repens* (Sonn.) Baill) and its phytochemical analysis by 4D GCXGC TOF-MS, Biomed Pharmacother, 91, 2017, 191-201.

[36] Majdalawieh AF, Carr RI. *In vitro* investigation of the potential immunomodulatory and anti-cancer activities of black pepper (*Piper nigrum*) and cardamom (*Elettaria cardamomum*), J Med Food, 13(2), 2010, 371-381.

[37] Nair S, Nagar R, Gupta R. Antioxidant phenolics and flavonoids in common Indian foods, J Assoc Physicians India, 46, 1998, 708-710.

[38] Gomaa AA, Makboul RM, El-Mokhtar MA, *et.al.* Terpenoid-rich *Elettaria cardamomum* extract prevents Alzheimer-like alterations induced in diabetic rats via inhibition of GSK3β activity, oxidative stress and pro-inflammatory cytokines, Cytokine, 113, 2019, 405-416.

[39] Paul K, Ganguly U, Chakrabarti S, *et.al.* Is 1,8-cineole-rich extract of small cardamom seeds more effective in preventing Alzheimer's Disease than 1,8-cineole alone?, Neuromolecular Med., 22(1), 2020, 150-158.

[40] Qiblawi S, Dhanarasu S, Faris MA. Chemopreventive effect of cardamom (*Elettaria cardamomum* L.) Against Benzo(α)Pyrene-induced forestomach papillomagenesis in Swiss albino mice, J Environ Pathol Toxicol Oncol., 34(2), 2015, 95-104.

[41] Jamal A, Javed K, Aslam M, *et.al.* Gastroprotective effect of cardamom, *Elettaria cardamomum* Maton fruits in rats, J Ethnopharmacol, 103(2), 2006, 149-153.

[42] Bajpai M, Pande A, Tewari SK, *et.al.* Phenolic contents and antioxidant activity of some food and medicinal plants, Int J Food Sci Nutr, 56(4), 2005, 287-291.

[43] Khan A, Safdar M, Khan AMM, *et.al.* Cinnamon improves glucose and lipids of people with type 2 diabetes, Diabetes Care, 26 (12), 2013, 215-218.

[44] Das DR, Sachan AK, Vishnoi G, *et.al.* A Review on Surveillance of Herbal Medicines, International Journal of Phytopharmacology, 7(2), 2016, 68-72.

[45] Ammon HP. Cinnamon in type 2 diabetics, Med. Monatsschr. Pharm., 31(5), 2008, 179–183.

[46] Pieroni A and Torry B. Does the taste matter? Taste and medicinal perceptions associated with five selected herbal drugs among three ethnic groups in West Yorkshire, Northern England, J. Ethnobiol. Ethnomed., 3, 2007, 21.

[47] Dugoua JJ, Seely D, Perri D, *et.al.* From type 2 diabetes to antioxidant activity: A systematic review of the safety and efficacy of common and cassia cinnamon bark, Can. J. Physiol. Pharmacol, 85(9), 2007, 837–847.

[48] Duke JA, Bogenschutz-Godwin MJ, de Cellier J *et.al. Cinnamomum verum* J. Presl (Lauraceae) Ceylon cinnamon, Cinnamon, in CRC Handbook of Medicinal Spices, CRC Press, Washington DC, 2003, 114–115.

[49] Ranasinghe P, Pigera S, Premakumara GA, *et.al.* Medicinal properties of 'true' cinnamon (*Cinnamomum zeylanicum*): a systematic review, BMC Complement Altern Med.,13, 2013, 275.

[50] Matan N, Rimkeeree H, Mawson AJ, *et.al.* Antimicrobial activity of cinnamon and clove oils under modified atmosphere conditions, International Journal of Food Microbiology, 107(2), 2006, 180–185.

[51] Hili P, Evans CS, and Veness RG. Antimicrobial action of essential oils: the effect of dimethylsulphoxide on the activity of cinnamon oil, Letters in Applied Microbiology, 24(4), 1997, 269–275.

[52] Parthasarathy H and Thombare S. Evaluation of antimicrobial activity of *Azadirachta indica*, *Syzygium aromaticum* and *Cinnamomum zeyalnicum against* oral microflora, Asian Journal of Experimental Sciences, 27(2), 2013, 13–16.

[53] Abu El Ezz NMT, Khalil FAM, Shaapan RM. Therapeutic effect of onion (*Allium cepa*) and cinnamon (*Cinnamomum zeylanicum*) oils on cryptosporidiosis in experimentally infected mice, Global Vet, 7, 2011, 179–183.

[54] Shreaz S, Wani WA, Behbehani JM, *et.al.* Cinnamaldehyde and its derivatives, a novel class of antifungal agents, Fitoterapia, 112, 2016, 116–131.

[55] Yang CH, Li RX, and Chuang LY. Antioxidant activity of various parts of *Cinnamomum cassia* extracted with different extraction methods, Molecules, 17(6), 2012, 7294–7304.

[56] Li HB, Wong CC, Cheng KW, *et.al.* Antioxidant properties *in vitro* and total phenolic contents in methanol extracts from medicinal plants, LWT-Food Science and Technology, 41, (3), 2008, 385–390.

[57] Kim SH, Hyun SH, and Choung SY, Anti-diabetic effect of cinnamon extract on blood glucose in db/db

mice, Journal of Ethnopharmacology, 104(1-2), 2006, 119–123.

[58] Jarvill-Taylor KJ, Anderson RA, and Graves DJ, A hydroxychalcone derived from cinnamon functions as a mimetic for insulin in 3T3-L1 adipocytes, Journal of the American College of Nutrition, 20(4), 2001, 327–336.

[59] Anderson RA, Broadhurst CL, and Polansky MM, Isolation and characterization of chalcone polymers from cinnamon with insulin like biological activities, American Journal of Clinical Nutrition, 84(3), 2006, 1432–1436.

[60] Hayward NJ, McDougall GJ, Farag S, *et al*. Cinnamon shows antidiabetic properties that are species-specific: Effects on enzyme activity inhibition and starch digestion, Plant Foods Hum Nutr, 74(4), 2019, 544-552.

[61] Ranasinghe P, Jayawardana R, Galappaththy P, *et al*. Efficacy and safety of 'true' cinnamon (*Cinnamomum zeylanicum*) as a pharmaceutical agent in diabetes: a systematic review and meta-analysis, Diab Med, 29, 2012, 1480–1492.

[62] Zhu R, Liu H, Liu C, *et al*. Cinnamaldehyde in diabetes: A review of pharmacology, pharmacokinetics and safety. Pharmacol Res, 122, 2017, 78-89.

[63] Schink A , Naumoska K , Kitanovski Z, *et al*. Anti-inflammatory effects of cinnamon extract and identification of active compounds influencing the TLR2 and TLR4 signaling pathways, Food Funct, 9(11), 2018, 5950-5964.

[64] Kim ME, Na JY, Lee JS. Anti-inflammatory effects of trans-cinnamaldehyde on lipopolysaccharide stimulated macrophage activation via MAPKs pathway regulation, Immunopharmacol Immunotoxicol, 40(3), 2018, 219-224.

[65] Lee SH, Lee SY, Son DJ, *et al*. Inhibitory effect of 2-hydroxycinnamaldehyde on nitric oxide production through inhibition of NF-kappa B activation in RAW 264.7 cells. Biochem Pharmacol, 69(5), 2005, 791-799.

[66] Hariri M, Ghiasvand R. Cinnamon and chronic diseases, Adv Exp Med Biol, 929, 2016, 1-24.

[67] Eidi A, Mortazavi P, Bazargan M, Zaringhalam J. Hepatoprotective activity of cinnamon ethanolic extract against CCI4-induced liver injury in rats, EXCLI J, 11, 2012, 495-507.

[68] Moselhy SS, Ali HK. Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats, Biol Res, 42(1), 2009, 93-98.

[69] Kwon HK, Hwang JS. So JS, *et al*. Cinnamon extract induces tumor cell death through inhibition of NFkB and AP1, BMC Canc, 10, 2010, 392.

[70] Yang XQ, Zheng H, Ye Q, *et al*. Essential oil of Cinnamon exerts anti-cancer activity against head and neck squamous cell carcinoma via attenuating epidermal growth factor receptor - tyrosine kinase, J BUON, 20, 2015, 1518- 1525.

[71] Han X, Parker TL. Antiinflammatory activity of cinnamon (*Cinnamomum zeylanicum*) bark essential oil in a human skin disease model, Phytother Res, 31, 2017, 1034-1038.

[72] Kwon HK, Jeon WK, Hwang JS, *et al*. Cinnamon extract suppresses tumor progression by modulating angiogenesis and the effector function of CD8+ T cells, Cancer Lett, 278, 2009, 174-182.

[73] Hussain A, Brahmbhatt K, Priyani A, *et al*. Eugenol enhances the chemotherapeutic potential of gemcitabine and induces anticarcinogenic and anti-inflammatory activity in human cervical cancer cells, Cancer Biother Radiopharm, 26, 2011 519-527.

[74] Jaganathan SK, Mazumdar A, Mondhe D, *et al*. Apoptotic effect of eugenol in human colon cancer cell lines, Cell Biol Int, 35, 2011, 607-615.

[75] Yoo CB, Han KT, Cho KS, *et al*. Eugenol isolated from the essential oil of *Eugenia caryophyllata* induces a reactive oxygen species-mediated apoptosis in HL-60 human promyelocytic leukemia cells, Cancer Lett, 225, 2005, 41-52.

[76] Ghosh R, Ganapathy M, Alworth WL, *et al*. Combination of 2-methoxyestradiol (2-ME2) and eugenol for apoptosis induction synergistically in androgen independent prostate cancer cells, J Steroid Biochem, Mol Biol, 113, 2009, 25-35.

[77] Sadeghi S, Davoodvandi A, Pourhanifeh MH, *et al*. Anti-cancer effects of cinnamon: Insights into its apoptosis effects. Eur J Med Chem, 178, 2019,131-140.

[78] Pal D, Banerjee S, Mukherjee S, *et al*. Eugenol restricts DMBA croton oil induced skin carcinogenesis in mice: downregulation of c- Myc and H-ras, and activation of p53 dependent apoptotic pathway, J Dermatol Sci, 59, 2010, 31-39.

[79] Kaur G, Athar M, Alam MS. Eugenol precludes cutaneous chemical carcinogenesis in mouse by preventing oxidative stress and inflammation and by inducing apoptosis, Mol Carcinog, 49, 2010, 290-301.

[80] Wu SJ, Ng LT, Lin CC. Cinnamaldehyde-induced apoptosis in human PLC/ PRF/5 cells through activation of the proapoptotic Bcl-2 family proteins and MAPK pathway, Life Sci, 77, 2005, 938-951.

[81] Samarasekera R, Kalhari KS, Weerasinghe IS. Mosquitocidal

activity of leaf and bark essential oils of ceylon *Cinnamomum zeylanicum*. J Essent Oil Res, 17, 2005, 301-303.

[82] Yang YC, Lee HS, Lee SH, *et al*. Ovicidal and adulticidal activities of *Cinnamomum zeylanicum* bark essential oil compounds and related compounds against *Pediculus humanus capitis* (Anoplura: Pediculicidae), Int J Parasitol, 35, 2005, 1595–1600.

[83] Debjit B, Kumar KP Sampath, Yadav A, *et al*. Recent trends in Indian traditional herbs *Syzygium aromaticum* and its health benefits, J Pharmacogn Phytochem, 1(1), 2012, 6-9

[84] Daniel AN, Sartoretto SM, Schmidt G, *et al*. Anti- inflammatory and antinociceptive activities of eugenol essential oil in experimental animal models, Revista Brasileira de Farmacognosia, 19, 2009, 212- 217.

[85] Bhat KS, Vivek K. Biocidal potential of clove oils against *Aedes albopictus* – A comparative study, Afr J Biotechnol, 8(24), 2009, 6933-6937.

[86] Delaquis PJ, Stanich K, Girard B, *et al*. Antimicrobial activity of individual and mixed fractions of dill, cilantro, coriander and eucalyptus essential oils, Int J Food Microbiol, 74(1-2), 2002, 101-109.

[87] Duke JA, Bogenschutz-Godwin MJ, deCellier J, *et al*. *Syzygium aromaticum* (L.) Merr. and L. M. Perry (Myrtaceae) Clavos, Clove, Clovetree, in *CRC Handbook of Medicinal Spices*, CRC Press, 2003, Washington DC, 281.

[88] Balch P, Balch J. Prescription for Nutritional Healing, 3rd Ed. Very Publishing, 2000, 94.

[89] Hu Q, Zhou M, Wei S. Progress on the antimicrobial activity research of clove oil and Eugenol in the Food Antisepsis Field, J Food Sci, 83(6), 2018, 1476-1483.

[90] Marchese A, Barbieri R, Coppo E, *et al*. Antimicrobial activity of eugenol and essential oils containing eugenol: A mechanistic viewpoint, Crit Rev Microbiol, 43(6), 2017, 668-689.

[91] Adefegha SA, Oboh G, Adefegha OM, *et al*. Antihyperglycemic, hypolipidemic, hepatoprotective and antioxidative effects of dietary clove (*Szyzgium aromaticum*) bud powder in a high-fat diet/streptozotocin-induced diabetes rat model, J Sci Food Agric, 94(13), 2014, 2726-2737.

[92] Luvuno M, Mbongwa HP, Khathi A. The effects of *Syzygium aromaticum*-derived triterpenes on gastrointestinal ghrelin expression in streptozotocin-induced diabetic rats, Afr J Tradit Complement Altern Med, 13(4), 2016, 8-14.

[93] Chua LK, Lim CL, Ling APK, *et al*. Anticancer potential of *Syzygium* species: a review, Plant Foods Hum Nutr, 74(1), 2019, 18-27.

[94] Kubatka P, Uramova S, Kello M, *et al*. Antineoplastic effects of clove buds (*Syzygium aromaticum* L.) in the model of breast carcinoma, J Cell Mol Med, 21, 2017, 2837–2851.

[95] Liu H, Schmitz JC,Wei J, *et al*. Clove extract inhibits tumor growth and promotes cell cycle arrest and apoptosis. Oncol Res 21, 2014, 247–259.

[96] Dwivedi V, Shrivastava R, Hussain S *et al*. Comparative anticancer potential of clove (*Syzygium aromaticum*) – an Indian spice – against cancer cell lines of various anatomical origin, Asian Pac J Cancer Prev, 12, 2011, 1989–1993

[97] Das A, Harshadha K, Dinesh Kannan SK, *et al*. Evaluation of therapeutic potential of eugenol-A natural derivative of *Syzygium aromaticum* on cervical cancer, Asian Pac J Cancer Prev, 19(7), 2018, 1977-1985.

[98] El-Hadary AE, Ramadan Hassanien MF. Hepatoprotective effect of cold-pressed *Syzygium aromaticum* oil against carbon tetrachloride (CCl4)-induced hepatotoxicity in rats, Pharm Biol, 54(8), 2016, 1364-1372.

[99] Chniguir A, Zioud F, Marzaioli V, *et al*. *Syzygium aromaticum* aqueous extract inhibits human neutrophils myeloperoxidase and protects mice from LPS-induced lung inflammation, Pharm Biol, 57(1), 2019, 56-64.

[100] Rali S, Oyedeji OO, Aremu OO, *et al*. Semisynthesis of derivatives of oleanolic acid from *Syzygium aromaticum* and their antinociceptive and anti-inflammatory properties, Mediators Inflamm, 2016, 2016, 8401843.

[101] Shekhar S, Yadav Y, Singh AP, *et al*. Neuroprotection by ethanolic extract of *Syzygium aromaticum* in Alzheimer's disease like pathology via maintaining oxidative balance through SIRT1 pathway, Exp Gerontol, 110, 2018, 277-283.

[102] Jeon SJ, Kim E, Lee JS, *et al*. Maslinic acid ameliorates NMDA receptor blockade-induced schizophrenia-like behaviors in mice, Neuro-pharmacology, 126, 2017, 168-178.

[103] Kim SR. Control of granule cell dispersion by natural materials such as eugenol and naringin: A potential therapeutic strategy against temporal lobe epilepsy, J Med Food, 19(8), 2016, 730-736.

[104] Goni P, Lopez C, Sanchez R, *et al*. Antimicrobial activity in the vapour phase of a combination of cinnamon and clove essential oils, Food Chem, 116(4), 2009, 982-989.