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RADIO-PROTECTIVE POTENTIAL AND ANTIMICROBIAL ACTIVITY OF PUDINA. (MENTHA SPP. /MINT)

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ABSTRACT

Pudina (mentha piperita) belongs to the family Labiate is a perennial herb growing in the hilly regions or in the cold climatic region in India. Pudina (mentha arvensis L.) is used as carminative, anti-peptic ulcer agent, antispasmodic, and has been used to treat indigestion, skin diseases, coughs and colds in folk medicine. Mint has vitamin A. Simple changes in diet can lead to significant reduction in disease burden without adding cost. Plants and herbs have been used for the healing purposes and maintaining a good health. Oil as well as the extract of mentha piperita possesses significant radio protective properties. Pudina is used as an antidote to poison. Pudina extract demonstrated an antimicrobial activity against streptococcus mutans.

KEYWORDS: Mint, antimicrobial activity, radioprotection, mentha piperita.

INTRODUCTION

Plants and herbs have been used for healing purposes and maintaining good health. Pudina (Menthaspicata L.) and their products prepared from the extracts are some of the highly marketed naturopathic ayurvedic medicines. Pudina leaves are used as an antidote to poison.[1] Research has shown that Mint Leaves are beneficial for human health as it contains significant amount of micronutrients, vitamins, antioxidants, photochemical and fiber content that may help protect against degenerative diseases and micronutrient malnutrition. Many valuable medicinal herbs are becoming rare and precious information regarding their health benefits is lost.[2] Mint is a common herb used in Indian kitchen. It is cheap, commonly available, and simple herb. It contains number of vitamin and minerals, which are vital to maintain a healthy body. Mint is rich in vitamin A and vitamin C and also contains smaller amounts of vitamin B2.[3] Study done by the researchers have determined that mint can be a

cheaper alternative for vitamin A.Although most people only use a small amount of herbs in cooking, nutritional benefits of mint and other herbs can add up.[3] The herbal drugs offer an alternative to the synthetic compounds and are considered either non-toxic or less toxic than their synthetic counter parts. Plants and their phytochemicals, especially with free radical scavenging, antioxidant properties, and immune-stimulatory effects have been evaluated for their radio-protective effects. Studies have shown that some commonly used medicinal plants and their photochemical possess radio-protective effects.[4] The essential oils of *Mentha* plants have anti-inflammatory, antimicrobial, antioxidant, anti-carcinogenic, insecticide and analgesic properties.[5] and also used in the perfumery, pharmaceutical and food industries.[6] Essential oil bearing plants belonging to Mentha species, (Menthaarvensis) locally known as pudina[7] constitutes the most important source of therapeutic agents and is used in the alternative systems of medicine.[8] The mint plant contain many active ingredients such as menthol (40-50 %)[9] Carvone (67.3 %), limonene (13.5%), 1, 8- cineole (5.4%), linalool (2.8 %), menthone (2.9 %), and isomenthone (1.2 %)[10] Which provide positive effects on health and productivity[11] Study conducted by[12] also showed that *Menthaarvensis* has significant hepato-protective activity. Methanolic extract of pudina can be prepared by cold extraction method. Pudina extract demonstrated an antimicrobial property against streptococcus mutans.[13]

WHO reported that 70% of the population of developing countries depends on natural product drugs for health care.*Menthaarvensis* L. (Lamiaceaea) is distributed throughout the western Himalayas and is cultivated throughout world for use as a vegetable. It is an erect aromatic herb that grows up to 60 cm in height with suckers; the stem is cylindrical and the leaves are simple and opposing type. *Menthaarvensis* L. is used as a carminative, anti-spasmodic, anti-peptic ulcer agent, and has been given to treat indigestion, skin diseases, coughs and colds in folk medicine. Inspite of increasing advancement in the field of medicine and molecular diagnosis it is estimated that 80% of the world population is still dependant on the plant derived pharmaceuticals. WHO report that plant based products or its derivatives accounts for nearly 28% of drugs available in the market.[14] Natural products as such and their derivatives have historically been exploited as a valuable source of novel therapeutic agents.[15] Pudina (menthaarvensis L.) is used as carminative, antispasmodic, anti-peptic ulcer agent and has been given to treat indigestion, skin diseases, coughs and colds in folk medicine.[16]

HISTORY AND SPECIES

The benefit of pudina with its therapeutic advantages and healing properties is surviving for over 4000 years.[17] Experiments on the antimicrobial properties of plant components were first documented in the late 19th century.[18] Different parts of pudina have been used to cure specific ailments. Today in Japan and many Asian countries pudina is commonly used as an ingredient in commercially available yogurt and food beverages. There are also many companies which produce pudina beverages and flavours. Essential oils and extracts from pudina plant species control microorganisms related to skin, dental caries and food spoilage, including Gram-negative and Gram-positive bacteria.[19] Pudina was widely acclaimed as carminative, digestive, aromatic and an anti-emetic agent (that allays nausea and vomiting), and is valued as a stimulant, expectorant, antispasmodic killer of intestinal worms and a mildly analgesic herb.[20] Recently it is proved thatit is mosquito repellent[21] and has anti-nematodal,[22] antiviral,[23] antifungal[24] properties.

There are more than 25 species in the genus Mentha and this contains both pure species, *Menthaarvensis* (Japanese Peppermint), *M. asiatica* (asian mint), *M. australis* (Australian mint), *M. cervina* (Hart's Pennyroyal), *M. citrato* (bergamot mint), *M. crispata*(wrinkled leaf mint), *M. aquatica* (water mint), *M. laxiflora* (forest mint), *M. longifolia*or *M. sylvestris* (horse mint), *M. lulegium*(pennyroyal), *M. requienii* (corsican mint), *M. sachalinensis*(garden mint), *M. satureioides* (native pennyroyal), *M. spicata*or *M. cordifolia*(spearmint), *M. suaveolens* (apple mint), *M. vegans* (gray mint)] and the hybrid species, the most important being peppermint *M. piperita,* a cross between the *M. aquatica* (water mint) and *M. spicata* (spearmint); and the ginger Mint *M. gracilis* a cross between *M. arvensis* sand *M. spicata* (spearmint)[25]

A RADIOPROTECTIVE AGENT- MINT

Mentha is an important culinary plant with immense medicinal use. The plant which was originally a native to Europe was carried to different parts of the world through travellers, warriors, and traders. Today, Mint is cultivated in North America, Africa, Australia, and Asia mainly for its pharmaceutical, medicinal, and culinary uses. Globally, the essential oil obtained by steam

Figure 1: Photograph of a mint plant.

Distillation of the fresh leaves is used as a flavouring agent, an ingredient for some cosmecutical preparations, and as a medicinal agent.[25]

MINT IN TRADITIONAL MEDICINE AND SCIENTIFICALLY VALIDATED STUDIES

Peppermint is known to relieve digestive ailments and is a popular remedy in the various traditional and folk medicines in Europe, China, Arabia, and the Indian subcontinent. The leaves are carminative and are used to treat digestive disorders such as dyspepsia (e.g. spastic complaints of the upper gastrointestinal tract), bacillary dysentery, flatulence, gastritis, and enteritis. It is also used as a cholagogue, emmenagogue, vermifuge, to enhance lactation, and as a sedative. The leaves are useful in the treatment of bronchitis, diabetes, diarrhoea, fevers, hypertension, jaundice, nausea, pain, respiratory, and urinary tract infections.[25]

Studies have shown that mint and its oil reduces smooth muscle contractions through a calcium channel blocking effect. This then causes the antispasmodic effect on the smooth muscles of the gastrointestinal tract.[26,27] It also relaxes the smooth muscles of the gastrointestinal tract by reducing the cellular calcium influx[25] Menthol, the active principle is reported to be antibacterial, stimulates bile flow, reduces the tone in the oesophagealsphincter, facilitates belching, and acts as a carminative.[25,28] It also possesses neuromodulatory and performance-enhancing properties.[29] Mint oil modulates the calcium channel-dependent processes in intestinal, neuronal, and cardiac preparations.[30] It decreases travel sickness, stimulates bile flow, and assists digestion[31] mint also possess cancer preventive properties[32] and benzo[a]pyrene-induced lung tumours in mice[33] mint is effective in ameliorating the various gastrointestinal disorders to avoid or mitigate the

irritable bowel syndrome and in preventing digestive disorders like dysentery, flatulence, and gastritis.[25]

PHYTOCHEMICALS PRESENT IN MINT

Irrespective of the plant species, the phytochemicals present in the various species of Mentha are the same while their ratios may alter. Mint plants contain over 40 distinct chemical compounds.[25] The essential oil of peppermint is mostly made up of menthol, menthone, menthol esters, 3-carene, carvone, *cis*-carane, *cis*pinane, isomenthone, limonene, menthanol, myrcene, and the monoterpene derivatives pulegone, piperitone, menthofuran, trans-cinnamic acid, oleanolic acid, *p*-cymene, physcion, terpinolene, and urosolic acid [Figure 2]. Mint also contains α-pinene, β-pinene, cineole, jasmone, ledol, limonene, neomenthol, piperitone, pulegone, and viridiflorol[Figure 2]. Menthol and menthol acetate are responsible for the pungent and refreshing odour while the ketones menthone, pulegon, menthofuran have a less delightful fragrance. Traces of jasmone improve the oil's quality [Figure 2].[25] The mint plants also contain the flavonoids acacetin, chrysoeriol, diosmin, eriocitrin (eriodictoyl-7-o-rutinoside), hesperidin, hesperidoside, isorhoifolin, linarin, luteolin, menthoside, methyl rosmarinate, rutin, tilianine, narirutin, and nodifloretin. The phenolic acids present are caffeic acid, lithospermic acid, rosmarinic acid, protocatechuic acid, protocatechuic aldehyde, phytosterols, β-sitosterol, and daucosterol; the anthraquinones aloe-emodin, chrysophanol, emodin, and tannins are the other compounds present [Figure 2].[25]

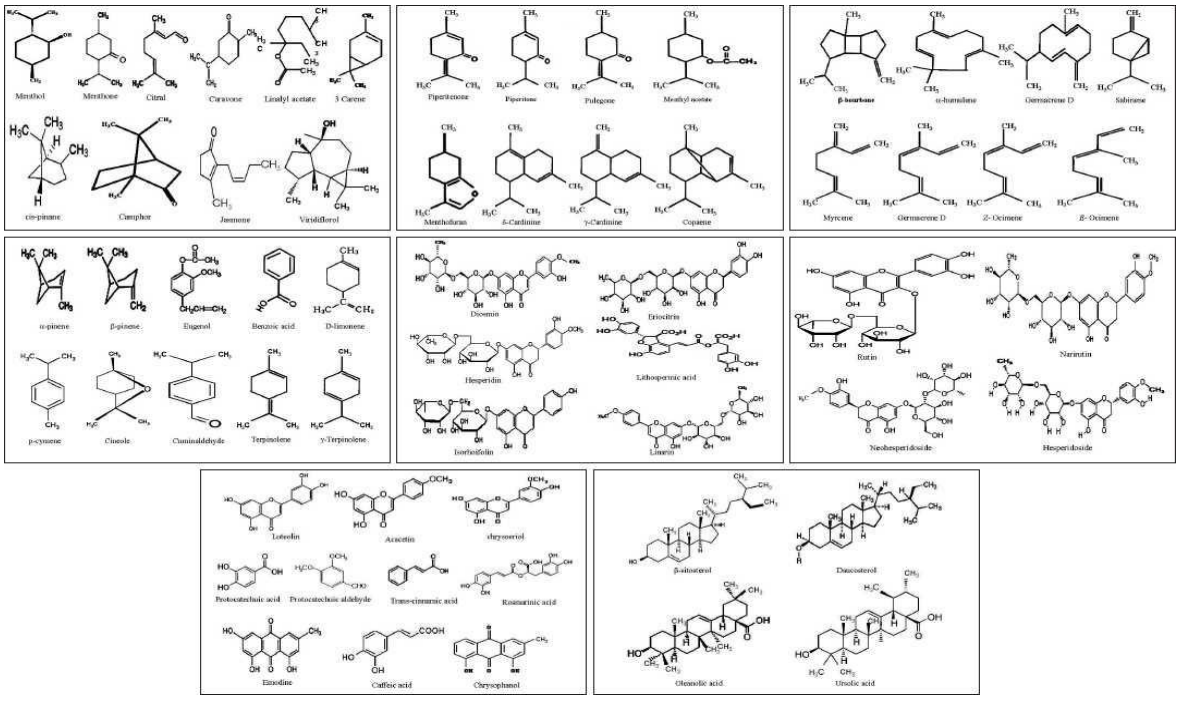

Figure 2: Chemical structure of some phytochemicals present in mint.

SURVIVAL STUDIES OF *M. ARVENSIS* AND *M. PIPERITA* AND RADIOPROTECTIVE POTENTIAL

Among all available experimental assays, animal survival as the end point is the most confirmatory in radio protective study because this assay clearly indicates both quantitative and qualitative degree of the radio-protective effects of a test compound. The chloroform extract of *M. Arvensis* protected mice against the radiation-induced sickness and mortality.[34] Oil as well as the aqueous extract of *M. Piperita* possesses significant radio-protective properties.[35,36] Oral administration of the oil and the aqueous extract of the plant for three consecutive days protected mice against the radiation-induced sickness and mortality.[37,36] In rodents, death within 10 days post-irradiation is due to the gastrointestinal epithelial damage, while that from 11 to 30 days post-irradiation is because of hematopoietic damage.[34] From these studies, it is evident that both *M. arvensis* and *M. Piperita* protected mice against both gastrointestinal and bone marrow deaths. Mint also prevented radiation-induced weight loss and emaciation in these studies suggesting that, irrespective of the polarity (chloroform and aqueous extracts), the radio-protective effects were significant. A series of preclinical studies by Ashok Kumar, Ravindra Samarth and colleagues have shown that mint protects the vital organs against the radiation-induced ill effects.

Mint Protects against the Radiation-Induced Hemopoetic Syndrome and Gastrointestinal Syndrome

The lympho-hematopoietic elements are among the highly replicating tissues and are the most radiosensitive life supporting organs.[38] Oral administration of the aqueous extract of *M. Piperita* as well as mint oil increased total erythrocyte and leucocytes counts, haemoglobin concentration, and hematocrit values.[37,36] An increase in the number of bone marrow cells; the leucoblasts, myelocytes, metamyelocytes, band/stab forms, polymorphs, pronormoblasts, and normoblasts, lymphocytes, and megakaryocytes in bone marrow; and the levels of erythropoietin in serum[39] and increase in the weight of the spleen and in the number of endogenous colonies (CFU-S) was found. The pre-treatment with the mint extract protected the lympho-hematopoietic elements from the deleterious effects of ionizing radiation, possibly through the free radical, antioxidant, and anti-inflammatory effects.[37,38]

Ionizing radiation is rarely used to treat localized gastrointestinal (GI) tumors, and is done with great caution and care.GI tract is exposed to scatter radiation when treating for cancer of the colon, rectum, prostate, and other closely linked sites.[40,41] The gastrointestinal protective

effects of *M.piperita* in mice by evaluating the villus height, goblet cells/ villus section, total cells, mitotic cells, and dead cells/crypt section in the mouse jejunum from day 1 to day 20 post irradiation.[41] Exposure to radiation alone caused a decrease in the villus height, number of total cells, and mitotic cells/crypt section with a concomitant increase in goblet cells and dead cells.[41] Pretreatment with *M. piperita* reversed these changes, indicating entero-protective effects.

Mint mitigates Radiation-Induced Behavioral Perturbations in Rats and reduces the Radiation-Induced Testicular Damage in Mice

Exposure to ionizing radiation causes change in the behavioral perturbations such as emesis, conditioned taste aversion, performance decrement, learning and memory impairment.[42] Radiation-induced conditioned taste aversion has been defined as a behavioral endpoint that is mediated by the toxic effects of radiation on the peripheral systems, primarily the gastrointestinal system.[43] Radiation causes aversion to the taste of saccharin in rodents. This is controlled by the same pathway(s) that control nausea and vomiting in man and shares many similarities with emesis. The conditioned taste aversion has been proposed as a standard procedure and a reliable paradigm for evaluating behavioral alterations induced by radiation or other environmental agents/toxins.[44,45] Observed that the oil from *M. spicata* mitigated the radiation-induced conditioned taste aversion inrats. Intra-peritoneal administration of the oil before exposure to radiation offered significant radioprotection against conditioned taste aversion. Mint oil blocked the saccharin avoidance response within 5 post-treatment observational days and demonstrated that mint oil may be of use in preventing the radiation-induced behavioral changes.[45]

Testis is a radiosensitive organ and the degree and permanency of the damage depend on the treatment field, schedule of radiation, and the total received dose. The spermatogonia are the most radio-sensitive germ cells as exposure to a low dose of 0.1-0.2 Gy of ionizing radiation causes detectable changes, while at higher doses (>4 Gy) causes permanent azoospermia.[46,47] Recently, Samarth and Samarth investigated the protective effect of the aqueous extract of *M. piperita* against the radiation-induced testicular damage in mice by measuring biochemical parameters (lipid peroxidation, acid phosphatases, and alkaline phosphatases) and evaluating the histological alterations at various time points (day 1, 3, 7, 14, and 30 post-irradiation).Exposure of animals to radiation alone caused a significant increase in the levels of lipid peroxidation and acid phosphatase activity at all available assay

points (days 1 to 14). The histopathological results also supported the biochemical observations for massive damage to the various testicular cells.[48] Pretreatment with the extract partially/completely reversed the biochemical parameters depending on the assay time .Histological studies also showed a normal testicular morphology with regular arrangement of germ cells and slight degeneration of the seminiferous epithelium.[48] These observations clearly suggest the effectiveness of *M. piperita* in protecting against the deleterious effects of ionizing radiation.

Mechanism of Action [Figures 3]

Free radical scavenging

The anti-oxidative properties of the aqueous extracts of various species of Mentha and observed that the *M. x piperita*"Frantsila" extract was better than the other extracts and that this activity was strongly associated with the phenolic content.[49] The total antioxidant activity was highest in ethyl acetate and aqueous, and least in hexane and chloroform fractions. Correlation with chemical analysis indicated that the antioxidant effects were dependent on the phenolic content in the fractions.[50] The ethyl acetate, acetonitrile, and aqueous soluble extracts of *M. piperita* leaves were also observed to scavenge 1, 1'diphenyl-2-picrylhydrayl, 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonate) (DPPH), and hydroxyl radical scavenging assays; while the aqueous and dichloromethane-soluble extracts were effective in the β-carotene-linoleic acid bleaching inhibition assay. The essential oils from *M. aquatica, M. longifolia*, and *M. piperita* also possessed free radical scavenging effects and the oil of *M. piperita* was effective in both DPPH and OH radical scavenging assays.[25] The aqueous and chloroform extract of *M. arvensis* were potent scavengers of nitric oxide *in vitro.*[51] The polyphenolic compounds isolated from the aqueous extract of peppermint leaves, namely eriocitrin, luteolin-7- O-rutinoside, diosmin, hesperidin, narirutin, isorhoifolin, rosmarinic, and caffeic acids were studied for their antiradical activity in the DPPH assay. The study showed that luteolin-7- O-rutinoside, eriocitrin, androsmarinic acid possessed good activity, while caffeic acid, hesperidin, isorhoifolin, narirutin, and diosmin showed lesser activity. In the anti-H2O2 activity, good activity was observed for eriocitrin, rosmarinic acid, luteolin-7-O-rutinoside, and caffeic acid, while hesperidin, diosmin, narirutin, and isorhoifolin were not as effective.[25] Independent studies also showed that monoterpene ketones, menthone, and isomenthone were the most powerful scavenging compounds in the oil of *M. longifolia* and *M. piperita*, while 1, 8-cineole in the oil of *M. aquatic.*[51]

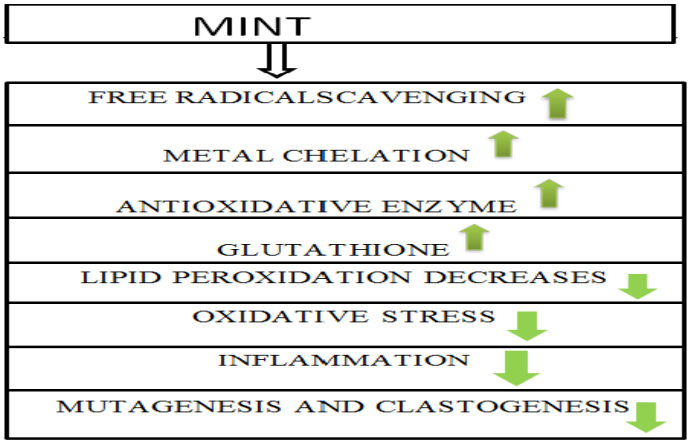

Figure 3: Mechanisms responsible for the radio-protective effects of Mint (Arrow up depicts increase while arrows down depict decrease).

Metal chelation activity

The water-soluble extracts from the various species of Mentha were screened for their potential iron (III) reduction and iron (II) chelation effects. *M. aquatica*, *M.arvensis*var. *japanensis*, *M.* x *dalmatica*, *M.* "Native Wilmet", *M.* "Morocco", and *M. x Verticillata* were better than *M. spicata* var. *crispa*, *M.* x *piperita*"Frantsila" and also that *M. haplocalyx* was better than the other extracts.[49] The extracts of *M. piperita* with different polarities were studied and observed that the petroleum ether, methanolic, and aqueous extracts demonstrated the best iron chelating activity. Mint possess iron chelating effects and may contribute for the radio-protective effects.[52]

Anti-mutagenic Effects increases DNA Repair

In *vitro* studies using *S. typhimurium* strains TA98 and TA1535 have shown that *M. piperita* was devoid of mutagenic effects.[53] Mint is reported to be anti-mutagenic and to inhibit the mutagenicity of the carcinogens/mutagens like benzo[a]-pyrene, alpha toxin B1, methyl-methane-sulfonate and extract of shamma, a complex mixture of powdered tobacco, slaked lime, ash, oils, spices and other additives, which has been linked to oral cancer in Saudi Arabia.[32] The phytochemicals linalool, eucalyptol, and myrcene present in mint are observed to prevent oxidant induce genotoxicity and that this effect was mediated by their free radical scavenging activities.[25] Luteolin is also reported to prevent the formation of strand breaks and protect PC12 cells against oxidative DNA damage.[54] Emodin, another important constituent of Mentha inhibited the formation of 1-nitropyrene-induced DNA adducts in *S. typhimuriumTA98* in the 32P-post labeling study, indicating it blocks and/or suppresses the

mutagenicity of 1-nitropyrene.[25] In association with the direct scavenging, blocking and/ or suppressing mutagenic effects, Mint is also reported to enhance the error-free repair and this may also contribute to the anti-mutagenic activities. The alterations in O6-methylguanine-DNA methyltransferase (MGMT) activities of the water-soluble and alcohol-soluble constituents of spear Mint (*M. viridis*) in human peripheral blood lymphocytes and cancer cell lines. Enhanced levels of MGMT effectively remove the highly mutagenic adducts formed by alkylating agents and the authors observed that the extracts marginally increased their levels and activities. Rosmarinic acid, an important constituent of mint, is also reported to increase the repair of oxidized nucleotide bases induced by the photosensitizer [R]-1-[(10-chloro-4-oxo-3- phenyl-4H-benzo[a]quinolizin-1-yl)carbonyl]-2-pyrrolidine -methanol (Ro 19-8022) by increasing expression of the OGG1 repair gene in PC12 cells.[54]

Mint protects against Radiation-Induced Clastogenicity

Studies by[39] have shown that pretreatment with the aqueous extract of *M. piperita* decreased the radiation induced chromatid breaks, chromosome breaks, centric rings, dicentrics, exchanges, and acentric fragments at all the time points studied.[33] Concurrently, a quantitative decrease in the levels of micronucleus frequencies was also observed reinforcing the results of chromosomal aberrations for the anticlastogenic effects.[39] All these studies clearly indicate that the observed anti-mutagenic, induction of DNA repair, and anticlastogenic effects of mint extract and by some of its compounds may have partly contributed to the observed radio-protective effect.

ANTI-INFLAMMATORY ACTIVITY

Studies have shown that *M. piperita* possess an anti-inflammatory effect against both acute (xylene-induced ear edema) and chronic (cotton-pellet granuloma) models of inflammation. The terpenoid oxide 1, 8-Cineole, present in mint, possess an inhibitory effect in carrageenan-induced inflammation and cotton pellet-induced granuloma in rats. Luteolin is also reported to inhibit arachidonic acid and 12-O-tetradecanoylphorbol-13-acetate-induced ear edema and oxazolone induced allergic edema in mice.*In vitro* studies with the menthol, eucalyptol, luteolin,β-myrcene, menthone, limonene, rosmarinic acid, and cineole have shown to suppress the production of inflammatory mediators. Additionally, menthone also suppressed the LPS, 12-O-tetradecanoylphorbol-13-acetate, hydrogen peroxide, okadaic acid, and ceramide-induced nuclear factor kappa-B(NF-kβ) activity in the HaCat cells.[25]

Mint decreases Radiation-Induced Lipid Peroxidation and also restores Glutathione levels

Aqueous extract of the various species of Mentha were tested for their ability to inhibit iron (III)-ascorbate-catalyzed hydroxyl radical-mediated brain phospholipid peroxidation *in vitro.* It was observed that the extract of *M. piperita* was better than the other extracts.[49] Studies have also shown that the aqueous extract of *M. piperita* decreases the radiation-induced lipid peroxidation in the mice liver, blood, and testis.[25] The oral administration of Mentha extract before exposure to γ radiation caused a significant increase in GSH content when compared to the radiation alone group on day 10 post-irradiation in the blood, liver, and testis of mice and contributed to the radio-protective effects.[25]

Mint increases Levels of Antioxidant Enzymes and also reduces Serum Phosphatases

The pretreatment with the aqueous extract of *M. piperita* before exposure to 8 Gy of γ irradiation caused a significant increase in the activities of the antioxidant enzymes the superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione S-transferase when evaluated 30min post-irradiation.[36] Studies by[55,56] have shown that both oil as well as the aqueous extract of *M. piperita* modulated levels of serum phosphatases at different assay time points (6 h and30 days post-irradiation). Exposure of Swiss albino mice to lethal dose of γ irradiation (8.0 Gy) caused a marked increase in the activities of serum phosphatases and acid phosphatase. Administering mentha oil (40 µl/animal/day) and aqueous extract (1 g/kg body wt) orally for 3 consecutive days prior to irradiation significantly decreased the levels of these enzymes. Further, the normal values were attained earlier than that for the radiation alone group.[56,55]

Applications of Mint

Fresh pudina leaves, on chemical analysis, are found to have moisture, protein, carbohydrates and minerals like calcium, phosphorus, iron and a volatile oil. Different varieties of pudina contain different active substances. Menthol and peppermint give a tingling cool sensation and its derivatives are extensively used in the modern pharmaceutical industry. Pudina is famous for its use indigestive upsets like nausea, vomiting, indigestion and diarrhea. Simple and remedial uses are.[16] Widely acclaimed as carminative, digestive, aromatic and an antiemetic agent, pudina is valued as a stimulant, expectorant, anti-spasmodic killer of intestinal worms and a mildly analgesic herb.[57] Pudina cure itchy skin rashes or urticarial originated due to food allergies. Take a few leaves of pudina by mashing it with a few pieces

of black pepper and a pinch of ajwain it immediately neutralizes the incompatibility of any food. Simply chewing a few leaves of fresh pudina controls bad odour of the mouth. "Sat pudina" or peppermint is an essential ingredient of many popular tooth powders. Another of its kind can be made at home by finely crushing together ash of almond shell 250 gm., nagarmotha, bark of moulsiri, kattha and hararh 50 gm each and clove, ash of phitkari and dalchini each 25 gm. Just add and crush 10 gm of peppermint to this powder. To fight bad breath and conditions like spongy gums, this makes an excellent tooth powder. Equal quantities of "sat pudina" and "sat ajwain", if put in a small glass bottle, and kept in the sun with a closed cap for an hour get liquefied a unique combination is achieved which can be used both internally and externally in a number of ailments. A few drops of it in a cup of warm water act as a good digestive and antispasmodic aid, whereas if applied externally it is an effective pain balm. Old timers will recall the famous "amritdhara" drops of the pre-Partition era. This is the exact formula of once very popular and effective medicine.[58] The antibacterial activity and chemical composition of the leaf essential oil of *mentha-rotundifolia* from morocco. The antimicrobial activities were tested in vitro by in a bioassay on nine bacterial strains: *Escherichia coli, Staphylococcus aureus, Staphylococcus intermedius, Klebsiella pneumonia, Pseudomonas aeruginosa, Bacillus subtilis,Streptococcus mutans, Micrococcus luteus*, and *Proteus mirabilis* and were evaluated.[59] The composition and antimicrobial properties of essential oil obtained from *Mentha longifolia* and *Mentha arvensis* growing wild in East Serbia were examined by Mimica-Dukic., 1997.

CONCLUSIONS

Pre-clinical studies suggest the usefulness of mint in preventing the toxic effects of ionizing radiation at non-toxic concentrations. Studies have been with mice and validated mint's clinical applicability to humans; *in vitro* studies with relevant propagatory cell lines and primary cultures will help in understanding the molecular mode of action responsible for the radioprotection. When considering DRF as the yard stick, the radio-protective effects of mint is very high for any plant reported to possess radio-protective effects. The observations of[37] are that the mint affords a DRF of 1.78 is more than the other plants with radio-protective effects (*Hippophaerhamnoides, Ocimumsanctum, Panaxginseng, Podophyllumhexandrum, Emblicaofficinalis, Tinosporacordifoila, Syzygiumcumini, Zingiberofficinale, Ageratumconyzoides, Aeglemarmelos*and *Aphanamixispolystachya*)[25] and is highly encouraging. Observations have shown that both polar and non-polar fractions are effective in preventing radiation-induced sickness and lethality suggesting that mint contains both

polar and non-polar compounds with radio-protective effects.[34][37] Among the non-polar compounds it is possible that the antioxidant and anti-inflammatory compounds like menthol, eucalyptol, luteolin, β-myrcene, Mentone, limonene, rosmarinic acid, and cineole may have been responsible for the observed effects experimental studies are needed to validate this. Among the water-soluble compounds, mint contains flavonoids like rutin,hesperidin, caffeic acid, carnosic acid, carnosol, and rosmarinic acid, which have all been reported to possess radio-protective effects.[58,60] it is possible that the presence of these compounds in the aqueous extract might have contributed to the observed high DRF of the aqueous extract of mint. Preliminary investigations by the author indicate that mint possess differential radio-protective effects in mammalian cells *in vitro*. However, further studies on determining the radio -protective activity of mint and its active components should be with tumor-bearing animals of different histological and metastatic potentialities, principally to observe for the normal tissue protection. Most published radio-protective studies have been withγ-radiation and Swiss albino mice, similar experiments are performed with other sources of ionizing radiations, especially the high LET sources and with other species of experimental animals as only then will the radio-protective spectrum be understood. Studies are performed to understand whether in combination; mint could enhance the radio-protective effect and also as whether mint could prevent the systemic toxicity and delayed cytogenetic damage of the clinically used dose without impairing the protective efficiency. If mint is effective in enhancing the radio-protective effects of low doses or decrease the systemic toxicity it will be of immense help in clinics and will also reduce the treatment cost.

Apart from applications in the clinics, mint can be used as a radiation counter measure in the management of radiological/ nuclear incidents e.g., for the protection of defense personnel from nuclear weapon radiations; for protecting reactor workers and rescue crew; protection of astronauts from exposure to space radiation; protection of embryos against maternal exposure during pregnancy; protection against radiation induced genomic instability, and radiation carcinogenesis.Human intervention trials as its effectiveness against as radio-protective agent in occupational exposure and flight attendants must also be investigated.

Due to its abundance, low cost, and safety in consumption, mint remains an herb with tremendous potential and countless possibilities for further investigation. It has the potential to develop as a non-toxic radio-protective agent, but only when gaps in the existing knowledge are bridged.

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