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THERAPEUTIC RELEVANCE OF AEGLE MARMELOS: A REVIEW

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Aegle marmelos, Therapeutic, Ethnobotany, Phytoconstituents, Ethnomedicinal, Pharmacological activities

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ABSTRACT: Aegle marmelos, commonly known as Bael or Bilva, is a traditional tree belonging to the family Rutaceae with enormous value in ethnobotany, Ayurveda, and has been used since time immemorial for its spiritual significance as an offering to Lord Shiva while worshipping. Looking at its religious perspective and medicinal benefits, people have conserved trees of Bael in sacred groves. It is a sub-tropical tree and grows wildly in the dry, dry dipterocarp and mixed deciduous forests on the plains and hilly regions. Researchers have used and studied almost all the parts like root, bark, fruit, leaves, and seeds of this significant tree because of the varied phytoconstituents isolated from them, like alkaloids and terpenoids, amino acids, fatty acids, coumarins, etc. Substantial experiments were conducted on Aegle marmelos owing to many phytoconstituents found in it and they were found to exhibit potential therapeutic responses in many pharmacological activities like anti-diabetic, anti-hyperlipidemic, analgesic, antimicrobial, antipyretic, anti-inflammatory, radioprotective, anti-ulcer, anticancer, gastroprotective, antidiarrheal, etc., to name a few. Many pharmaceutical herbal industries have been formulating preparations using different parts of Aegle marmelos for quite a long. Still, there are yet many segments that have been overlooked, leaving big grounds for cutting-edge work. Hence, it was worthy of putting forward a consolidated and updated overview of the pharmacognostic aspect of Aegle marmelos, incorporating its phytoconstituents, therapeutic properties, and ethnomedicinal benefits for aiding the scientists, students, and aspiring researchers for futuristic research on this significant plant, for promoting its rigorous large scale cultivation and ethno conservation and also for manifesting the potential of this plant in the pharmaceutical industry for herbal formulations.

INTRODUCTION: Aegle marmelos is a traditional tree belonging to the family Rutaceae, having substantial ethnobotanical significance owing to its diversified medicinal properties and spiritual relevance.



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It is commonly known as Bael and is known by distinct names in different languages, namely Assamese (Bael, Bel); Hindi (Bael); English (Bael tree, Bel tree, Bengal Quince, Stone Apple, Wood Apple, Indian Bael, Elephant Apple, Holy Fruit Tree); Kannada (Bilvapatre, Kumbala, Malura); Malayalam (Koovalam, Koolakam, Mavilavu, Vilvam); Telugu (Maredu); Gujarati (bil); Tamil (Kuvalam); Bengali Cambodia (Pnoi, Phneou); Sanskrit (Shivapala, Bilva, Sriphal, Shivadruma); Vietnamese (Mbau Nau, Trai mam); Thai (Matum, Mapin); Malay (Pokok Maju Batu); Urdu (Bel); Burmese (Opesheet, Ohshit); Indonesia (Maja

batuh, Maja); Marathi (Kaveeth); Nepali (Bel, Gudu); Sinhalese (Beli) 1, 2, 3.

Origin and Geographical Distribution: It is a subtropical plant. It can naturally survive at an altitude up to 1200m. It can thrive well in conditions where other trees cannot survive, like in temperature variation between 50 to -7 degrees Celsius, without showing any retardation in growth. It can grow even in soil with a pH between 5-10 and withstand waterlogging. Though it is trusted to have originated in India in central India and the Eastern Ghats, its existence in other countries can be due to human activities in the past. A Chinese Buddhist pilgrim named Hiuen Tsiang, who visited India in 1629 AD is known to have detected the existence of the Bael tree here 3, 4, 5. It is grown mainly in the vicinity of temples due to its mythological connection. It grows wildly in the dry, dry dipterocarp and mixed deciduous forests on the plains and hilly regions. It is widely distributed in India, Sri Lanka, China, Cambodia, Ceylon, Nepal, Bangladesh, Vietnam, Myanmar, Laos, Philippines, Pakistan, Indonesia, Tibet, Malaysia, Thailand, Java, and Fiji. In India, it can be seen along the Himalayan foothills, in the states of Uttar Pradesh, Chhattisgarh, Bihar, Madhya Pradesh, Jharkhand, Uttaranchal, Jammu and Kashmir, Karnataka, Kerala, Punjab, Tamil Nadu, East Coast, Deccan Plateau and West Bengal ^{4, 5, 6}.

Botanical Description: Bael is a deciduous, medium-sized tree grows slowly, has a short trunk, and attains a height of about 12-15m. It has a short trunk; the bark is grayish or pale brown, thick, finely fissured with flaking or smooth textured. Its branches spread out; young ones are laden with stiff and straight spines the lower branches mostly droop downwards. Thorns are axillary, about 2.5 cm long. A gummy and clear sap exudes from its wounded branches, which gradually hangs down and becomes solid. It resembles gum Arabic. At first, it tastes sweet but later starts to irritate the throat 6, 7, 8. The leaves of Bael are alternate, compound, or single. They are usually trifoliate with three leaflets and occasionally with five leaflets when compound. The leaflets are ovatelanceolate or ovate shaped, with pointed or tapering tips and measuring 5-14 cm long and 2-6cm wide. The terminal leaflet has a long petiole, around 1-2.5 inches long, while the lateral ones lack a petiole.

The new foliage appears pinkish-maroon, exhibiting a glossy appearance. The mature leaves are smooth and dark green. When bruised, the mature leaves give off a displeasing odor. Each leaflet bears 4 to 12 pairs of side veins joining at the margins ^{4, 6, 7, 8}. The flowers are aromatic, bisexual, pale green or yellowish, measuring 1.5 to 2 cm in length, present as unbranched, drooping, and short clusters at the end of leaf axils or the twigs. They usually appear along with new leaves. The flowers are oval, oblong, thick, and blunt, and each bears five (rarely four) fleshy and curved petals with 50 or more stamens which are greenish-yellow in color. The calyx is shallow, having short five sepals, pubescent outwards 3, 5, 8, 9.

The fruit is a little pear-shaped or globose, has a diameter of 5-12 cm, and has a very hard rind on the outside, which does not break open even on ripening. It is green when unripe and turns yellowish-brown when fully ripe. Inside, it has 8-20 less defined segments, triangular-shaped, having dark and thick walls that are orange in color. These segments contain a pale orange, resinous, aromatic, pasty, sweet, somewhat astringent pulp with 10-15 seeds. Seeds are about a cm long, flattened oblong, have wooly hairs, and are embedded in a transparent and adhesive mucilage sac that gets solidified on drying ⁵.

Uses of Aegle marmelos in Ayurveda: Aegle marmelos, commonly known as Bilva, has been used in Ayurveda extensively, owing to its medicinal properties in treating various inflammatory disorders and its spiritual importance for ages. There has been the use of fruit, root, leaves, stem, flower, and bark in preparation for formulations. The unripe fruit of Aegle marmelos is used in boosting digestion and pitta while the ripen fruits have been used to treat diarrhea and dysentery. The leaves are useful for balancing the Vata to cure dyspepsia, sinusitis, cold, and gastric indigestion. Its pith is utilized for stabilizing the Vata and Kapha, alleviating the colic pain and indigestion in the digestive tract. Its stem is incorporated in formulations to diminish the cold and cough, treat rheumatoid arthritis, as a carminative, aids in digestion by balancing the digestive enzymes, and as a cardiac tonic. The flower of Bilva is used to treat diarrhea and dysentery, control emesis, and alleviate thirst.

The oil obtained from the flowers is used to mitigate cold and congestion in the chest, inflammation. and pain, and enhance complexion. Roots of the plant stabilize the tri dosha and relieve the colic pain and vomiting sensation. However, the roots of Aegle marmelos hold an exceptional and valuable place in Ayurveda as a paramount component of the group called Dashamoola, which is a formulation of ten important plant roots used in Ayurveda, imparting its anti-inflammatory properties to the preparation. A few important formulations that incorporate parts of this important plant in their preparation are Kutajavaleha (for piles, irritable bowel syndrome, and other ailments related to the gut), Bilwa Taila (for treating ailments related to the ear, like hearing difficulty, tinnitus, etc.), Vilwadi Gulika (to treat insect bites and certain infections). Gangadhara Churna (for treatment of diarrhea and dysentery, ailments of the digestive tract), *etc.*, to name a few ^{10, 11, 12, 13, 14}.

Ethnobotanical uses of Aegle marmelos: It has been used traditionally and ethnobotanically by the indigenous and conventional people to heal and treat several diseases and disorders, a curative learned by the indigenous measure and conventional people their experiences and their inquisitive and experimentative survival techniques. Habitually and gradually, people got convinced of the thought that the healing provided by the natural sources would never harm their body in any sense; hence they used all the available plant resources for food and fodder, building houses, and useable items and their medicinal properties. Amongst many such plants and trees listed in ethnobotany and ethnomedicine, Aegle marmelos finds a very prominent place. Its ethnobotanical usage and ethnoconservation have been done since time immemorial. People have conserved trees of Bael in sacred groves. They regarded the leaves of this tree as sacred because of its trifoliate shape, giving it a resemblance to Trishul of Lord Shiva, Trikal (The three Lords Brahma, Vishnu, and Mahesh), the three eyes of the Supreme Shiva, three lingas, Trishakti (Knowledge, action, and desire) and three syllables a, u and m of Omkar. It is believed to have emerged from the body of Goddess Parvati, and hence it is affectionate to Lord Shiva. The leaves, when offered to the Idol of Lord Shiva, are believed to cease all bad karmas of

a person, and if it is brought in the vicinity of a person, then it would ward off all the negative energies and emit Sattva or the positive vibes all around. In ethnomedicine, people used all the parts of Aegle marmelos to treat various ailments. The fruit of the Bael tree has been used to treat issues like diarrhea, dysentery, constipation, epilepsy, high blood pressure, intestinal parasites, and ulcers. It has been used as an effective tonic for the brain and heart. The tribals also used the dried powder of fruit and mixed it with mustard oil to treat skin burns. People have consumed the fruit in its ripe and unripe form. The tribals and locals have traditionally used the root bark to stop the recurrence of intermittent fever, treat cases of fish poisoning, dog bite, amoebiasis, rheumatism, cardiac palpitations, and other cardiac ailments and state of melancholia. People used the juice of root bark and mixed it in milk along with cumin seeds to improve the quantity of seminal fluid.

The flowers of the Bael tree have been used to treat gastrointestinal diseases, as an anti-diabetic natural source, local anesthetic, *etc*. The leaves have been used to cure diabetes, ulcers, cardiac problems, beriberi, acute bronchitis, emesis, asthma, cuts, wounds attributable to animal interactions, abscess, dropsy, eye infections, cold, and cough, infections of the respiratory tract, *etc*. The leaves have been used as a tonic to manage healthy hair by incorporating its oil with cumin seeds and rubbing it on the scalp. The tribals used the seeds even for healing wounds of animals and as fodder for them. The oil obtained from the seeds has been used for its antibacterial and antifungal activities ¹⁵.

The extensive use of Bael in ethnomedicine and Ayurveda had evoked much interest in the inquisitive minds of the herbal industry. This is the reason behind extensive research in the formulation of medicines and supplements using their different parts. It is evident from the trending sales of herbal products worldwide that people are inclined to use herbal products and supplements to maintain general wellness and treat several diseases and disorders of physical and mental state. Using herbal products over synthetic products is now an open secret. Nearly one lac people die annually succumbing to the toxic effects of synthetic drugs ¹⁶. There are minimal side effects with the use of herbal remedies, provided care is taken to not take

them alongside any medicine of some other system of medicine and no over-usage is done. The herbal preparations are to be taken after consultation of a health practitioner only to avoid any impact of contraindications, adverse effects associated with their interaction with food and other drugs, and side effects associated with their usage beyond permissible doses. Attributing to this tree's medicinal properties, big giants of herbal industries herbal been manufacturing various preparations using Bael as their ingredient like Bael Patra powder, Bael fruit powder, Bael tablets, Capsules, Churna, Sharbat, Murabba, Candy, Hair tonic, Bael fruit tea, Bael prash, Bael tincture, etc., to name a few.

There has been extensive research on this tree to prove more of its medicinal properties, isolate the phytoconstituents present in it to prove and establish their association with various pharmacological activities displayed by the plant, elucidate the structure of various phytoconstituents, and validate of methods used in the research work. This will pave the way for clinical trials of the drug; after successful completion, the industry can formulate a medicine for treating those ailments.

Chemical constituents: Aegle marmelos has been found to contain many alkaloids, coumarins, flavonoids, steroids, essential oils, etc., present in different parts of the plant, like its fruit, leaves, root, and bark. All parts of the plant are found to contain many phytoconstituents of therapeutic value. Based on vast research done on Aegle marmelos to date, the following chemical constituents have been isolated-

1. Fruit: The alkaloids isolated from the Bael fruit are Aegelinine, marmeline, aegelin, marmesiline, O-methyl halfordinol, and O-(3,3-dimethylallyl) halfordinol. The coumarins isolated are 6-(4acetoxy-3-methyl-2-butenyl)-7-hydroxyl coumarin, 6-(2-hydroxy-3-hydroxymethyl-3-butenyl)-7hydroxycoumarin, 8-[(3-methyl-2-oxo-3-buten-1yl) oxy]-7H-furo[3,2-g] benzopyran-2-one, 6formylumbilliferone, 8-hydroxysmyrindiol, decursinol, isofraxidin, alloimperatorin, demethylsuberosin, isogosferol, psoralen, marmelonine, isophellodenol marmesin. scoparone, marmelosin, Scopoletin, xanthotoxin, umbelliferone. xanthotoxol xanthoarnol. and

Flavonoids and Phenolic acids isolated are namely ferulic acids, chlorogenic acid, gallic acid, ellagic acid, quercetin, kaempferol, and protocatechuic acid. Several volatile compounds found are dehvdro-p-cymene. (E)-2-Octenal. citronellal. citral, caryophyllene oxide, carvone, carvyl acetate, acetoin, 3,5-octadiene-2-one, dihydro-beta ionone, hexanal, limonene, eugenol, humulene oxide, hexadecane, linalool oxide, alpha humulene, alphacubebene, p-cymene, isoamyl acetate, pulegone, verbenone, beta-ionone, beta-caryophyllene, betaphellandrene, beta-cubenene, (E)-6,10-dimethyl-5.9-undecadien-2-one. (E, E)-2,4-Heptadienal. Carbohydrates isolated are glucose, sucrose, galactose, arabinose, fructose, L-rahaminose, and uronic acid. Vitamins that are found are riboflavin and ascorbic acid. Organic acids found are tartaric acid, malic acid, and oxalic acid. Tannin isolated is skimmianine. Terpenoid found is an alphaphellandrene ^{7, 8, 17, 18}.

- **2. Seeds and Gum:** The seeds and gum of Bael fruit are found to contain coumarin luvangtin, carbohydrates like glucose, galactose, arabinose, rhamnose, galacturonic acid, xylose, and threose. Various fatty acids isolated are stearic acid, oleic acid, palmitic acid, linoleic acid, myristic acid, linolenic acid, and ricinoleic acid ¹⁸.
- **3. Leaves:** Alkaloids isolated from the leaves are O-(3,3-dimethylallyl) halfordinol, Aegelin, marmeline, N-2-ethoxy-2-(4-methoxyphenyl) ethylcinnamamide, aegelinosides A and B, N-2methoxy-2-[4-(3',3'-dimethylallyloxy) phenyl], anhydomarmeline, N-2 - methoxy -2 - (4methoxyphenyl) ethylcinnemamide. Phenvlpropanoids that are found are hydrocoumarins, phenylpropenes, Aegelinine, lignans. Marmesin. Marmelosin, marmesinine, rutin and beta-sitosterol-beta-D-glucoside are also found in the leaves. The terpenoids are alpha-phellendrene, p-menth-1-en-3,5-diol, p-cymene, sitosterol, and limonene. Other constituents found present in the leaves are rutaretin, montanine, N-pcis-and trans-coumaroyltyramine, betulinic acid, valencic acid, 4-methoxybenzoic acid, and transcinnamic acid 6, 17, 18
- **4. Bark:** Constituents isolated from the bark are coumarins *viz*. Umbelliferone, Marmesin, Marmin, Aegelinol. Alkaloids found are Gamma-Fagarine,

Skimmianine. Other compounds which have been found are Gamma-Sitosterol, Skimmiarepin A, and Skimmiarepin C 18 .

5. Roots: The roots are found to contain coumarins like Umbelliferone, Xanthotoxin, Psoralen, Scopoletin, Marmin, Marmesin and Aegelinol. Alkaloids isolated are Gamma-Fagarine, Tembamide, haplopine, dictamine and skimmianine 18

Pharmacological Activities: Aegle marmelos is a plant of immense medicinal use. Since time immemorial, almost all parts of the plant have had the therapeutic potential to cure several ailments because of the potent phytoconstituents present in them. Researchers isolated these phytoconstituents and pharmacological activities were performed to prove that the plant exhibits the potential of curing many diseases due to its phytoconstituents.

- 1. Anticancer Activity: Methanolic and acetone extracts of *Aegle marmelos* were found to be effective against tumor cells HEp-2 and MDA-MB-231saving the normal Vero cells, hence exhibiting anticancer potential ¹⁹.
- **2. Analgesic Activity:** Stem bark aqueous extract of *Aegle marmelos* was found to exhibit a dosedependent analgesic effect in the acetic acidinduced writhing in mice and tail-flick test in rats ²⁰.
- **3. Antipyretic Activity:** The ethanolic leaf extract of *Aegle marmelos* at the dose 200 and 400mg/kg body weight was found to reduce the raised temperature (p<0.001) of albino rats in Brewer's yeast induced pyrexia in a dosedependent way, succeeded by the aqueous extract. The antipyretic activity was comparable with paracetamol taken as standard ²¹.
- **4. Anti-inflammatory Activity:** The hydroalcoholic extract of *Aegle marmelos* leaves showed remarkable anti-inflammatory activity in acute carrageenan-induced rat paw edema compared to standard drug indomethacin ²²
- **5. Anti-malarial Activity:** Alcoholic extract of *Aegle marmelos* was found to be effective against the NK 65 Strain of Plasmodium

berghei by exhibiting schizontocidal activity both in vivo and in vitro at a dose of 1g/kg for four consecutive days and 100microgram/kg ²³.

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- **6. Antioxidant Activity:** The high concentration of total phenolic and total flavonoid content in the leaf extract of *Aegle marmelos* was found to be responsible for scavenging the free radicals and exhibiting potent antioxidant activity comparable to the standard vitamin C ²⁴.
- **7. Hepatoprotective Activity:** The leaf extract of *Aegle marmelos* at a dose of 100mg/kg was found to exhibit potent hepatoprotective activity in PCM-induced hepatotoxicity in Wistar rats, comparable to the silymarin group. When Piperine was co-administered with a low dose of 25mg/kg of *Aegle marmelos* extract, the hepato-protective effect was found to have got potentiated ²⁵.
- **8. Antidiabetic Activity:** The methanolic extract of leaves of *Aegle marmelos* remarkably reduced the oxidative stress in alloxan-induced diabetes in albino rats. The extract was found to significantly reduce hydroperoxide levels, conjugated diene, and lipid peroxidation in the liver and serum-induced by alloxan, thereby lowering the total blood sugar level ²⁶.
- **9. Antimicrobial Activity:** Acetone and methanolic extracts of *Aegle marmelos* were found to exhibit potential anti-microbial activity against the tested microbes, especially against S. marcescens due to the presence of biologically operating chemical constituents ¹⁹.
- of *Aegle marmelos* was found to have remarkably reduced the ulcer index, gastric volume, and free acidity in aspirin and pylorus ligation induced gastric ulcers in rats. The extract was found to decrease ulceration in indomethacin-induced ulcers significantly. The water immersion stress test induced ulcers in rats at a dose of 200-400mg/kg body weight ²⁷.
- 11. Gastroprotective Activity: The aqueous extract of the ripen fruit pulp of *Aegle marmelos* was found to have provided gastric mucosal protection in gastric ulceration induced by aspirin, cold restraint stress, and cerebellar

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nodular lesion in adult albino rats by significantly increasing the 5-hydroxytryptamine level and enterochromaffin cell count ²⁸.

- **12. Antidiarrheal Activity:** The decoction of the dried unripe fruit pulp of *Aegle marmelos* was found to show potent antidiarrheal activity in infectious diarrhea by affecting the production and activity of specific enterotoxins and the colonization of bacteria in the epithelium of the gut. The extract also affected the generation of cholera toxins, binding both labile and cholera toxins to the Ganglioside monosialic acid receptor GM1 ²⁹.
- **13. Cardioprotective Activity:** The aqueous leaf extract of *Aegle marmelos* was found to have shown remarkable cardioprotective activity in doxorubicin-induced cardio-toxicity in Wister albino rats, due to the presence of certain flavonoids in it. This was found to be comparable to the existing synthetic standard drug carvedilol ³⁰.
- **14. Radioprotective Activity:** The leaf extract of *Aegle marmelos* was found to exhibit potent radioprotective activity by reducing the symptoms of sickness induced by radiation and increasing the survival in Swiss male albino mice, possibly by scavenging the free radicals and arresting peroxidation of lipids along with increasing glutathione ³¹.
- **15. Anti Spermatogenic Activity:** The extract of leaves of *Aegle marmelos* was found to exhibit potent anti-spermatogenic activity by withstanding the process of spermatogenesis and decreasing the motility of the sperms in rats ³²
- **16. Anti-anxiety and Antidepressant activities of** *Aegle marmelos*: The methanol leaf extract of *Aegle marmelos* was found to show remarkable anxiolytic and antidepressant activity, probably due to the rising level of monoamines at the postsynaptic sites and it was also found to intensify the anxiolytic and antidepressant activity of the standard drugs imipramine and fluoxetine ³³. The methanolic leaf extract of *Aegle marmelos* was found to show dosedependent, significantly increased anxiolytic

activity, possibly due to GABA facilitatory action of certain phytoconstituents present in the leaves of *Aegle marmelos* like flavonoids, phenols, tannic acid marmesinin, saponin, *etc* ³⁴. The extract of *Aegle marmelos* showed potent anxiolytic activity when given in higher doses to test animals, as shown by the standard drug Diazepam. The anxiolytic effect produced by *Aegle marmelos* did not show any impairment in motor coordination, contrary to the skeletal muscle relaxation shown by diazepam. *Aegle marmelos* can thus be used as an effective remedy for anxiety without showing side effects, unlike standard synthetic drugs available ³⁵.

The aqueous extract of the drug Aegle marmelos, when given at a low dose of 75mg/Kg and a high dose of 300mg/Kg, showed appreciable antidepressant activity on the fourteenth day in comparison to the standard drug Fluoxetine given at a dose of 20mg/Kg to the test animal ³⁶. The ethanol leaf extract of the drug Aegle marmelos showed significant anti-anxiety and antidepressant activity compared to standard when given to animal Wister albino rats. phytochemical screening of extract was found to show the presence of alkaloids, saponins, and steroids, which were thought to be accountable for the pharmacological activity of the plant ³⁷. The aqueous and ethanol extracts of Aegle marmelos showed remarkable anxiolytic activity in the Light Dark Model and the Open Field Test Models and even in the biochemical estimation, comparable with the standard drug Diazepam. The drug exhibited this activity possibly owing to GABA-dependent facilitation of various phytoconstituents present in the drug viz. flavonoids, saponin, marmesinin, tannic acid phenols, etc. 38.

17. Antihyperlipidemic Activity: The ethanolic, aqueous, and chloroform extracts of leaves of Aegle marmelos, when given at a dose of 250mg/kg to triton instigated hyperlipidemic rats, was found to reduce their level of triglycerides, low and very-low-density lipoproteins and total cholesterol and increased the level of high-density lipoprotein considerably, possibly due to the presence of

phytoconstituents like saponins, flavonoids, beta-sitosterol, tannins and polysaccharides ³⁹.

CONCLUSION: Aegle marmelos has not only been a plant of immense ethnobotanical and spiritual importance but has been researched by many people for its other medicinal uses owing to the presence of a large number of phytoconstituents present in various parts of the plant. It has been thus seen at large as a plant of economic importance by various pharma companies and the herbal drug industry for the preparation and selling of its formulations for use in humans. It has been researched widely for its various therapeutic activities; however, there is still a lot of scope for advanced research on its psychotropic properties so that herbal preparations can be formulated for the human population to fight some diseases belonging to this category and reduce the reckless and addictive use of the available synthetic drugs used by people nowadays to combat the outcome of their stressful lifestyle.

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