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Review Article

PISTACIA LENTISCUS: A REVIEW ON PHYTOCHEMISTRY AND PHARMACOLOGICAL PROPERTIES

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ABSTRACT

Pistacia lentiscus Linn. (Family - Anacardiaceae), commonly known as mastic tree or mastagi, has been used in traditional system of medicines for treatment of various kinds of diseases since long-standing time. Its various parts contain a variety of chemical constituents which are medicinally important such as resin, essential oil, gallic acid, anthocyanins and flavonol glycosides, nortriterpenoids, *α*-tocopherol and arabino-galactan proteins. It has antiatherogenic, antimicrobial and antimutagenic, antioxidant, antifungal, lipid lowering, hepatoprotective, anticancer, anthelmintic, wound healing, hypotensive, antiarthritic, antigout activity and also in the treatment of functional dyspepsia.The aim of this review is to further highlight the discovered pharmacological effects and phytochemical details of this plant *Pistacia lentiscus* which may further provide the way to promote study and research.

Keywords: Gallic acid, Anthocyanins, Antioxidant, Hepatoprotective, Hypotensive, *Pistacia lentiscus.*

INTRODUCTION

Herbal drugs are still the spine of about 75–80% of the world's population, mainly in developing countries, for treatment of many diseases due to better compatibility with the human body and producing lesser adverse effects. It has been assessed that approximately one quarter of prescribed drugs contain plant extracts or active ingredients obtained from plant chemical constituent such as Atropine (Anticholinergic), cardiac glycosides (cardiotonics), artimisinin (antimalarial), Opium alkaloids (analgesics), quinine (antiparasitic), taxol (antineoplastic), vincristine and vinblastine (antineoplastic)[1]. Herbal plants have wide therapeutic value since long time and still a lot of research is going on which further explore the use to improve the human health value. These plant-derived drugs were discovered through the study of traditional remedies and conventional knowledge of indigenous people and some of these could not be substituted despite the huge advancement in synthetic chemistry[2].

Pistacia lentiscus Linn. (Family- Anacardiaceae) is widely distributed in Mediterranean Europe, Morocco and Iberian peninsula and in the west through southern France, Turkey, Iraq and Iran. The resin part of this plant known as Mastic resin and plant called as mastic tree[3,4]. It has a great medicinal value and already been used in traditional system of medicines like Unani and Ayurveda system[5].

TAXONOMICAL CLASSIFICATION

Kingdom : *Plantae*

Division : *Magnoliophyta*

Order : *Sapindales*

Family : *Anacardiaceae*

Genus : *Pistacia*

Species : *Pistacia lentiscus.*

Binomial name: *Pistacia lentiscus* L.

BOTANICAL DESCRIPTION

Mastic tree is diocious, found in Mediterranean Europe, Mediterranean region, Morocco and Iberian peninsula in the west through southern France, Turkey, Iraq, Iran and India . It is also native to the Canary Islands[6].

This is a shrub or tree, with separate male and female plants, evergreen, 1 to 5 m height, with pinnate leaves and small (4-5 mm. Diam.) globose black drupes. It has a strong smell of resin. It yields mastic resin which is imported into India. The aromatic, ivory coloured resin, also known as mastic, is harvested as a spice from the cultivated mastic trees grown in Greek island, where it is also known by the name Chios Tears. Originally liquid, it is sun dried into drops of hard, brittle, translucent resin, when chewed; the resin softens and becomes bright white and opaque gum. The resin exudes naturally from the bark but for commercial purposes, it is obtained by making small vertical incisions in it and picking off the hardened product about three weeks later. Average annual yield of resin per tree is 3.6-5.4 kg. Mastic is globular, pyriform or elongated tears, 4-8 mm. in diameter, pale yellow, clear and glassy when fresh, becoming dull and brittle on keeping; it has an aromatic odour and agreeable taste[3].

SYNONYMS

Common name of *Pistacia lentiscus* L. in Hindi -Rumi Mastagee, Rumi Mastiki, Mastagee; English – Mastic; Gujrati - Rumi Mastagi; Sanskrit-Rumi mastagee Urdu – Rumee Mastagee, Unani - mastagee.

PHYTOCHEMISTRY

The most important component of *Pistacia lentiscus* L. are resin which was analysed by GC & GC-MS to obtain α- pinene, β- pinene, limonene, terpene-4-ol and terpeneol[7]. Essential oil from leaves contain β- caryophylline (31.38%), germaerene (12.05%) and γ-cadinene(6.48%)[8]. Hydrodistilled oil from leaves was analysed by GC-MS and contain α- pinene, γ-terpene and terpene-4-ol[9]. Polyphenols from the leaves are gallic acid and galloylderivatives[10], flavonol glycoside and anthocyanins (delphinidine 3-O-glucoside and cyanidine 3-O- glucoside). Traces amount of myrcetine derivative and catechin are also present[11]. α-tocopherol is also found from the leaves[12]. The gum oil contain 90% monoterpene hydrocarbon named as 79% of α- pinene and 3% β- myrcene and leaf oil contain 50% monoterpene hydrocarbon as 11% of α- pinene and 19% β- myrcene. It is also containing 25% sesquiterpenes whereas unripe fruits contain 22% of α- pinene and 54% β- myrcene and ripe fruits contain 11% of α- pinene and 72% β-myrcene[13].Volatile oil obtained from fruits was analysed by GC-MS contain α-pinene, myrcene and limonene; sesquiterpene, ketones and aliphatic esters and phenolic compound (thymol, carvacrol) whereas dimyrcene (0.5-4.4%) is found in all types of oil[14]. Mastic oil also has Verbenone, α- terpineol, linalool[15].Two novel nortriterpenoid *i.e.* malabaricane and polypodane types were found in neutral fraction of gum mastic[16]. Mastic resin was also containing polymer of a monoterpene- 1,4-poly-β-myrcene which was first time reported known example of polymer monoterpene[17] and Chios mastic gum also contain arabino galactane protiens (AGPs) which prevents infection of H. Pyroli[18]. Figure 1 shows the chemical structures of various major chemical constituents found in the plant.

PHARMACOLOGY

Antiatherogenic activity

According to Dedoussis *et al,* accumulated level of ox-LDL may play important role in the initiation and progression of atherosclerotic lesions. Under oxidative stress, ox-LDL attracts blood monocytes beneath the endothelium. Uptake of ox-LDL occurs through CD36 receptor that binds to its lipid moiety. These monocytes (macrophages) are more susceptible to apoptosis, nucleus shrinks, organelles change, and membrane loses integrity. Macrophages converted to foam cell, full of cholesterol and oxidized lipid.In this study it was reported that triterpenoid fraction of *Pistacia lentiscus* through GSH restoration and down regulation of CD36 mRNA expression is helpful in the treatment of atherogenesis[19].

Antimicrobial activity

The crude extract (Pet ether, $CHCl_3$, Ethyl acetate and Ethyl alcohol) obtained from the leaves of *Pistacia lentiscus* L. has reported to inhibited the growth of *phythium ultimum* and *Rhizoctania solani* fungus significantly and further study revealed that all extract are more effective on *P. ultimum* than *R. solani*[20]. The efficacy has also been reported against (90-100%) *M. cavis, T. mentagrophytes* and *T. violaceum* at MICs of the plant in the range from 0.6-40 microgram/ml[21]. Essential oil from aerial parts which contain terpineol and α-terpineol was also found to be effective against mycelian growth of *A. flavus*[22].

Literature reports that the leaf Extract of *Pistacia lentiscus* L. was tested for antimicrobial and antioxidant property and it has been observed that it has a strong antifungal but weak antibacterial activity. Apart from that its ethanolic extract also has high reducing power capacity and a weak scavenging activity for superoxide anions[23.] In another study, *Pistacia lentiscus* L. has found to be effective against *Sarcinalutea, Staphylococcus aureus* and *E. coli* and it also has antimycotic activity[24]. Its essential oil which is obtained from leaves, twigs and mastic gum by steam distillation showed in vitro antimicrobial activity[25] and antifungal activity against *rhizoctania solani*[7]. It's aqueous and flavonoid enriched extract and essential oil from leaves has marked inhibitory effect against *Salmonella typhi murium* and lower inhibitory effect on *Staphylococcus aureus, Pseudomonas aeruginosa* and *Salmonella enteritidis*[26]. It has been illustrated that the acetone extract of mastagi gum has more significant antibacterial activity against *S. Mutans* and *Mutans streptococci* in vitro and in vivo so it is useful in prevention of careis which was shown in a clinical study on 25 periodontally healthy volunteers[27]. Essential oil from mastic gum is also effective against Gram positive and Gram negative bacteria *i.e. Staphylococcus aureus, Lactobacillus plantarum, Pseudomonas flagi* and *Salmonella enteritidis*in broth and in model food system (silk milk at 37°C) and when EDTA added in coliform broth increased the inhibitory activity but did not have any increased effect on model food system[28].

Antioxidant activity

Natural antioxidants present in the plants scavenge harmful free radicals from our body. Synthetic antioxidants like butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA) commonly used in foods have side effect and are carcinogenic. Plant phenolic acids act as antioxidants has been extensively investigated[29]. A lot of studies have been reported on the antioxidant property of *Pistacia lentiscus*[30]. Essential oil which was collected at flowering stage contain high monoterpene hydrocarbon fraction (45-68.35%) showed highest free radical scavenging activity and antioxidant capacity[31,32,33]. Natural resin and bioactive triterpenes from essential oil also showed antioxidant property so these are used in functional food due to this property[34].

In another study it was reported that its antioxidant activity is due to digallic acid which has ability to scavenge the free radical ABTS (+), to inhibit XO which involved in generation of free radical and also for inhibition of lipid peroxidation which is induced by H_2O_2 in the K562 cell line[35] and its gallic acid constituent and 1, 2, 3, 4, 6-Pentagalloyl glucose also showed antioxidant effect[36]. Galloylquinic acid isolated from leaves of this plant was found to have antioxidant property because it was strongly reduced the oxidation of LDL which was determined by relevant LDL test[37].

Liubuncic *et al* also proved the antioxidant effect of *Pistacia lentiscus* which was determined by measuring their ability to supress the extent of iron induced lipid peroxidation in rat liver homogenate and also was found that it is most effective in suppressing iron induced lipid peroxidation and it was also non-toxic[38].

Lipid lowering effect

Andrikopoulos and co-workers reported that the Gum and resin part of *Pistacia lentiscus* was the most efficient in protection of human LDL from the oxidation and it inhibit LDL oxidation at the minimum dose of 2.5 mg (75.5%) and at the maximum dose of 50 mg (99.9%)[39].

Hepatoprotective activity

Janakat and Al- merie reported that the aqueous extract of *Pistacia lentiscus* (both boiled and nonboiled) showed marked hepatoprotective activity against CCl_4 by reducing the activity of 3 enzymes (Alkaline phosphatase (ALP), Alanine amino transferase (ALT), Aspartate amino transferase AST) and level of bilirubin. Nonboiled aqueous extract was found to be more effective than boiled[40].

In further study, Mansoor *et al* reported that the resin exudates of *Pistacia lentiscus* were found to be effective in treatment of gastric ulcer. Mastic at an oral dose of 500 mg/kg produces a significant reduction in the intensity of gastric mucosal damage which is induced by pyloric ligation, Aspirin, Phenylbutazone and Reserpine. It produce a significant decrease of free acidity in 6 hr pylorus-ligated rats and has a marked cytoprotective effect against 50% ethanol in rats. It does not produce any significant effect on duodenal ulcer[41].

Antiarthritic and Antigout activity

Bhouri *et al* reported that the digallic acid obtained from the fruit *Pistacia lentiscus* L. exhibits an inhibitory activity against the xanthine oxidase.It is also having free radical scavenging activity (99%) and protection against lipid peroxidation (68%)[35].

In another study, Berboucha *et al* reported that *Pistacia lentiscus* used in several inflammatory diseases such as rheumatism, arthritis and gout. Total phenolic content of seed and leaves of this plant were estimated. Its aqueous fraction from hexane and chloroform extraction inhibited XO activity by mixed mechanism i.e. competitive and noncompetitive both and due to its XO inhibition activity, it is used in treatment of gout[42].

Wound healing activity

According to Boulebda *et al,* Wound contraction i.e. healing of wound was significantly ($P<0.05$) enhanced in the presence of *Pistacia lentiscus* L. oil and unsaponifiable oily fraction. It was more pronounced in case of the oily unsaponifiable fraction-treated group of animals so it is considered as active healing agent.Topical application of the *Pistacia lentiscus* L. fruits fatty oil and its unsaponifiable fraction is helpful in the treatment of wound[43].

Anticancer activity

Balan *et al* reported that 50% ethanolic extract of chios mastic gum (CMG) of *Pistacia lentiscus* inhibited proliferation and induce death of HCT116 human colon cancer cells in vitro. CMG exerts concentration dependent apoptosis by directly or indirectly inducing cell arrest at G_1phase followed by DNA damage.In vitro, CMG causes cascade of cellular events ultimately result in the interruption of matrix adhesion and triggering (anoikis form) irreversible cell death[44].

Dimas *et al* also reported that hexane extract of mastic gum is also used in the treatment of colorectal tumours[45].

Merilan He *et al* reported that gum mastic inhibit proliferation of LNCaP (Androgen responsive human prostate cancer cell line) cells by androgen via AR (androgen receptor) which was used to treat

prostate cancer. It inhibit expressions of the 3AR gene i.e. PSA, Hk2, NKX3.1, inhibit AR transcriptional activity function on androgen regulated genes. Gum suppressed the AR- mediated action. It inhibits both the expression at transcriptional level and function of the AR in LNCaP cells[46].

Other pharmacological actions of *Pistacia lentiscus* L. is as hypotensive effect due to procyanidine[47], as aphrodiasac[48], in the treatment of functional dyspepsia[49], as antiasthmatic in allergic asthma by inhibiting eosinophilia and reducing airway hyper-responsiveness and suppressing the productionof inflammatory cytokines (IL-5 and IL-13) as well as chemokines (eotaxin and eotaxin2) in broncho alveolar lavage fluid[50], in chron's disease[51], in treatment of *H. Pylori* infection by inducing blebbing, morphological abnormalities and cellular fragmentation in *H. Pylori* cells[52], anthelmitic activity[53] and in treatment of inflammatory bowel disease[54].

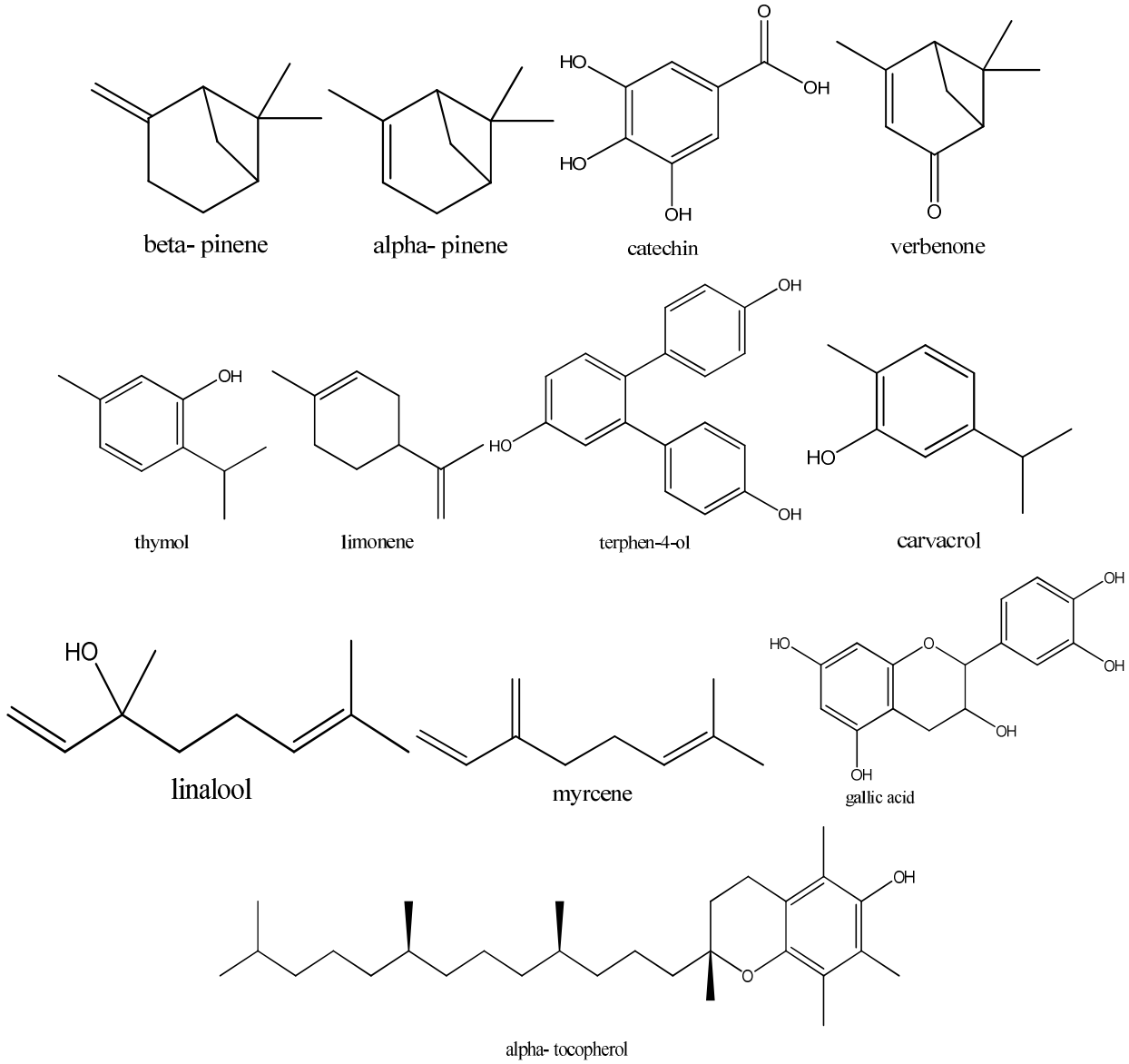

Fig. 1: Chemical structure of some important chemical constituents of *Pistacia lentiscus* L.

CONCLUSION

Pistacia lentiscus is used for various medicinal properties. The extract of the different parts of the plant shows various activities like antiatherogenic, antiinflammatory, antioxidant, antimicrobial, hypotensive, anticancer, antiarthritis and antigout and in treatment of wound, antiasthmatic and anthelmitic activity. This review further highlighted the discovered pharmacological effects and phytochemical details of *Pistacia lentiscus* which provide way to further studies and research.

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