

AN UPDATED OVERVIEW ON PEPPERMINT (*MENTHA PIPERITA* L.)Paul Rita<sup>2</sup> and Datta K. Animesh<sup>1\*</sup><sup>1</sup>Department of Botany, Cytogenetics and Plant Breeding Section, University of Kalyani, Kalyani, West Bengal, India<sup>2</sup>Department of Botany, Charuchandra College, Kolkata- 29, India

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## ABSTRACT

*Mentha piperita* L. (Family: Lamiaceae; Synonym: *M. balsamea* Wild; commonly known as peppermint) is a natural hybrid (*M. aquatica* × *M. spicata*) with immense therapeutic uses (oldest known medicinal plant species, “medicinal plant of the year 2004”, known as “heirba Buena” meaning good herb) apart from possessing other potential uses (as flavoring agent from chewing gum to after dinner mints, in cosmetics and pharmaceutical products). The plant species is a perennial herb, propagating through stolons and yield peppermint oil (extremely used of all the volatile oils) of commerce (used parts: leaf, whole plant). Considering the essentiality of *M. piperita* an overview is conducted involving nearly all aspects to provide unabridged repository of references to present and future researchers for effective exploration of the species in human health benefits and commerce.

**KEY WORDS:** *Mentha piperita*, overview, Lamiaceae

## INTRODUCTION

*Mentha piperita* L. (Family: Lamiaceae; Synonym: *M. balsamea* Wild; commonly known as peppermint) is an important medicinal herb (“medicinal plant of the year 2004”<sup>1</sup>; oldest known medicinal plant species in Eastern and Western traditions although first described in 1753 by Carolus Linnaeus) worldwide<sup>2</sup>, apart from its potential uses as flavoring agent (from chewing gum to after dinner mints), in cosmetics, pharmaceutical products amongst others. The species is a natural interspecific (*M. aquatica* × *M. spicata*) hybrid<sup>2</sup>. *M. piperita* (known as “heirba buena” meaning good herb) yield peppermint oil (principal component is menthol – C<sub>10</sub>H<sub>18</sub>OH, mw: 156.27, waxy white crystalline monoterpene substance, solid at room temperature, produced and accumulated specifically in the peltate glandular trichomes of the aerial parts) of commerce (extremely used of all the volatile oils<sup>3</sup>). Although peppermint oil is obtained from three species namely, *M. arvensis* L. var. *piperascens* malinvaud, *M. piperita* L. var. *piperita* and *M. spicata* L., oil quality of *M. piperita* (ISO 856: 2006<sup>4</sup>) and efficacy are reported to be the best<sup>5</sup>, India is the dominant source of mint oil and menthol in the world market; however, despite the quantity of peppermint being at par with world standards much headway in export trade could not be made due to fierce competition from USA (out of 4000 tonnes total world’s production, India produces about 200 tonnes)<sup>6</sup>.

An overview on *M. piperita* (possessing potential and significant uses) covering nearly all essential aspects is documented in the text with the view that present and future researchers may explore the plant species for human benefits and to enhance trade.

## Local names around the world

Arabic: Nana; Bogota: Yerba Buena; Brazil: Nortela pimento; Chinese: Po Ho; Danish: Pebermynte; Dutch: Pepermint; English: Brandy Mint, Pepper Mint; French: Menthe, Menthe anglaise; Hungarian: Borsus menta; Italian: Menta piperita; Mexico: Menta piperita; North America: Lamb Mint, Brandy Mint, Lam Mint, Peppermint; Norwegian: Peppermynthe; Polish: Pepparminta; Portuguese: Hortelana pimentosa; Russian: Myata perechnaya; Spanish: Mentainglesa, Menta Piperita; Swedish: Pepparmynt; Turkish: Nana; Uruguay: Menta.<sup>7</sup>

## Local names in Indian languages

Hindi, Bengali, Gujarati, Punjabi, Urdu, Marathi, Tamil and Telugu: Pudina; Kashmiri: Pudyam; Malayalam: Puthina.

## Distribution

The plant is indigenous to Europe and widespread in cultivation throughout all regions of the world. It is found wild occasionally with its parent species. It is an invasive species in Australia, the Galapagos Islands, New Zealand and United States.<sup>8</sup>

### Cultivation, Harvesting and Yield

Peppermint generally thrives in moist, shaded locations and grows best with a good supply of water. Being a hybrid, it is usually sterile, producing very few seeds and reproduces almost vegetatively, spreading quickly by underground runners (rainy season) and stolons (winter). Plantation is done during last week of December to last week of January by live juicy stolons (8-10 cm. long, 400-450 kg stolons per ha, with 40-60 cm. spacing). The species is often planted in areas with part-sun to shade. Harvesting is done twice – in June (first after 100-120 days of growth) and in October (second about 80-90 days following first harvest) on bright sunny days (since decrease in menthol content occur on cloudy/rainy days).<sup>8,9</sup> Average yield is 20 tonnes of fresh herbage per ha which in turn yield around 250 kg oil per year. India is the leading producer, consumer and exporter of Mentha oil in the world with around 14000 metric tons production (followed by China and Brazil) and 3000 metric tons exports annually of around 100 corers rupee – the data is of 2003 and of total Mentha oil irrespective of the species.<sup>9</sup>

### Common cultivars for garden use

*Candymint*- stems reddish; *Citrata* (orange mint)- leaves aromatic, hairless; *Crispa*- leaves wrinkled; *Lime mint*- foliage lime-scented; *Variegata*- leaves mottled green and pale yellow; *Chocolatemint*- flowers open from bottom up.<sup>10</sup>

### Commercial cultivars

*Dulgo pole*<sup>11</sup>, *Zefir*<sup>11</sup>, *Bulgarian population #2*<sup>11</sup>, *Clone 11-6-22*<sup>11</sup>, *Clone 80-121-33*<sup>11</sup> and *Mitcham Digne 38*<sup>12</sup>, *Mitcham Ribecourt 19*<sup>12</sup>, *Todd's #x2019*<sup>12</sup>.

### Used parts

Leaf, whole plant.

### Products

Peppermint oil, peppermint tea, peppermint candy, mints chocolate, chewing gum, candy care, insect repellent amongst others.

### Plant description

Rhizomatous perennial herb, about 30 to 90 cm in height; stem square erect or ascending, branched, upper portion always quadrangular; rhizomes wide-spreading, fleshy with fibrous roots; leaves 4 to 9 cm long and 1.5 to 4 cm broad, opposite, petiolate, ovate-oblong to oblong-lanceolate, serrate, pointed, dark green on the upper surface; flowers 6 to 8 mm long, purplish, occur in thick, terminal, spicoid racemes of verticillasters; calyx tubular with 5 sharp, hairy teeth, purplish, irregular; corolla four cleft; stamens 4, short; ovary four celled, style projecting ending in a bifid stigma; fruit consists of four ellipsoidal nutlets.<sup>13</sup>

### Leaf anatomy

Leaves being the most important part from which oil is extracted, the anatomical characters are relevant. Upper epidermis composed of large, clear epidermal cells with sinuous, vertical walls and possessing few or no stomata, few glandular trichomes present; palisade parenchyma, comprising a layer of columnar cells rich in chloroplasts; spongy parenchyma, of 4-6 layers of irregularly shaped chloroplastid- containing cells and intercellular air-spaces. Lower epidermis of small epidermal cells with sinuous, vertical walls and numerous diacytic stomata; in the region of veins and midrib, exhibits non-glandular and glandular trichomes as outgrowths; non-glandular trichomes uniseriate, papillose, 1-8-celled; glandular trichomes have 1-2-celled stalk and 1-8-celled glandular head containing the essential oil. Calcium oxalate crystals absent.<sup>13</sup>

### Chemical composition

Peppermint oil is composed primarily of menthol (37.4%), menthyl acetate (17.4%) and menthone (12.7%)<sup>14</sup>. Other constituents include pulegone, menthofuran and limone<sup>15</sup>; flavonoid glycosides namely, narirutin, hesperidin, luteolin-7-o-rutinoside, isorhoifolin, diosmin<sup>16,17</sup>; 5,7-dihydroxycromone-7-o-rutinoside<sup>16</sup>; polyphenols like eriocitrin<sup>16,17,18</sup>, rosmarinic acid<sup>16,17,18,19</sup>; cinnamic acid, caffeic acid and naringenin-7-o-glucoside<sup>18</sup>; salvianolic acid, dedihydro-salvianolic acid, luteolin-glucuronide, luteolin-diglucuronide, luteolin-glucopyranosyl-rhamnopyranoside, eriodictyol-glucopyranosyl-rhamnopyranoside<sup>19</sup> were also isolated from the aerial parts. Besides these, the herb also contain<sup>20</sup> 1,8-cineole,  $\alpha$ -amorphene,  $\alpha$ -cadinene,  $\alpha$ -carotene,  $\alpha$ -copaene,  $\alpha$ -gurjunene,  $\alpha$ -pinene,  $\alpha$ -terpinene,  $\alpha$ -terpineol,  $\alpha$ -thujone,  $\alpha$ -tocopherol, amyl-valerate, anethole, azulene,  $\beta$ -betulenol,  $\beta$ -carotene,  $\beta$ -caryophyllene,  $\beta$ -copaene,  $\beta$ -ionone,  $\beta$ -pinene,  $\beta$ -thujone,  $\beta$ -ylangene, betaine, bicycloclemene, bisabolene, cadinene, camphene, carvacrol, carveol, carveol-acetate, carvone, caryophyllene-oxide, cedrene, cedrol, choline, cineole, cinerol, cis-piperitol, cis-roseoxide, cis-sabinol, citronellol, cryptone, flavons hymenoxin, isoamyl-phenylacetate, isomenthol, isomenthol-acetate, isomenthone, isomenthyl-acetate, isopulegol-acetate, isovaleraldehyde, isovaleric-acid, isovaleric-acid-n-octyl-ester, jasmone, lavandulol, ledol, limonene, linalool, luteolin, menthoside, menthyl-isovalerate, menthyl-valerate, myrcene, myrtenol, neoisomenthol-acetate, neomenthol, neomenthone, neomenthyl-acetate, nerolidol, nevadensin, octan-3-ol, p-cymene, p-cymol, pectin, pent-cis-2-en-1-ol, perillyl-alcohol, phellandrene, phenylethanols, phenyl-propyl-pyridines, pinene, piperitenone, piperitone, piperitone-oxide, pyridine,

sabinene, sabinene-acetate, sabinene-hydrate, salvigenin, sideritoflavone, terpinolene, thymol, trans-piperitol, trans-roseoxide, vanillin, viridiflorol, xanthomicrol.

#### Oil extraction

Oil is extracted from the whole plant above ground just before flowering. Cultivated plants are selected for more and better oil content than wild forms. The oil can be extracted by the classical procedure like steam distillation (yield: 0.1 – 1.0%) or with organic solvents from the fresh or partly dried plant. But due to some drawbacks of the two processes, recently superficial fluid extraction, direct thermal desorption, hydroalcoholic extraction and atomization techniques are used<sup>21</sup> to extract menthol from leaf of *M. piperita*. There is a significant effect of the combination of pressure and temperature to achieve the effective isolation and fractionation of the less and most volatile compounds using superficial fluids<sup>21,22</sup>.

#### Factors affecting plant growth, oil yield and oil composition

Plants grown with 1.5/3.0 mmol L<sup>-1</sup> K showed greater development of the above ground part<sup>23</sup>. Mechanical or combined (with chemical) treatments control weeds and provides good plant growth<sup>24</sup>. *Ex vitro*<sup>25</sup> and *in vitro*<sup>26</sup> grown plants displayed enhanced vegetative growth upon an ascomycetous (member of Pyrenomycetes) endophytic association. Oil yield/quality or both are reported to be enhanced following a) grown in shade, b) drying the plant before distillation, c) maturing of the plant – end of blooming, d) higher mean temperature, e) application of phosphorus to soil, f) application of organic manures and sodium nitrate as fertilizers and g) sandy soil<sup>27</sup>. Clark and Menary (1980)<sup>28,29</sup> reported high oil yield with the attributes like, a) high rate of nitrogen fertilizer (100, 200 and 300 kg/ha), b) high level of irrigation (50 mm/week), c) long days (16 h light), d) high photon flux density (1200  $\mu\text{Em}^{-2} \text{ s}^{-1}$ ) and e) high night temperature. Fahlen *et al.* (1997)<sup>30</sup> were of opinion that 21-3h photoperiod gives higher concentration of menthol and night temperature had little effect on the menthol levels under 21h photoperiod regime; however, menthol and menthone percentage were significantly higher in 3<sup>rd</sup> to 5<sup>th</sup> leaf compared to top leaf pair position. Peppermint oil is reported to be enhanced at full bloom (menthol – 43 to 54%, menthone – 12 to 30%) and ground drying of the plants led to slight decrease in oil yield but quality is not affected<sup>31</sup>. Sharafi *et al.* (2010)<sup>32</sup> suggested that harvesting in late June compared to late August enhanced menthol but decreased menthone content. Hussain *et al.* (2010)<sup>33</sup> reported oil content as 12.2 g kg<sup>-1</sup> in summer and 10.5 g kg<sup>-1</sup> in winter crops.

UV-A (360nm; during day time<sup>34</sup>) and UV-B<sup>35</sup> are recommended to enhance oil content in *M. piperita*. Maffei and Scannerini (2000)<sup>36</sup> reported that UV-B radiation significantly increases total phenolic compounds, menthone, menthofuran, methyl acetate, gerinacene D,  $\beta$ -caryophyllene but decreases menthol content. Dolzhenko *et al.* (2010)<sup>37</sup> were of opinion that UV-B radiation differentially modulates the expression of genes involved in peppermint essential oil biogenesis and UV-B absorbing flavonoids. On the contrary, Wu *et al.*<sup>38</sup> noted reduction of photosynthetic capacity under UV-B radiation stress.

#### Diseases of peppermint

Nelson (1950)<sup>39</sup> reported that *Mitcham American* and *White Mitcham* varieties were more susceptible to *Verticillium* wilt (*F. albo-atrum* var. *menthae* n. var.) and plantation of sugar beets and potatoes before mint, tilling and loose seed beds may control wilt. Juronis and Snieskiene (2004)<sup>40</sup> reported fungal pathogens (*Puccinia menthae*, *Erysiphe biocellata* and *Verticillium* sp.) and phytophagous pests (*Tetranychus urticae*, *Eupteryx atropunctata*, *Ovatus crataegarius*, *Polia persicariae*, *Agrotis lineatus*, *Chrysomela coerulans*, *Cassida viridis*, *Longitarsus hycopi*) causing severe loss in peppermint. Szczeponek and Mazur (2006)<sup>41</sup> observed that *Puccinia menthae* (rust disease) causes major problems to peppermint growers apart from *Epicoccum purpurascens*, *Alternaria* sp. and *Sphaceloma menthae* as the dominating population on the diseased leaves. Besides these insect pests like *Diacrisia obliqua* (nature of damage: eat undersurface of leaf; control measure: application of Thiodan or Malathion), *Agrotis flammata* (damage young plants at collar region; soil treatment with Phorate before planting), *Aulocophora foenicollis* (feeds on growing leaves and buds; spraying Malathion), *Syngamia abruptalis* (folds the leaf; spraying Thiodan) and fungal pathogens like *Macrophomina phaseoli* (stolon rot; crop rotation with rice and wheat), *Fusarium oxysporum* (wilt; application of Benlate, Bavistin and Topsin), *Alternaria* sp. (leaf blight; application of copper fungicide) also cause major loss of peppermint<sup>6</sup>.

#### Cryopreservation of mint germplasm

Uchendu and Reed (2008)<sup>42</sup> recommended three cryopreservation protocols (controlled rate cooling, encapsulation dehydration and vitrification) for effective storage of *in vitro*-grown plants and suggested that controlled rate cooling as the most efficient and successful technique; however recovery of shoot tips from the other two processes was also high and may also be used for cryogenic storage of mint germplasm. Volk and Caspersen (2007)<sup>43</sup> studied the extent of cellular damage and plasmolysis during cryopreservation process

following the use of cryoprotectant plant vitrification solution 2 - PVS2 (30% glycerol, 15% dimethyl sulfoxide, 15% ethylene glycol, 0.4 M sucrose) prior to liquid-nitrogen exposure and found that the young meristematic cells were least damaged and thus provides a high survival rates. Senula *et al.* (2007)<sup>44</sup> evaluated for regrowth after cooling in liquid nitrogen using shoot tips from *in vitro* grown plantlets and a simple vitrification protocol with aluminium foil as a carrier, the influences of plant preculture, loading solution and loading time and of the effects of the cryoprotectant PVS 2 on plant regrowth after re-warming were also investigated.

#### Therapeutic uses

Herbalists consider peppermint as an astringent, antiseptic, antipruritic, antiemetic, carminative, vermifuge, diaphoretic, analgesic<sup>45</sup>. The plant extract possesses radioprotective<sup>46,47</sup>, antioxidant<sup>17,48,49</sup>, anticarcinogenic<sup>50,51,52,52</sup>, antitumorigenic<sup>51</sup>, antinociceptive<sup>53</sup>, antiandrogenic<sup>54</sup>, antiallergic<sup>16</sup>, antispasmodic<sup>55</sup>, antidiarrheal<sup>56,57</sup> properties amongst others. Peppermint oil vapour is used as an inhalant for respiratory congestion. Peppermint tea is used to treat coughs, bronchitis and inflammation of oral mucosa and throat. Essential oil can be used in complex patients with infiltrative pulmonary tuberculosis<sup>58</sup>. Traditionally the species is used to treat a variety of digestive complaints such as colic in infants, flatulence, diarrhea, indigestion, nausea and vomiting, morning sickness and anorexia and to reduce gas and cramping. Peppermint is used to treat irritable bowel syndrome<sup>59</sup>, Crohn's disease, ulcerative colitis, gallbladder and biliary tract disorders and liver complaints<sup>60,61</sup>, menstrual cramps<sup>62</sup>, headaches, migraines and chicken pox<sup>57,60</sup>. Plant extract can also reduce the arsenic-induced toxicity<sup>63</sup>, glucose, cholesterol, LDL-c and triglycerides levels (in diabetic rat<sup>64</sup>); uric acid level, cholesterol/HDL and LDL/HDL ratios<sup>32</sup>; iron absorption<sup>65</sup>; malodor and volatile sulphur compounds in intensive care unit patients<sup>66</sup>.

Clinically it is proven that peppermint is effective against nausea and vomiting tendency usually in the first few months of pregnancy<sup>67</sup>. In a placebo-controlled study of gynecological surgery patients there was a statistically significant effect of peppermint in reducing postoperative nausea<sup>68</sup>.

The volatile oil of peppermint are useful in invigorating mind, improving mood, relaxing tension-filled and anxiety-ridden nervous system<sup>45</sup>; psychological change in attentional behavior<sup>69</sup>; promoting general arousal of attention<sup>70</sup> and enhancing memory<sup>71</sup>.

#### Other potential uses

The plant extract of *M. piperita* possesses anti-viral (Influenza A virus<sup>72</sup>, Newcastle disease virus<sup>72</sup>, Vaccinia

virus<sup>72</sup>, Herpes simplex virus type 1 and 2<sup>73,74</sup>, X4<sup>75</sup>, R5<sup>75</sup> and HIV-1<sup>75</sup>, Vesicular stomatitis virus<sup>75</sup>, Ecotropic murine leukemia virus<sup>75</sup>), antibacterial (bactericidal against *Staphylococcus pyogenes*<sup>45</sup>, *Streptococcus pyogenes*<sup>45</sup>, *Serratia marcescens*<sup>45</sup> and *Mycobacterium avium*<sup>45</sup>; in order of *E. coli* > *Staphylococcus aureus* > *Pseudomonas aeruginosa* > *S. faecalis* > *Klebsiella pneumoniae*<sup>32</sup>, bacteriostatic against *Streptococcus thermophilus*<sup>76</sup>, *Lactobacillus bulgaricus*<sup>76</sup>, *E. coli* O157:H7<sup>77</sup>, *Streptococcus mutans*<sup>78</sup>, *S. pyogenes*<sup>78</sup>, against *Helicobacter pylori*<sup>79</sup>, *Salmonella enteritidis*<sup>79</sup>, *Listeria monocytogenes*<sup>80,81</sup>, *Staphylococcus aureus*<sup>82</sup>), antifungal (*Trichophyton mentagrophytes*<sup>83</sup>, *Fusarium moniliforme*<sup>84</sup>, *Rhizoctonia solani*<sup>85</sup>, *Pythium ultimum* var. *ultimum*<sup>85</sup>, *Fusarium solani*<sup>85</sup>, *Colletotrichum lindemuthianum*<sup>85</sup>, *Yarrowia lipolytica*<sup>86</sup>, *Aspergillus niger*<sup>87</sup>, *Rhizopus stolonifer*<sup>87</sup>, *Botrytis cinerea*<sup>87</sup>, *Aspergillus candidus*<sup>88</sup>, *Penicillium sp.*<sup>88</sup>, *Fusarium culmorum*<sup>88</sup>, *Candida albicans*<sup>89,90</sup>), anti-protozoal (against *Giardia lamblia*<sup>91,92</sup>), anti-nematodal (against *Meloidogyne arenaria* race 2<sup>93</sup>, gastrointestinal nematodes of goats<sup>94</sup>) and larvicidal (larvicidal in order of *Culex quinquefasciatus* > *Aedes aegypti* > *Anopheles stephensi*<sup>95</sup>, female adults of *A. aegypti*<sup>96</sup>, mosquitocidal against *C. quinquefasciatus*<sup>97</sup>, *A. aegypti*<sup>97</sup>, *Anopheles tessellatus*<sup>97</sup>; repellent against *Culex pipiens*<sup>98</sup>; repellent, larvicidal and pupicidal against the housefly, *Musca domestica*<sup>99</sup>) properties. Mint due to its flavor is used in confectionary, soap and shampoos; in honey production from nectar as well.

#### Pharmacology

Peppermint oil and menthol exert their antiemetic effect at least partly by acting on the 5-HT(3) receptor of ion-channel complex, probably by binding to a modulatory site distinct from the serotonin binding site<sup>100</sup>. Peppermint's antispasmodic properties are found to produce a total and immediate resolution of blockage of Oddi's sphincter (located in the intestinal tract of animals). It induces Ca<sup>2+</sup> influx in a subset of sensory neurons from dorsal root and trigeminal ganglia, due to activation of TRPM8 of cation channels<sup>101</sup>. Animal model studies demonstrate a relaxation effect of the herb on gastrointestinal (GI) tissue, analgesic and anesthetic effects in the central and peripheral nervous system<sup>102</sup>. Immunomodulatory effect of peppermint oil is exerted through 1-menthol, menthone, and 1, 8-cineole suppressed antigen-induced histamine release<sup>103</sup>. The oil stimulates cold receptors on the skin and dilates blood vessels, causing a sensation of coldness and an analgesic effect<sup>104</sup>. Menthol, thymol, and methyl salicylate caused decreases in blood pressure but had no effects on respiration, heart rate, or blood flow in the femoral artery

or gastrocnemius muscle<sup>105</sup>. The principal pharmacodynamic effect of peppermint oil relevant to the gastrointestinal tract is a dose-related antispasmodic effect on the smooth musculature due to the interference of menthol with the movement of calcium across the cell membrane; the oil is relatively rapidly absorbed after oral administration and eliminated mainly via the bile - the major biliary metabolite is menthol glucuronide, which undergoes enterohepatic circulation<sup>106</sup>. Clinical effectiveness of peppermint oil in the treatment of irritable bowel syndrome results from inhibition of the hyper contractility of intestinal smooth muscle, thereby returning the muscle to its proper tone. The smooth muscle spasmolytic effect is exerted primarily on the neuromuscular junction. Futami (1984)<sup>107</sup> reported that menthol blocks smooth muscle contraction induced by serotonin and substance P58, and also blocks neuromuscular transmission. Hawthorn *et al.* (1988)<sup>108</sup> suggested that the vasodilatory effect of peppermint oil is mainly due to Ca<sup>2+</sup> channel blocking properties. The oil stimulates the upper airway cold receptors causing a reflex inhibition of respiration and inhibits upper airway accessory respiratory muscle activity<sup>109</sup>. Haahr *et al.* (2004)<sup>110</sup> reported that flavor released to the retronasal compartment was dependent on masseter muscle activity and chewing frequency and influenced by the volume of saliva present in the mouth. Pournemati *et al.* (2009)<sup>111</sup> suggested that inhaling peppermint odor during acute intensive exercise showed no significant effect on pulmonary indexes and physical performance. Leaf extract of menthol is very good bioreductant for the synthesis of silver and gold nanoparticles and synthesized nanoparticles active against clinically isolated human pathogens<sup>82</sup>.

### Toxicology

Peppermint oil has few side effect - it can cause heartburn or perianal irritation and is contraindicated in patients with bile ducts obstruction, gallbladder inflammation, and severe liver damage<sup>60</sup> and caution should be taken in patients with GI reflux, hiatal hernia and kidney stones<sup>102</sup>. Menthol products used directly under the nose of small children and infants may undergo the risk of apnea, laryngeal and bronchial spasms, acute respiratory distress with cyanosis and respiratory arrest<sup>112,113</sup>. Menthol can cause jaundice in newborn babies and in some cases is linked to glucose 6 phosphatase dehydrogenase deficiencies<sup>114,115</sup>. Allergic reactions to peppermint are reported. Pulegone and Menthol are the potentially toxic compounds in peppermint. Safe use of peppermint in cosmetic formulations can be done only if the concentration of pulegone does not exceed 1%<sup>15</sup>. The toxicities vary from

one cultivar to another<sup>116</sup>. Patients with achlorhydria should use peppermint oil only in enteric coated capsules<sup>117</sup>.

### In vitro studies

Krasnyanski *et al.* (1998)<sup>118</sup> produced somatic hybrid following protoplast fusion between peppermint (*M. piperita* L. cv. *Black Mitcham*) and spearmint (*M. spicata* L. cv. *Native Spearmint*). Sato *et al.* (1993)<sup>119</sup> through leaf derived protoplast culture developed the whole plants. Chung *et al.* (1994)<sup>120</sup> studied continuous suspended cell culture of *M. piperita* in cell-recycled air-lift bioreactor and recorded substantially higher essential oils in this system than batch culture. Chang *et al.* (1998)<sup>121</sup> observed improved menthol production from chitosan-elicited suspension culture of *M. piperita* and inferred that chitosan elicitation may activate the conversion of pulegone to menthol. Faure *et al.* (1998)<sup>122</sup> showed mannitol and thidiazuron improve *in vitro* shoot regeneration from peppermint leaf disks. Krasnyanski *et al.* (1999)<sup>123</sup> produced stable transformants (with high-menthone, menthofuran and pulegone and low menthol content) peppermint plants (*M. piperita* L. cv. *Black Mitcham*) following *Agrobacterium* mediated and direct gene (*limonene synthase gene* into protoplast using PEG) transfer. Paolicchi *et al.* (2002)<sup>124</sup> studied the influence of gravity on axillary shoot formation and adventitious root regeneration using *in vitro* culture system. Sunandakumari *et al.* (2004)<sup>125</sup> reported an efficient and economic protocol (using commercial sugar and tap water in MS media) for rapid multiplication of *M. piperita* through axillary bud multiplication and *ex vitro* rooting. Chakraborty and Chattopadhyay (2008)<sup>126</sup> studied the impact of several parameters (like menthone precursor or  $\gamma$ -cyclodextrin feeding alone or both together, fungal elicitor, *Agrobacterium* gall mediated calli) on the stimulation of menthol production in the cell suspension culture of *M. piperita*. Thul and Kukreja (2010)<sup>127</sup> recorded multiple shoot formation (with an average of 7 shoots per explant on MS medium supplemented with zeatin) within three weeks from 85% *in vitro* culture explants, and the plantlets exhibited 96% survival.

### Chromosome number

Chromosome number of *M. piperita* is variable with 2n counts of 66, 72, 84 and 120<sup>10,128</sup>.

### Polyploid

Lutkov *et al.* (1966)<sup>129</sup> reported first high-yielding polyploid variety *Priluki 6* with 100% greater content of essential oil than the diploid parent. Few fertile varieties (C64-56, 27/1, 38/5 and 29/98) were bred from the spontaneous polyploids. Beljaeva *et al.* (1970)<sup>130</sup> obtained natural polyploid form with 60-72 bivalents and

1-4 multivalent(s) along with various irregularities in spindle and tetrad formation. Pollen fertility reported was 66-72%. About 60% of the polyploid forms had  $2n=144$ , while, the others showed various aneuploid chromosome numbers. Savchenko (1980)<sup>131</sup> found a fertile allopolyploidy form of *M. piperita* which proved resistant to fluctuations in soil moisture and formed fertile flowers at both 100% and 50% full field capacity; however, a decrease in soil moisture after meiosis led to a reduction in the number of fertile flowers.

#### Interspecific hybrids

Lutkov et al. (1966)<sup>129</sup> raised  $F_1$  hybrid from crosses between allopolyploids of *M. piperita* ( $2n=144$ )  $\times$  *M. arvensis* var. *piperascens* ( $2n=96$ ) and *M. piperita*  $\times$  *M. sachalinensis* ( $2n=96$ ) and noted the hybrids were bushy and vigorous with high essential oil contents. Bugaenko et al. (1980)<sup>132</sup> also obtained  $F_1$  hybrids between polyploid *M. piperita* ( $2n=144$ ) and three wild forms of *M. spicata* ( $2n=48$ ) and found that about 81.7 to 84.2% of the plants were with  $2n=96$ ; while, the rest had  $2n=72$ , 78, 84 and 91 due to disturbed meiosis.

#### Molecular studies

Transgenic peppermints were obtained by *Agrobacterium* mediated transformation<sup>133,134</sup>. Son et al. (1998)<sup>135</sup> suggested that in biotransformation [(--)-isopiperitenone to ((-)-7-hydroxyisopiperitenone)] induction of  $P_{450}$  mediated by jasmonic acid as a signaling molecule. Fuchs et al. (1999)<sup>136</sup> studied stereo selectivity in the bioconversion of pulegone into menthone and isomenthone. Mahmoud and Croteau (2001)<sup>137</sup> demonstrated that essential oil quantity and quality can be regulated by metabolic engineering-alteration of the committed step of the mevalonate-independent pathway that leads to increase in monoterpene production, and antisense manipulation of a selected downstream monoterpene biosynthetic step also improve oil composition. Croteau et al. (2005)<sup>138</sup> reported that the organization of menthol biosynthesis is complex, involving four subcellular compartments; regulation of the pathway appears to reside largely at the level of gene expression and genetic engineering to up-regulate a flux-limiting step and down-regulate a side route reaction led to improvement in the composition and yield of peppermint oil. Ringer et al. (2005)<sup>139</sup> cloned and characterized (-)-isopiperitenol/(-)-carveol dehydrogenase of peppermint; random sequencing of an oil gland secretory cell cDNA library revealed a large number of clones that specified redox-type enzymes including dehydrogenases. Wildung and Croteau (2005)<sup>140</sup> employed two genes (*dxr gene* - deoxyxylulose phosphate reductoisomerase gene and *mfs gene* - menthofuran synthase gene) and two expression

strategies to create transgenic peppermint plants with improved oil composition and yield. Davis et al. (2005)<sup>141</sup> and Prosser et al. (2006)<sup>142</sup> cloned and characterized menthone reductases and cis-muroladiene synthases respectively from peppermint. Gobert et al. (2006)<sup>143</sup> studied nuclear DNA (ITS), chloroplast DNA (non-coding regions *trn L* intron, intergenic spacers *trn L-trn F*, and *psb A-trn H*) and AFLP and ISSR markers from hybrid, diploid and polyploid genome in order to reconstruct the phylogeny of mints related to *M. piperita*. Results suggested differential of introgression of different genome regions in mint hybrids.

#### CONCLUSION

*M. piperita* is a natural hybrid and propagated through stolons, therefore genetic diversity is limiting which may be a hindrance to improve peppermint oil yield and quality. Therefore attempts should be taken to enhance gene pool of the existing varieties following conventional (methodology of induced mutagenesis or polyploidy may be adopted) and biotechnological approaches and to select desirable clones with enriched oil content and composition. Present overview on *M. piperita* is an endeavor in this regard providing unabridged repository of references on different aspects, which may be helpful to researchers to design experiments for exploring the species for maximizing trade.

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