



REVIEW ARTICLE



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Prospective Role in Treatment of Major Illnesses and Potential Benefits as a Safe Insecticide and Natural Food Preservative of Mint (*Mentha* spp.): A Review

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Abstract

Apart from its use for culinary purposes and as a home remedy for minor ailments, not many people are aware of the other "great" benefits of mint (*Mentha* spp.). Through this review article an attempt has been made to explore the emerging potential of mint (*Mentha* spp.) for treatment of various major diseases and promising action as an insecticide and repellent, as well as its potential application as a natural food preservative. This article justifies the emerging notion regarding adoption of safer and natural alternatives to the conventional antibiotics, medications and synthetic food preservatives carrying hazards in the form of numerous undesirable side effects.

Keywords: Mint, *Mentha*, medicine, analgesic, antimicrobial, anti-inflammatory, natural, repellent, insecticide, food preservation

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INTRODUCTION

Mint (Genus: *Mentha* spp.) is closely related to a variety of oil yielding plants like *sage*, *marjoram*, *basil*, *lavender*, *rosemary* and *thyme*. Like them *mint* is also included in the family *Labiatae* (*Lamiaceae*). And included within the genus *Mentha* spp. are above 25 species of *mint*; most common of them are: *peppermint*, *spearmint*, *wild mint*, *curled mint*, *American mint*, *bergamot*, *Korean mint*, *curled mint*, etc. These species thrives in the temperate cultivating zones of Australia, Eurasia and South Africa [1,2]. Since ancient times the tantalizing and mesmerizing aroma with additional benefits to human health by providing relief from common colds, fever, flu, indigestion and motion sickness, makes *mint* a popular kitchen herb in the numerous world regions [3]. Separation and subsequent identification of compounds such as flavonoids, phenolic acids, terpenoids and other volatile constituents from various extracts of *mint* was attempted by innumerable researchers. These constituents are of considerable dietary medical repute and several species of *mint* have them in common [1]. In the present day, *mint* consumption is staggering due to its multitude of uses. The economic importance of *mint* is well evident from the fact that its various compounds and constituents obtained from the desiccated and fresh plants and their essential oils forms part of numerous items of daily use like confectionary, cosmetics, oral hygiene products, pharmaceuticals, pesticides, and as a flavor enhancing agent in toothpastes, chewing gums and beverages, to name but a few [2,4,5].

Countless medical and pharmacological benefits have led to an enormous induction of research oriented interest in this amazing herb. Accordingly through this review article an attempt has been made to comprehensively elaborate the traditional and medicinal uses of *mint*.

TRADITIONAL USAGE AS A CULINARY HERB AND IN POPULAR MEDICINE

As a matter of interest some traditional benefits and uses of this aromatic herb is outlined here. Traditionally, *mint* is a very beneficial and important plant, as since ancient times it is extensively used in cuisines, medicaments and cosmetics [6]. In ancient times, spearmint was utilized for scenting the baths and as a restorative agent for regaining health and vigor. During 1300s, *mint* was used to restore the whiteness of dull and stained teeth. Its distilled oil still to this day forms part of confectionaries, chewing gums and toothpastes, as due to the aroma and taste of *mint* they get a soothing flavor. The same also imparts soaps with a ravishing perfume [1].

In India, culinary delights are made more appetizing and delectable by adding *mint*; known in this region for its savoring aroma and a taste laden with freshness and

warmth. Decoction prepared by boiling leaves of *mint* is effective in seeking relief from gastric distension, flatulence, dizziness, pregnancy related vomiting and as a cure for various bodily inflammations including bronchitis [4]. As a condiment and salad dressing called *chutney*, Indians grinds *mint* into a paste along with onion, garlic, ginger, tomato, raw mango and an array of spices including fennel seeds, black salt, black pepper and chillies. The tartness and sweet acidity of tomatoes in its soup can be complimented by adding fresh *mint* leaves in the chopped form. During blistering Indian summers, protection from heat strokes can be ensured by taking a refreshing drink obtained by crushing sugarcane with *mint* leaves or by eating yogurt with addition of powdered dried leaves of *mint* [1]. In a number of countries as a tea flavouring agent, *Mentha spicata* L. (spearmint) leaves are popularly used [2].

Both in pharmaceutical preparations and as a seasoning agent, *Mentha piperita* (peppermint) has a longish credibility of safe use. Numerous potent and beneficial constituents are part of peppermint such as menthyl esters, dimethyl sulfide, cadinene, amyl alcohol, acetaldehyde, pinene, pugelone, phellandrene and limone. Alpha- and beta-thujone, alpha-pinene, terpinolene, sabinene, gamma-terpinene, fenchene, citronellol, ocimene are the trace constituents contained within the *mint*, together with isolation of other numerous and varied compounds of potential health benefits. In folk medicine, *mint* has the credibility of successful alleviation of ailments such as parasitosis, headache, stomach cramps, flatulence and indigestion, nausea and vomiting, menstrual cramps and dysmenorrhea. The herb was found to be of a great therapeutic benefit when employed as a counteracting agent to flu and inflammation inducing processes of the oropharyngeal region, sinus tracts and cavities and of hepatobiliary and gastrointestinal origin [7,8].

A dull yellow liquid with a pungent aromatic taste but having a pleasant smell is obtained from the leaves of *M. piperita*. This liquid is the essential oil and better known as peppermint oil, with menthol as its principal constituent. Important addition of peppermint oil in medicines and widespread use as a flavoring agent, especially in confectioneries has helped it to gain the status of a popular compound. Complementary as well as traditional medicines deems it of considerable efficacy at treating fungal and bacterial infections of the human skin of mild intensity, headache syndromes and postherpetic neuralgia [9,10].

Traditionally, the flowering parts of *Mentha pulegium* (pennyroyal) have the antimicrobial reputation in combating tuberculosis, sinusitis, bronchitis and foodborne illnesses. The same were also used as expectorant, antitussive, diuretic and carminative [11].

In northeastern Brazil, the natives for use as medicinal plant grow *Mentha x villosa* that emerged due to hybridization of *Mentha suaveolens Ehrh.* and *Mentha spicata L.* It is commonly known as small-leaved mentha or creeping mentha. The decoction of its leaves is used in that particular part of world as an anxiolytic, for relief of menstrual colic and treating bloody diarrhea. *Mentha x villosa* has also demonstrated to be a potent antiparasitic in various parasitic conditions such as urogenital trichomoniasis, schistosomiasis, giardiasis and amebiasis [12].

In South Africa, Zulu people utilizes *Mentha aquatica* (water mint) for spiritual reasons specially in protection against evil spirits and also as a household remedy for curing respiratory ailments including common colds [13].

In Thailand *Mentha cordifolia* Opiz ex Fresen is not simply a famous kitchen herb due to its tantalizing aroma, in fact it has additional benefits of helping people to seek relief from influenza, fever, indigestion and motion sickness. Thai people preserve its leaves by desiccation achieved through either hot air drying or sun drying [3].

MEDICINAL ACTIVITY

Besides the traditional use of *mint* for culinary purposes and home remedies, it has the promising potential as a medicinal herb for treating complex medical ailments. Table 1 summarizes the important medical effects of the various species of *mint* evaluated through research studies.

Antidiarrhoeal and positive digestive effects

In the underdeveloped nations, diarrhea is a leading cause of mortality and morbidity among adolescents. Therefore international health organization like WHO are taking the initiatives of supporting the studies based on conventional medicines pertaining to the prophylaxis and treatment of this killer disease. In this direction, plants with a therapeutic value can be of potential help. For this purpose an investigation was carried out in Egypt on plant extracts (in dosages of 200 and 400 mg kg⁻¹) of six indigenous medicinal plants for their overall antidiarrhoeal effect and also for their effect on motility of isolated rabbit's duodenal musculature. A significant ($P < 0.01$) antidiarrhoeal effect against castor oil-induced diarrhea was found in rats on oral administration of methanol based preparation of *Mentha microphylla* extract in a dose of 400 mg kg⁻¹. While in rabbits a dose-dependent (0.4–2.8 mg ml⁻¹) relaxation of the duodenum got evident from the same extract.

On phytochemical evaluation of plant extracts the dominant constituents that were revealed includes: unsaturated sterols/triterpenes, flavonoids, tannins, proteins, carbohydrates and lactones. And it was concluded that curtailment of the diarrhoeal activity by the extract of *Mentha microphylla* could be ascribed, at

least moderately to its content of tannins which form protein tannate that reduces intestinal secretion [14]. Spearmint is known to be as an effective carminative and gastro-stimulant. The boiled leaves extract or water distillate relieves hiccup, flatulence, giddiness of indigestion as well as controls vomiting during pregnancy [1,2,4].

Medical benefits	Species of mint	Preparation(s) used
Antidiarrhoeal effect [14]	<i>Mentha microphylla</i>	Methanol extract
Gastrointestinal antispasmodic [7]	<i>Mentha piperita</i>	Essential oil (peppermint oil)
Non-ulcer dyspepsia, gastro-esophageal reflux disorder, intestinal infections (bacterial & candidal) [15]	<i>Mentha piperita</i>	Enteric-coated peppermint oil
Relief of indigestion, epigastric bloating, flatulence [16]	<i>Mentha piperita</i>	Essential oil (peppermint oil)
Generalized bacterial infections [7]	<i>Mentha piperita</i>	Essential oil (peppermint oil)
Antibacterial activity against Gram -ve bacilli [6, 19]	<i>Mentha piperita</i>	Juices of leaves & stem, essential oil
Antibacterial activity against Gram +ve species [11]	<i>Mentha pulegium</i>	Essential oil
Antigiardial activity [8]	<i>Mentha piperita</i>	Methanolic, dichloromethane & hexanic extracts
Antiviral effect [10]	<i>Mentha piperita</i>	Essential oil
Antibacterial & antifungal effect [15]	<i>Mentha spicata</i>	Carvone isolated from essential oil
Anti- <i>Candida</i> activity [18]	<i>Mentha arvensis</i>	Essential oil
Anti-inflammatory activity [4]	<i>Mentha spicata</i>	Ethanol extract
Antioxidant activity [1, 4]	<i>Mentha spicata</i>	Essential oil
Antinociceptive effect [23]	<i>Mentha microphylla</i>	Methanolic extract
Haemostatic and pain relieving properties [4]	<i>Mentha spicata</i>	Ethanol extract
Antihypertensive & myorelaxant activity [12, 27]	<i>Mentha villosa</i>	Essential oil

Table 1: Evaluated medical benefits of various species of mint (*Mentha* spp.)

Physiological alteration of the GI musculature by peppermint makes it of a potential value for their role in clinical trials for the treatment of barium enema related colonic spasm. Two sixty nine (269) healthy individuals were a part of nine studies in which they were exposed to peppermint through any one of the method of administration i.e. either orally or by topical intraluminal approach through stomach or colon. The results revealed of the following effects due to it: reduction of the slow wave frequency in the esophagus and small intestine, which slows peristaltic movements,

effective inhibition of the potassium depolarization-induced responses in the intestine, decrease in the total gastrointestinal transit or gastric emptying, lessening of the basal tone in the gastrointestinal tract. So the results of this directed to the conclusion that the administration led to the relaxation of the lower esophageal sphincter. Therefore peppermint can of use as an antispasmodic agent for double-contrast barium meal examination and in patients with dyspepsia [7]. Moreover improvement of gastrointestinal activity may be achieved by enteric-coated peppermint oil (ECPO) in subjects suffering from a functional affliction of the large bowel; irritable bowel syndrome (IBS). A few more ailments like gastrointestinal colonization by *Helicobacter pylori* (a bacterium associated with stomach cancer) and *Candida albicans*, gastro-esophageal reflux disorder and non-ulcer dyspepsia were found to successfully respond to ECPO. Further to the point, a combination of peppermint and caraway oil may also be helpful during episodes of esophageal spasm and intestinal colic. A few clinical studies have suggested that this combination of the two essential oils can even help to dissolve gallstones [15].

Peppermint is laced with numerous active compounds such as limonene, menthone, menthofuran and menthol, and on clinical assessments these constituents were found to have an elevated medicinal worth especially in the treatment of the gastrointestinal complaints. It is interesting to note that people are now getting used to the adoption of peppermint oil or peppermint tea as remedy for indigestion, dyspepsia, flatulence and epigastric bloating [16].

Antimicrobial activity

The proliferation of antibiotic resistant bacterial strains is one of the reasons that pose a serious threat in achieving an effective elimination of microbial diseases. Since times immemorial plant extracts including their essentials oils have induced tremendous research interest for exploring their potential health benefits including the antimicrobial activity. The main driving force for invoking this interest is the notion that the medicinal components derived from plants are non-hazardous and economical, in contrast to the exorbitantly priced synthetic medicines having numerous adverse effects. Most importantly World Health Organization (WHO) has also noted that a major chunk of world's population relies on traditional medicine for acquiring essential healthcare. This importance led to an increased focus on assessment of the potential benefits of aromatic plants as remedial agents in infectious ailments [6,17]. An *in vitro* as well as *in vivo* biological activity of extracts and essential oil of plants, beneficial in many terms have been reasonably demonstrated through various studies. Based on this optimistic demonstration, there has been a justification of conducting more focused research

related to the estimation of the antimicrobial action of the plant derivatives [18]. A naturally existing cyclic terpene alcohol by the name of "menthol" with a molecular weight of 156 and chemical formula of $C_{10}H_{20}O$ imparts the various species of *Mentha* with a characteristic aroma and flavor. Menthol also demonstrated to have appreciable antibacterial effects against *Enterobacter aerogenes*, *Clostridium sporogenes*, *Klebsiella pneumonia*, *Salmonella pullorum*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Comamonas terrigena* and *Streptococcus faecalis* [7].

Above 10% of the indigenous bacterial flora consists of Gram -ve bacilli hence making them omnipresent. Variations in humidity and temperature and declining counts of the normally occurring Gram +ve organisms encourages a speedy gaining of the ground by Gram -ve bacilli ultimately leading to development of the range of anaerobic clinical infections like brain abscesses, wound infections, urinary tract infection (UTI), nosocomial bloodstream infections. For their treatment, an array of antibiotics is in usage. However their increased dependence has resulted in the emergence of resistant strains of the microbes. The multiple drug resistance has led to an accelerated demand for finding out medicines that can be potent against the resistant species of bacteria. The juices of leaves and stem of peppermint were examined for their antibacterial effects towards 56 isolates which are part of 11 various species of Gram-ve bacilli: *Klebsiella pneumonia*, *Salmonella typhi*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella paratyphi A*, *Salmonella paratyphi B*, *Proteus vulgaris*, *Enterobacter aerogenes*, *Yersinia enterocolitica* and *Shigella dysenteriae*. These isolates were cultured from varied laboratory specimens of urine, stool, blood and pus. The topmost antibacterial activity was exhibited by the extract of leaves with an average zone of inhibition $17.24 \text{ mm} \pm 0.87 \text{ SD}$, while the least effect was demonstrated by the extract obtained from the stem of *mint* with an average zone of inhibition $15.82 \text{ mm} \pm 3.56 \text{ SD}$ [19].

In another study conducted later on by Saeed et al. in which effects of various formulations of peppermint viz., juice, aqueous infusion, essential oil and decoction were researched against 11 different strains of Gram -ve bacilli viz., *Klebsiella pneumonia*, *Salmonella typhi*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Salmonella paratyphi A*, *Salmonella paratyphi B*, *Proteus vulgaris*, *Enterobacter aerogenes*, *Yersinia enterocolitica* and *Shigella dysenteriae*. The investigation involved the procedure of standard disc diffusion. With the 11.78 mm mean zone of inhibition the highest activity against bacteria was displayed by essential oil. Then with an inhibition zone of 10.41mm, the antimicrobial activity of peppermint juice specific to Gram -ve bacilli remained next to oil. Lastly,

decoction and aqueous infusion failed to produce any significant action against any of the 100 isolates of the same microbe [6].

The ethnopharmacological relevance of *M. pulegium* (pennyroyal) for its antiseptic properties was determined through an investigational screening of the essential oil of the plant's flowering parts against numerous microbes. A significant activity particularly against Gram-positive bacteria was revealed through results exhibiting minimal inhibitory concentration values and inhibition zones in the ranges of 0.25–4 $\mu\text{l/ml}$ and 8–21 mm and, respectively. The antibacterial efficacy of oil was so significant that even a minute quantity of 1 μl was comparable to potent antibiotics (Vancomycin, Erythromycin, Gentamycin, Amphotricin B.) for *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Candida albicans* and *Aspergillus niger*. On its chemical analysis the major constituents found out to be were piperitone (38.0%), piperitenone (33.0%), terpineol (4.7%), and pulegone (2.3%). This study affirmed the significant antimicrobial efficacy of pennyroyal and based on it suggested the therapeutic application of it as antibiotic or alternative [11].

Bupesh et al. evaluated the anti-pathogenic effects of chloroform, ethyl acetate, petroleum ether and water extracts of the leaf of peppermint against *Bacillus subtilis*, *Pseudomonas aerogenosa*, *Pseudomonas aureus*, *Streptococcus aureus* and *Serratia marcesens*. This study involving the *in vitro* agar well diffusion technique confirmed that the organic as well as aqueous decoctions from the leaves were potent enough to eliminate the targeted pathogens. Meanwhile, the efficacy of ethyl acetate extracts remained significant due to the creation of large zones of inhibition ranging from 9mm [16].

Giardiasis is a disease of humans caused by a parasite "*Giardia lamblia*". Upper jejunum and duodenum are the preferred points of colonization for the parasite. The general medications currently in practice to address this disease include furazolidone, metronidazole and benzimidazoles. Notwithstanding their common usage, these medications subject their users with numerous side effects including gastrointestinal disturbances, headache, dizziness, vertigo and anorexia. Due to development of resistance, strains of *G. lamblia* do not respond adequately to the antimicrobials currently in practice. These factors compelled Vidal et al. to evaluate the effects of the fractions and extracts of peppermint on trophozoites of *G. lamblia*. This analysis ascertained the effects affecting the adhesion, morphology and multiplication of the parasites' trophozoites. Results revealed that dichloromethane, hexanic and methanolic extracts put forth IC_{50} values of 0.8, 2.5 and 9.0 $\mu\text{g/ml}$ after 48 hours of incubation, respectively. The aqueous extract

displayed no effect against the trophozoites with an $\text{IC}_{50} > 100 \mu\text{g/ml}$, however the aqueous fraction caused a moderate activity with an IC_{50} of 45.5 $\mu\text{g/ml}$. The best anti-giardial activity was shown by the dichloromethane fraction, with an IC_{50} of 0.75 $\mu\text{g/ml}$ after 48 hours of incubation. The adhesion and morphological assays disclosed that this fraction induced disparate alterations on plasma membrane surface of the parasite and restrained the adherence of *G. lamblia* trophozoites. Furthermore, no lethal impact on the intestinal cell line IEC-6 got evident on cytotoxic assays. The anti-giardial activity of *Mentha x piperita* brought forward through this study, indicated the herb's potential therapeutic value in giardiasis [8].

The Gram-negative bacterium *Helicobacter pylori* is the chief causative organism for peptic ulceration and chronic type B gastritis, with a strong linkage to stomach cancer. In the developed world the prevalence of *H. pylori* is near 40%, while in the developing nations the figures hovers around 80–90%. Currently conventional antibiotics are the mainstay treatment for eradication of the bacterium. The conventional regimen involves a combination of two antimicrobials and a proton pump inhibitor. Drug resistance is the main impediment in achieving a success rate surpassing 80% following this therapy and an alarming fact is that this rate is further declining. Moreover, this treatment involves administration of a couple of medications, which may lead to the causation of side-effects that together with increased treatment expenditure, ultimately contribute to inadequate drug concordance. These elements, in addition to antimicrobial resistance, emphasize the urgent need to track out novel anti-*Helicobacter pylori* medications. In the last couple of years there has been a considerable surge in the research studies focusing on the anti-*Helicobacter pylori* effects of the medicinal herbs and plants. To test the effects of various herbs and plants utilized in Mexican complementary medicine, aqueous and methanolic distillates of 53 distinct plant species were assessed *in vitro*. Aqueous extract (AE) of *Mentha piperita* as well as of *Artemisia ludoviciana subsp. mexicana*, *Ludwigia repens* and *Cuphea aequipetala* showed the highest inhibitory effect (Minimum inhibitory concentration (MIC) 125 to $< 250 \mu\text{g/ml}$); in contrast, methanolic extracts (MEs) of the same plants had insignificant effect against *Helicobacter pylori* (MIC 500 to $> 500 \mu\text{g/ml}$). The data obtained from this study provides valuable information necessary for the development of new anti-*Helicobacter pylori* therapies [20].

Herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) are characteristic microorganisms that induces epidermal lesions in the pharynx, mouth, esophagus, eye and genitals. Contact with infected saliva leads to transmission of HSV-1

causing herpes labialis, whereas sexual contact with an infected partner leads to transmission of HSV-2 resulting in neonatal and urogenital infections. In Germany, an assessment of the virucidal and inhibitory activities of peppermint oil against herpes simplex virus was undertaken. Technique of plaque reduction assay was employed *in vitro* to test the oil's inhibitory effect on RC-37 cells. At noncytotoxic concentrations, there have been significant reductions in plaque formation by the viruses at percentages of 82% and 92% for HSV-1 and HSV-2, respectively. For virucidal activity the viral suspension tests confirmed that at elevated concentrations the oil significantly curtails down the titers of the herpes viruses by more than 90%. Further through the same study, peppermint oil was found to be also potent against an acyclovir resistant strain of HSV-1 (HSV-1-ACV^{res}), as it considerably inhibited and thereupon brought down its titre by 99% [10].

Individual constituents derived from *mint* also have significant antimicrobial activity. Purification of essential oils of dill, caraway and spearmint achieved through chemical and biotechnological means yields 'carvone'. *In vitro* bioactivity demonstrated that its optical isomers were effective against a broad spectrum of pathogenic bacteria and fungi. L-Carvone or (4R)-(-)-carvone with a sweet odour is the main constituent of spearmint. At concentration of 10 µg/ml it was found to have a reasonable antimicrobial effect over *E. coli* and *Enterococcus faecium* and above a concentration of 10 µg /ml against *Aspergillus niger* [15].

As plants carries a wealth of compounds with antimicrobial properties it is expected that screening programs for some under-represented areas like anti-fungal activity may lead us to potential novel antifungal constituents located within them. *Candida albicans* is an opportunistic fungal pathogen that leads to a variety of local and systemic afflictions in compromised individuals such as persons with immunologic impairments and those on prolonged antibiotic treatment. It is important to note that so far there hasn't been the satisfactory utilization of the already present information focused on medicinal herbs effective in combating these yeast species, ultimately resulting in a dearth of antifungal formulations having effectual value. Ethanolic extracts and oil from leaves and/or roots of thirty five plants that have been under use as medicines in Brazil are tested for anti-*Candida albicans* activity. An appreciable anti-*Candida* activity was displayed by the essential oils of the thirteen out of the thirty five plants including peppermint and *Mentha arvensis* (Japanese mint). On the other hand the ethanolic extract failed to create a potent anti-*candidal* effect at any of the concentrations tested. The assessment outcome symbolizes a meaningful input to

the characterization of the anti-fungal activity of the essential oils and plant extracts [18].

Anticancerous activity

A monoterpene by the name of perillyl alcohol (POH) naturally occurs in essential oils of *mint*, as well as of gingergrass, lavender, cranberries, cherries, perilla, savin and sage. POH and its metabolite perillic acid (PA) have been reported to possess anti-tumor action against numerous forms of carcinoma in human. Their exact course of action has yet to be determined. Nevertheless *in vitro* studies showed that POH led to a reasonable inhibition of the growth of lung, breast and pancreatic cancer cells. Among both males and females, lung cancer tops the list for all cancer related mortalities. Above 80% of lung cancer incidences comprise cases of non-small cell lung cancer (NSCLC) that has a five year survival rate and that too of less than 15%. Presently therapeutic measures for tackling lung carcinoma consist of chemotherapy, radiation therapy and finally an option of surgery. Even though surgery is a last ditch solution, majority of the patients with lung carcinoma presents with an advanced form thereby making radical resection impossible. Consequently, there is an intense necessity to seek out efficacious and potent chemotherapeutic agents versus NSCLC. To this end, the effects of effects of POH and PA on the growth and multiplication of non-small cell lung cancer (A549, and H520) cells were examined. The results illustrated that both agents by evoking cytotoxicity, arresting cell cycle, induction of apoptosis and elevating the expression of bax, capase-3 and p21 action in both the cell lines of NSCLC are found to be sufficiently capable of suppressing the tumorous progression of NSCLC. The potentiality of these agents (POH and PA) as promising therapeutic agents for tackling lung carcinoma has led to an increased interest for testing them through clinical trials [21].

Anti-inflammatory activity

Arumugam *et al.* evaluated the *in vivo* effects of chloroform, hexanic, aqueous (AF) and ethyl acetate (EAF) fractions of ethanol extract of spearmint on cotton pellet (chronic) and carrageenan (acute) induced inflammation in rats. As positive control two commonly used anti-inflammatory medications (Indomethacin and Diclofenac), while as negative controls (25% DMSO and ddH₂O) were employed. Results showed that adequate suppression of chronic inflammation got evident in AF and EAF treated groups (greater than 52%) and this effect was comparable to the anti-inflammatory drugs (~74%). It was also found that these fractions by virtue of the containment of secondary metabolites like phenolics and flavonoids possessed considerable free radical scavenging effect which ultimately leads to an efficient curtailment of the formation of granulomas. The anti-inflammatory effect of the compounds can be due to the inhibition of

inflammatory mediators which are presumed to have role in the production of reactive oxygen species (ROS). Moreover, a two fold increase in the levels of antioxidants {Glutathione (GSH) and glutathione peroxidase (GPx)} was reported in both AF and EAF treated groups, in comparison to the values of the controls. In conclusion, this study suggested that fractions from the spearmint leaves based on ethanol can abate the process of chronic inflammation through their antagonistic effects on oxidation [4].

Antioxidant, free radical scavenger and radioprotective activities

Free radical species such as hydroxyl radicals ($\text{OH}\cdot$), superoxide anion radical ($\text{O}_2^{\cdot-}$) and non-free radical species such as hydrogen peroxide (H_2O_2) causes oxidative harm to organic molecules such as proteins, lipids, nucleic acids and carbohydrates. The ensuing cellular damage or oxidative injury seems to be a major predisposing factor behind a range of ailments like cardiovascular problems, inflammations, viral afflictions, autoimmune disorders, gastrointestinal disorders and diabetes [1,22]. Fortunately enough, against these oxidative insults there is a mechanism of antioxidant defense in all aerobic organisms including human beings. However, this natural mechanism can sometimes be inadequate to respond appropriately, and hence in order to boost this defense, ingestion of antioxidant compounds gets imperative. It has been documented that chemical constitution of *mint* includes effectual trace elements such as manganese, cobalt & zinc and potent organic components (such as carveol) in compound form. All these are believed to significantly contribute to the free radical scavenging effects of the *mint* extract [1]. In addition, it has been documented that monoterpenoids like limonene, menthol, menthone, carvone, *s*-carvone, pulegone and dihydrocarveol are comprised within the essential oil of spearmint. Together, flavonoid, phenolic and terpenoid complexes have been isolated from numerous distillates of spearmint. Antioxidant effects of some of these compounds were found to even exceed the same of α -tocopherol (Vitamin E). Due to their potential pharmacological role as natural antioxidants and free radical scavenger and together being an integral part of spearmint is garnering immense research interest and attention [1,4]. This might have compelled Choudhury *et al.* to subject the methanol, diethyl ether and dichloromethane distillates of *mint* to free radical scavenging activity tests and observed that diethyl ether extract of *mint* displayed approximately 100% antioxidant efficiency at $\sim 40\mu\text{g}/\text{L}$ while the remaining two extracts show very little activity [1].

Analgesic and antinociceptive effects

The analgesic/ antinociceptive agents reduce the sensitivity to painful stimuli. Pharmaceutically many

agents are in use as analgesics, however most of them produce infrequent side effects including gastrointestinal complexities spanning from mild-moderate symptoms (nausea, vomiting and diarrhea) to excruciating complications (ulcer, hemorrhage and perforation). This drug related side effects substantiate the need for developing non-toxic analgesics. Since a long time plant extract have been looked at as lucrative sources of agents for pain alleviation. To this end, a multitude of plants and herbs have reasonably demonstrated to possess analgesic efficacy [23]. The ethanolic distillates of eleven plants of Jordan that have been in traditional usage as medicines were researched for their antinociceptive effectiveness by employing tests of acetic acid-induced writhing and hot-plate tests in mice. Furthermore the anti-inflammatory and analgesic actions of the same plants were ascertained through tests of cotton pellet granuloma and xylene-induced ear oedema in rats. These tests revealed that *Mentha piperita* (peppermint), *Ruta graveolens*, *Cinnamomum zeylanicum*, *Eucalyptus camaldulensis* and *Apium graveolens* exerts an antinociceptive impact in opposition to both hot plate-induced thermal stimulation and acetic-acid induced writhing. Moreover, *M. piperita*, *Beta vulgaris*, *Commiphora molmol* and *Jasminum officinale* were found to be in possession of anti-inflammatory influence against acute (xylene-induced ear oedema) and chronic (cotton-pellet granuloma) inflammation. Additionally through the gathered results, a dose-dependent anti-inflammatory action of the extracts based on ethanol of *M. piperita* (dose-dependent), *B. vulgaris*, *C. molmol* and *J. officinale* versus both acute (exudative) and chronic (proliferative) inflammation, also got evident. Finally this data affirmed the traditional use of mint for painful and inflammatory conditions [24]. In another study of similar nature, methanolic decoctions (200 and 400 mg kg^{-1}) of eight plants (including *M. microphylla*) in use of Egyptian folk medicine were assessed for their antinociceptive action. This study was conducted in mice through tests of acetic-induced writhing and tail-flicking tests. *M. microphylla* in the largest dose (400 mg kg^{-1}) lent a protection of 45.8– 50.8% from painful provocation by acetic acid, although in comparison to the control the mean number of writhes was found to be significantly ($P < 0.05$) lower. More to the point, the tests revealed that there has been no let-up in pain in animals at the lowest dose (200 mg kg^{-1}) of the same plant extract. It was further found that there has been a significant ($P < 0.05$) increase in the latency to response of tail to thermal stimulation at an administered quantity of 400 mg kg^{-1} of the same plant extract. Phytochemical analysis pointed out the existence of dominant chemical entities of triterpenes, flavonoids, unsaturated sterols, glycosides and tannins within the extract of *M. microphylla*. The analgesic

effect of the extract of *M. microphylla* can be attributed to these constituents, as all of them were proved to have an appreciable analgesic effect in other plant extracts [23].

Solvent fractions (ethyl acetate, hexane, aqueous and chloroform) of spearmint's ethanol based decoction have been identified to possess numerous compounds that are known to have beneficial effects of anti-inflammation and as analgesics. These include flavonoids, terpenoids, water-soluble phenolics like acacetin, apigenin, diosmetin, ericitrin, glucoside, luteolin, sideritoflavone, thymonin and thymusin. In addition to them, newly isolated monoterpenoids (spicatoside A and B) were also found to have potent hemostatic properties in addition to giving relief from inflammation and pain [4].

Interestingly, a historical review on clinical approaches to headache used by practitioners in medieval Persia documented the oral administration of pennyroyal (*Mentha Pulegium*) oil as a cure for "shaqhiqeh"—a recurrent unilateral headache, as it was believed to have a nerve fortifying effect. Meanwhile for the same ailment, topical and nasal application of spearmint was advocated because of analgesic effect in *shaqhiqeh* [25].

All the evidences lend pharmacological credence to the promising applications of *mint* for managing conditions associated with pain and inflammation.

Cardiovascular, hypotensive effects

Wayward lifestyle including appropriate diet and excessive mental stress can lead to arterial thrombotic events. Therefore in the developed world, utmost attention is given to the prevention of thrombovascular disorders. For this purpose immense focus is directed on following a diet plan comprising food with antithrombotic effects, as regular consumption of such a diet provides an easy and controlling way of protection from cardiovascular diseases. Aggregation of platelets is a major contributing factor resulting in numerous cardiovascular diseases. So natural agents (including vegetables and fruits) presumably with antiplatelet action need to be researched. To this end, an investigation was aimed at screening the herbs for their antithrombotic action. This investigation involved a primary *in vitro* platelet function test and a secondary laser- induced *in vivo* carotid artery thrombosis test. Through this study, peppermint was found to have significant thrombolytic effects [26]. Through an investigation performed in rats to assess the hypotensive action of the essential oil of *Mentha x villosa* (EOMV) for lowering the hypertension induced by prolonged administration of deoxycorticosterone-acetate (DOCA)-salt, it became evident that there has been a dose-dependent reduction of blood pressure in the conscious hypertensive rats on intravenous (i.v.) administration of EOMV. And that this hypotensive

effect was found to be significantly marked when compared with uninephrectomized controls. This increased EOMV-induced hypotension could have been associated with heightened vascular reactivity to EOMV, instead of an association with an elevated sympathetic nervous system action [12].

Furthermore through an earlier study of Lahlou et al. conducted in 2001 dose-dependent reductions in heart rate and mean aortic pressure were reported on i.v. administration of EOMV in anesthetized rats. The study deduced that these diminishments could have been attributable to pipertenone oxide (PO); a major component of EOMV. Apparently these effects affecting cardiovascular system seemed to be independently occurring, as EOMV induced slowing of heart rate (bradycardia) is manifested as dependent upon the presence of a flawless and functional sympathetic nerve drive to the heart. Whereas EOMV-induced hypotension appeared to be free of the existence of a viable sympathetic nervous system, as it remained unaffected by i.v. induction of hexamethonium [27]. In folk medicine therefore the application of *Mentha x villosa* as an antispasmodic has been justified because of its myorelaxant activity [12].

Central Nervous System (CNS) effects

Acetylcholinesterase is an enzyme acting in the nerve synapses and responsible for the degradation of an important neurotransmitter; acetylcholine. As proposed by cholinergic hypothesis, cholinesterase inhibitors causes prolongation of the effect of acetylcholine that ultimately leads to the enhancement of the transmission of the impulses within the nerve synapses. By means of that cholinesterase inhibitors are being therapeutically employed for addressing myasthenia gravis and Alzheimer's disease with success. Based on these promising outcomes, an immense interest is evident for searching out novel inhibitors as there are only a few in clinical use. The inhibition of the acetylcholinesterase was investigated by Oinonen et al. by putting to test the capabilities of methanol extracts of different species of *mint* (*M. x piperita* L., *M. arvensis* L., *M. pulegium* L., *Mentha longifolia* L., *M. x gentilis* L. and *M. spicata* L.). For recognition of compounds straightaway from micro-fractionated extracts without the need of bothering for further purification, liquid chromatography combined with ion trap mass spectroscopy is a powerful screening implement. Firstly the enzyme inhibitory activity is evaluated by pre-screening the decoctions on thin layer chromatography (TLC), followed by tracking down the active compound by combining enzyme assay in 96-well plate to high performance liquid chromatography (HPLC) micro-fractionation. As a result the active compound in the flower extract of *M. arvensis* (wild mint or corn mint) was identified as linarin and the effect of fractionated flower extract on

acetylcholinesterase (AChE) activity in 96-well plate showed selective dose dependent inhibitory effect on acetylcholinesterase. The results of this investigation illustrated the potential applicability of the above defined method to track out and recognize the acetylcholinesterase inhibitors in extracts of the plants [28].

Moreover a sedative or anti-convulsive effect is produced, when a causative agent comes and attaches to the γ -aminobutyric acid (GABA) -benzodiazepine receptors, depending on the receptor subtype the agent is attaching to. Accordingly a screening was undertaken to check the affinity of the compounds from South African plants comprising tranquilizing effects to the GABA- benzodiazepine receptor. For that purpose, the compounds of *water mint*; viridiflorol from the essential oil and (*S*)- naringenin from an ethanolic extract were bounded to the GABA-benzodiazepine site. Of the two agents, viridiflorol was found to adequately restrain the binding of acetylcholinesterase, an enzyme often linked with Alzheimer's disease. Nonetheless, naringenin has also been able to possess many effects outside the CNS, such as being a mutagenic and genotoxicology inhibitor, a cancer chemopreventive agent and also possessing antibacterial, antiviral, antiallergic, antioxidant, hypocholesterolic, apoptotic and cytostatic activities [13].

Lately, peppermint has been found to enhance athletic efficiency, as well as there have been some particular claims of its capability in reducing drowsiness. In a few countries smelling on the oil vapors of the peppermint helps to rejuvenate the medical practitioners, fatigued from the extended working hours. This inhalation also helps to prevent the post-lunch lethargy and sluggishness. A widely published assertion appearing in the popular literature that mint has restorative and stimulating effects has been probed through objective appraisal of the diurnal drowsiness (daytime sleepiness). Having said that, pupillary unrest can be indexed through pupillary fatigue oscillations which serve as a standard of measuring daytime somnolence. On contrasting with the odorless state, the induction of peppermint oil leads to inhibition of sleepiness during eleven (11) minutes spent in an unlit room. A variation in subjective ratings of initial sleepiness from the Stanford Sleepiness Scale (SSS) was shown not to be connected to the marked difference in sleepiness between the mint oil and the odorless settings. Even though the existence of peppermint oil fades out the increase in daytime sleepiness linked with sitting in dark rooms, but still it is not apparent from this investigation that peppermint oil has actually anti-sleep-inducing actions or the competence to interrupt the inception of sleep. Therefore in order to support the viewpoints about the invigorating effects of

peppermint oil, there is a need to go for empirical research investigations related to the substantiation of claims of its capacity to keep people invigorated and active, especially during night-time work shifts [29].

Ethnoveterinary effects

M. piperita (peppermint) was found to have ethnoveterinary potential as it has been documented to address the abdominal troubles including the control of gastrointestinal parasites in cats, dogs and pigs of the British Columbian region of Canada. In addition to the production of relaxation effects on GI, various studies on the animal models undertaken in the region revealed of anesthetic and analgesic effects on the peripheral and central nervous systems and immunomodulating phenomenon. To this end, experiments established the high-level validity of peppermint for treating ailments connected to stomach, and its mid-level validity as an anthelmintic in the above referred animals. *In vitro* assay found principles (β -sitosterol and glucosides), from leaves of *M. cordifolia* to be effective against *Ascaris suum* (roundworm of pigs). This effect is almost similar to the one produced by mebendazole (anthelmintic drug). In addition, *Mentha* spp., have been found to comprise a reasonable combating activity against *Haemonchus contortus* (a pathogenic nematode of ruminants) [30].

POTENTIAL BENEFITS AS A NATURAL REPELLENT AND INSECTICIDE

Long-term polluting and contaminating effects of the conventional biocides (pesticides and insecticides) on the human health and environment resulted in a public concern and outcry leading to their availability being dwindled in the recent years. Therefore, researchers have become more ambitious in their search of novel biocides which obviously should be effective along with the properties of *biodegradability* and *eco-friendliness* [31]. Currently there has been spawning of interest in possible employment of plant extracts as substitutes to synthetic biocides. Essential oils top the list of the plant based substances, tested versus insects. Because of their versatile mechanism of action these plants based naturally occurring compounds may have the actions of repellents, contact insecticides, fumigants and antifeedants. They can act by various mode of action that affects the biological limits within the insects such as life span, growth rate, reproduction and cell biology [32]. As already mentioned, L-Carvone or (4R)-(-)-carvone is the principal component of spearmint. The numerous uses of carvone includes: in the agricultural field i.e. as potato sprouting inhibitor, in the food industry as for producing fragrance and flavors and its significance in the medical field as a potential antimicrobial agent. More to the interest, as an insecticide carvone can effectively act against the fruit fly, *Drosophila melanogaster*. All this has led to an

infusion of tremendous research interest for further exploration of this monoterpene [15].

As deer repellent the successful application of spearmint oil has been established through a patent application [33]. By mixing spearmint oil with water in an oil extender and spraying this mixture on vegetation keeps off deer from munching on the plants. It has been completely safe to use this spray on vegetables, fruits and ornamental plants [15].

Mosquitoes are a major source of transmission of many lethal diseases in humans, like dengue, malaria, yellow fever, encephalitis and filariasis. Around the world numerous municipalities have enforced various mosquito control procedures and programs to keep the mosquitoes in check. Use of aerosols and aerial spray of chemicals is included in such programs. However, resistance of mosquitoes to these chemicals and retraction from market of registered anti-mosquito agents due to adverse environmental and health related issues have led to drastic curtailment of options for controlling these blood sucking creatures. As a result of this, it gets all the more important to seek new ways for evolving effective strategies for elimination of mosquitoes which should also be environment friendly. Hence plant derivatives that have been in traditional use by different communities around the world against the various entomological species have been evaluated against mosquitoes particularly in the last ten years. The results of this evaluations revealed that phytochemicals sourced from plants have the potential to take up position as surrogate chemical agents for combating mosquitoes, as they possess mosquito repellent action and more importantly have pupicidal, larvicidal and adulticidal effects [31]. Indian researchers investigated the larvicidal activity of oil of *M. piperita* L. (peppermint) by inflicting different varieties of species of mosquitoes including: *Anopheles stephensi*, *Aedes aegypti* and *Culex quinquefasciatus*. *Cx. Quinquefasciatus* was found to be the most vulnerable followed by *An. stephensi* and *Ae. aegypti*. Administration of oil at 3ml/m² of water surface area for duration of 24 hours caused 100% elimination of *Cx. Quinquefasciatus*, 90% of *Ae. aegypti* and 85% of *An. stephensi*. 100% elimination of *Ae. aegypti* was acquired in 48 hours of application of oil at 3ml/m² or in 24 hours at 4ml/m². A 100 % rate of elimination was seen at 4ml/m² in 72 hours for *An. stephensi*. Another promising thing to note is that there has been an inhibition of emergence to a major extent at 3ml/m² and the few adults that were able to thrive were unable to ovipost even after feeding on a blood meal. On a direct application to the human skin, the oil displayed a marked repellent activity versus mature mosquitoes. The percentage rates of protection from *An. annularis*, *An. culicifacies*, and *Cx. quinquefasciatus* were 100%, 92.3% and 84.5%, respectively. This study convincingly

concluded that oil of peppermint was approximately as potent as Mylol oil, which is commercially available as a mosquito repellent [9]. Although Ansari et al. in 2000 demonstrated that the essential oil of mint has potent repellent activity to counter *Anopheles annularis* and *Anophales culicifacies*, which are accountable for causing the majority of cases of malaria across the rural part of northern India, however a Turkish investigation conducted by Erler et al. conducted in 2006 revealed a depressed repelling activity of the same essential oil. This variance in results of the two studies could be due to the investigation of Erler et al. focusing on a distinct specie of mosquito i.e. *Culex pipiens* [31]. Furthermore, an important constituent isolated from spearmint; (4R)-(-)-carvone was found to be having a strong capability for antagonizing mosquitoes particularly the mature female of *Aedes aegypti*, which is the prime transmitter of maladies like dengue, yellow fever and haemorrhagic dengue. (4R)-(-)-carvone is also of substantial value as a precursor of octyl and pentyl endoperoxide derivatives. *In vitro* analysis of these derivatives showed an appreciable eliminating action of them on HB3species of *Plasmodium falciparum* [15]. In recent times for establishing safer pest control strategies with a reduced environmental persistence and minimal mammalian toxicity, there has been a growing research emphasis pertaining the possible application of extracts of plants and herbs for controlling insects feeding on stored food products. Bruchidae and particularly *Acanthoscelides obtectus* has drawn the attention of numerous scientists primarily because of its destructible impact on the stored crops. Due to excellent adaptation to physiological variations, *A. obtectus* gets an edge in becoming the leading damaging pest of *Phaseolus vulgaris* L. (kidneybean), one of the most significant of leguminous crops of the Mediterranean and South American regions. The estimation of the annual damage caused by this pest comes to about 20–40% deficit within the total amount of stored seeds of the legume. Papachristos and Stamopoulos in 2002 tested the effects of oils (in vapour form) of *Mentha viridis*, *Mentha microphylla*, *Lavandula hybrida*, *Laurus nobilis*, *Citrus sinensis*, *Eucalyptus globulus*, *Apium graveolens* and *Rosmarinus officinalis* on *A. obtectus*. Few of the mentioned oils demonstrated a substantial lethal effect on the pest, with males emerging as more sensitive to the effects in comparison to females. For males, the most lethal oils were found to be that of *M. viridis* and *M. microphylla* [32].

AS A NATURAL AND “GREEN” ALTERNATIVE TO SYNTHETIC FOOD PRESERVATIVES

The augmented demand of consumers for natural and organic products as well as the deleteriousness of artificial antioxidants has guided the attention of researchers towards the edible herbs and plants as

natural resources of harmless and effectual antioxidants for use in food industry. In the same manner as other oil-water emulsions, dairy commodities also undergo oxidative and hydrolytic rancidities. The rancidity in foods is due to the reaction of oxygen with the food constituents particularly lipids. For depressing the rancidity of fats and oils, synthetic agents are widely employed such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA) and tertiary butyl hydroquinone (TBHQ) And also for inhibiting the oxidative degeneration of dairy items, antioxidants mainly in synthetic form have been extensively utilized. In India, a milk delicacy with a smooth consistency by the name of 'Sandesh' is popularly consumed as a traditional dessert. This sweet treat also offers a rich supply of proteins, fats, vitamins and carbohydrates. Sandesh is produced by heat desiccation of 'Chhana' (a heat-acid coagulated product of milk analogous to cottage cheese). Through a research study involving set of experiments, the capability of antioxidants (from natural sources) for controlling the deterioration of lipids happening through oxidation was evaluated. From the gathered results it got evident that *mint*, beet and ginger possess superior antioxidant properties, which were as good as that of TBHQ alone, and combination of BHT and BHA. Blending of *mint* or ginger with beet produced better retardation of lipid oxidation as compared to beet alone. Apart from the effectiveness, another greatest advantage of these antioxidants derived from natural sources unlike their synthetic counterparts is that they are free from undesirable health effects. Therefore in order to obtain health benefits from these well effective natural retardants of lipid oxidation, their adoption by the dairy industry may be advisable as well as worthwhile [34].

Based on the detrimental effects, the story is also not different concerning the widespread use of chemical preservatives by the food industry, as the demand by the consumer rights groups is gaining strength for completely abolishing their use by moving onto "natural-green" substitutes for extending the shelf life of food products. To this end, numerous herbs and spices can offer themselves as potential candidates since it has been established that their essential oils encompasses antimicrobial capabilities. This capability can help to maintain the quality of food items over an extended period of time by delaying the process of food deterioration through holding up the development of the food borne microorganisms. Accordingly the effects of the essential oil of peppermint in varying strengths (ranging from 0–1.2% v/v) on the survival and growth of *Staphylococcus aureus* and *Salmonella enteritidis* were assessed in nutrient broth. The conductance measurements and viable count method revealed a sufficient inhibiting action against these two food

borne bacteria, as concentration of essential oil as minimal as 0.4% seemed to be effective. Therefore it can be safely assumed that the specific oil can prove to be a promising stabilizer of foods [35].

CONCLUSION

Mint enjoying the foothold status of a popular & traditional kitchen herb, can also offer numerous benefits ranging from the medical arena to other areas having a strong association with health: spanning from the food industry to repellents and insecticides. The manuscript is hoped to dispel the impression that *mint* is only a simple culinary herb as commonly known. In fact it has the potential of taking the statuses of a potent curative herb, natural antioxidant for controlling food deterioration or as an insecticide; pesticide or a repellent for combating the menacing creatures. In conclusion, this review is expected to help understand the urgency of the need for an ambitious and in-depth dedicated research initiatives that can further explore and ultimately reveal the real "great" medical benefits of this amazing herb.

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