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Review Article

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A Pharmacologically Review on Celastrus paniculatus

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Abstract Celastrus paniculatus (CP), a traditional Ayurvedic medicinal plant used for centuries as a memory enhancing, anti- inflammatory, analgesic, sedative and antiepileptic agent. The seed extract has been extensively investigated in several laboratories for their neuropharmacological effects and a number of reports are available confirming their nootropic action. In addition, researchers have evaluated the anti-inflammatory, anticonvulsant and other pharmacological effects of CP preparations/extracts. Therefore, in view of the important activities performed by this plant, investigation must be continued in the recently observed actions described in this paper. Moreover, clinical studies have to be encouraged, also to evidence any side effects and possible interactions between this herbal medicine and synthetic drugs.

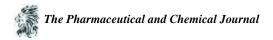
Keywords Celastrus paniculatus; Ayurvedic; Medicinal plant; Nootropic

Introduction

Herbal medicinal plants are used for the treatment of various diseases and it will not be an overstatement that use of these medicinal plants is as old as the mankind [1]. In USA, Australia and Canada, Market of herbal medicine has a turnover of about US\$ 30 billion in 2000 which was increased up to 5-15% by the turn of the century [2]. Worldwide annual market of herbal medicine has reached to \$60 billion. The industrialized societies have been discovered to the extraction of active constituents and the development of several drugs and chemotherapeutic from these plants as well as from traditionally used rural herbal remedies. *Celastrus paniculatus* is one of the plants which has a rich source of therapeutically and medicinally potential active constituents.



Seeds of Celastrus paniculatus



Description of Celastrus paniculatus

Binomial name

Celastrus paniculatus Wild.

Synonym

Celastrus dependens Wall.

Parts used

Seeds, leaves, root and stem

Family Celastraceae Genus Celastrus

Celastrus is a genus of woody, climbing shrub distributed over China, Japan, Australia, Tropical North America and Pacific Islands. There are seven species of Celastrus in India one of which is *Celastrus serratus* Hoechst present in Indian Botanical Garden Howrah. It is commonly known as Bittersweet or Staff tree. It is grown on almost each type of soil and situation [3].

Celastraceae

Celastraceae family is found in tropical and subtropical regions of the world, including North Africa, South America and many parts of East Asia, mainly in China [4-5]. Celastraceae is a family having 96 genera and 1350 species of herbs, wine and small tree. Celastraceae has five subfamilies Celastroideae, Hippocrateoideae, Parnassioideae, Salacioideae and Stackhousioideae. Some of the genera of Celastraceae are Celastrus, Kokoona, Salacia, Gymnosporia and Euonymus. Leaves are simple with an alternate pattern. Flowers are hermaphrodite and cymene. Seeds have fleshy endosperm with large embryo and dicotyledon. In the last thirty years, a number of secondary metabolites are isolated from Celastraceae, of which main constituents are sesquiterpenoids, phenyl alkyl amine and flavonoids [6].

Geographical distribution

Celastrus paniculatus grow in different variety of climates and environments. It is mainly found in India, especially in Punjab, Kashmir and hilly area distributed in Sri Lanka, Maldives, Philippines, Australia, China, Cambodia, Vietnam, Malaysia, Taiwan, Nepal, Thailand as well as in the Pacific Islands [7].

Organoleptic evaluation Leaves

Color: Green

Shape: Oval or elliptic Texture: Leathery and smooth Arrangement: Alternate

Margin: Toothed

Apex: Acute, acuminate Base: Obtuse or rounded

Bark

Color: Outer bark is pale or reddish-brown while the inner bark is light yellow in color

Surface: Rough and cracked

Flower

Color: Greenish White or yellowish-green, hermaphrodite, pubescent

Fruit

Fruits are globose, yellow in color with three to six seeds

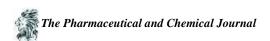
Seed

Color: Reddish brown

Shape: Ellipsoid in shape enclosed in orange, red fleshy aril and grows inside the fruits

Odor: Unpleasant Taste: Bitter Chemical constituents Seeds Sesquiterpene alkaloids

Celapanin, Celapagine, Celapanigine



Monounsaturated and polyunsaturated fats Sesquiterpene ester

 1α , 6β , 8β -triacetoxy- 9β -benzoyloxydihydro beta-agarofuran along with the some known compounds which are 1α , 6β , 8α -triacetoxy- 9α -benzoyloxydihydro-beta agarofuran angulatueoid C, and 1α , 6β , 8β , 14-tetra acetoxy- 9α -benzoyloxy dihydro beta-agarofuran from the carbon tetrachloride-soluble fraction of *Celastrus paniculatus* methanolic seed extract [8].

Triterpenoids Pristimerin [9]

Fatty acids Palmittic, Oleic, Linoleic and Linolenic acid. 80% of the methanolic extract of seed oil contain Malkanguinol, Malkangunin, Paniculatadiol.

Polyalcohol esters

Malkagunuin, Polyalcohol A, B, C and D [10-11]

Sterols

Vitamin C, minerals, carbohydrates and proteins are also found in the seeds [12, 13]

Stem

Alkaloid such as Wifornine F, Paniculatine A and B are isolated from the stem [14].

Root bark

Petroleum ether extract of the root bark of *Celastrus paniculatus* shows alkaloids such as n-triacontanol and pristimerin, benzoic acid, uncharacterized quinine and golden-yellow oil. Zeylaseral, zeylasterone, celastrol found as qunione, methide and phenolic triterpenoids in outer root bark [15]. Ethanolic extract of *Celastrus paniculatus* shows the presence of tannins.

Leaves

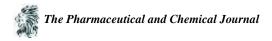
Leaves contain an alkaloid, a glycoside and a coloring matter. It contains dulcitol.

Traditional uses

Plants are used in the treatment of various ailments from the prehistoric times. Ayurveda is the ancient traditional system of medicine, which includes a large number of medicinal plants for the treatment of diseases. *Celastrus paniculatus* is one of the plants which are used in Ayurveda as a nervine tonic, tranquilizer and a diuretic, in treatment of rheumatism, gout, leprosy and asthma [16-17]. Charka Samitha and Sushruta Samitha describe its roots uses in headache, depression, as laxative, purgative and in urinary disorders, skin problems and in neurologic disorders [18]. In Unani and Siddha medicines, it is used for gout, lumbago and to relieve fatigue [19]. It is used in Chinese medicine to treat fever, joint pain, edema and rheumatoid arthritis [20, 21]. Powdered root bark is used in the treatment of malaria [22]. In an Indian traditional system of medicine *Celastrus paniculatus* is used as emetic, aphrodisiac, in treatment of anorexia, constipation, cough and skin infections [23].

Ethnobotanical study

In traditional Himalayan medicines *Celastrus paniculatus* is used to reduce the swelling of the veins of the anus and rectum, which causes discomfort and bleeding, in treatment of rheumatism, diarrhea and leprosy [24]. Crushed roots are used for pneumonia in folk medicines [25]. A Gond tribe of Uttar Pradesh uses the powdered root in the treatment of cancer [26]. In the Chendwara and Betul district of Madhya Pradesh powder of the root and decoction of seeds of *Celastrus paniculatus* used to treat rheumatism [27, 28]. The oil of seeds of *Celastrus paniculatus* is used by herbal therapist for hair growth and to make the hair silky [29]. Tribes of Purandhar [30] and tribes of Jalgaon and Nandurbar districts of Maharashtra [31, 32] use the seed oil on joints for the treatment of rheumatic pain. They also use the oil orally and topically for the treatment of paralysis in the morning and evening [33]. In the Mayurbhanj district of Odisha it is used for joint diseases, gout and rheumatism. Codified literature of Himachal Pradesh shows its uses as cardiotonic, carminative, anthelmintic and in the treatment of skin infections.



Reported activities of Celastrus paniculatus

Tranquilizing effect

Karanth et al., 1980 evaluated seed oil of Celastrus paniculatus at the dose of 200 mg/kg for its tranquilizing effect on mice [34]. The study revealed that it decreased the spontaneous motor activity, amphetamine-induced hyperactivity and consumption of oxygen in mice. It increased the effect of hexobarbitone and produce hypothermia in mice.

Antimalarial activity

Celastrus paniculatus extract from the root bark and stem was evaluated by Pavanand et al., 1989 for antimalarial activity against Plasmodium falciparum by in vitro method. In comparison to stem, root bark showed better antimalarial activity [9]. Further a quinonoid triterpene was isolated from a chloroform extract for in vitro antimalarial activity, but this was less active than conventional antimalarial drug tested.

Antifertility activity

Antifertility effect was studied on the liver and testis of rats by using the oily extract of seeds of *Celastrus paniculatus* by Bidwai *et al.*, 1990. Intraperitoneal treatment of 0.2 ml of *Celastrus paniculatus* oil for 30 d showed vacuolization, cell depletion and arrest of spermatogenesis [35].

Singh and co-workers, 2018 reported antifertility efficacy of ethanol extract of *Celastrus paniculatus* seed in male rats [36]. When a dose of 250 mg/kg was given orally to the rats for 45 d, the reproductive organ weight, sperm count and motility were decreased. Biochemical estimation showed that testicular enzymes lactate dehydrogenase and gamma glutamyl transpeptidase activity was increased while sorbitol dehyrogenase activity was decreased.

Anti-inflammatory activity

Inflammation is a defense mechanism of a tissue reaction to infection, injury or a foreign substance. *Ahmad and his colleagues*, 1994 used the methanolic extract of the flowers of *Celastrus paniculatus* for anti-inflammatory activity by using hot water tail immersion test in mice and carrageenan-induced edema in rats [37]. Results revealed that flowers have both analgesic and anti-inflammatory activity.

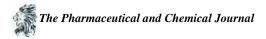
Alcoholic and methanolic extracts of *Celastrus paniculatus* seeds were used by *Parimala et al.*, 2009 for evaluating their anti- inflammatory activity [38]. Screening was done on rats of 150-250 gm by a carrageenan paw edema method using plethysmograph. The standard drug used was diclofenac sodium. Mean increase in the paw volume and percentage inhibition of inflammation revealed that *Celastrus paniculatus* seeds possess good anti-inflammatory activity.

Kulkarni and his coworkers, 2015 prepared the absolute alcoholic extract of seeds of *Celastrus paniculatus* and gave it to 120-150g male Wistar rats [39]. Experimental evaluation showed a significant anti-inflammatory effect of the alcoholic extract of *Celastrus paniculatus* seeds which may be related to inhibition of prostaglandin synthesis and IL-1β.

Cognitive enhancement activity

Gattu *et al.*, 1997 studied that chronic administration of *Celastrus paniculatus* seed oil when given orally reversed the declension of spatial memory produced by a central musurinic receptor blockade in rats [40]. While the acute administration did not significantly reverse this effect.

The same effects were evaluated by Bhagya *et al.*, 2016 using *Celastrus paniculatus* oil in Wistar rats [41]. They recorded the behavior of rats in the open field and then behavioral test was conducted in dimmed room, after that anxiety test was studied in elevated plus maze, partially baited radial arm maze and t-maze rewarded alteration task methods. Observations made by them showed that chronic dose of *Celastrus paniculatus* seeds oil exhibit neuroprotective effects on chronic stress induced cognitive impairment.



Nootropic activity

Gupta and Kumar, 2002 investigated aqueous, methanolic, chloroform and petroleum ether extracts of *Celastrus paniculatus* seeds at the dose of 200 mg/kg for nootropic effect in male Wistar rats by using a shuttle box, step through, step down and elevated plus maze paradigms [42]. After experimentation, it was observed that only aqueous extract improved the memory of rats.

Celastrus paniculatus is also reported as a nootropic drug by Bhanumathi and coworker, 2010. Methods used for nootropic activity were elevated plus maze and passive avoidance test [43]. In elevated plus maze method, they gave the aqueous extract of seed of Celastrus paniculatus by using doses of 350 and 1050 mg/kg and in passive avoidance test they gave the doses of 500 and 1500 mg/kg for the mice. The standard drug used was piracetam with a dose of 100 mg/kg and sodium nitrite was used to induce amnesia. Results obtained showed that the Celastrus paniculatus seed extract enhance the memory power by inhibiting acetyl cholinesterase enzyme, and thereby increase the acetylcholine level in the brain. Raut and Colleagues, 2015 evaluated the same activity using Celastrus paniculatus seed oil and an equal amount of ghee at a dose of 200 mg/kg/day orally in mice [44]. Evaluation demonstrated that *Celastrus paniculatus* oil with ghee has a potential drug in the treatment of dementia. Similar activity was evaluated by Jakka, 2016 by using whole plant of methanolic extract of Celastrus paniculatus using elevated plus, morris water maze on scopolamine and aluminum-induced amnesia and estimation of acetylcholinesterase enzyme activity [45]. After experimentation Jakka observed that Celastrus paniculatus extract significantly improved learning and memory power of rats as transfer latency in elevated plus maze and escape latency in the morris water maze model showed a declined. Further acetyl cholinesterase enzyme concentration in the brain was decreased and % of inhibition of acetylcholine activity in rat brain increased which shows the nootropic effect of Celastrus paniculatus.

Antioxidant activity

Gupta and Kumar, 2002 evaluated cognitive property of the seeds of Celastrus paniculatus in rats by using petroleum ether, chloroform, methanol and aqueous extracts and founded that only the aqueous extract show improvement in learning and memory power. As we know that memory loss is associated with oxidative stress they further tested the aqueous extract for antioxidant activity by using doses of 100, 200 and 300 mg/kg, out of that only 200 and 300 mg doses lead to a significant decrease in malanodialdehyde and the increase in glutathione and catalase level in the brain. Thus gave confirmation of memory-enhancing and antioxidant effect.

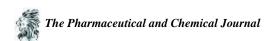
Alama and Haque, 2011 studied the antioxidant activity of seeds of *Celastrus paniculatus* by 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging method [46]. They done the extraction of seed with methanol and further fractioned it with water, chloroform and ethanol. The evaluation showed that ethanolic fraction shows highest activity in DPPH free radical scavenging activity and also inhibit activity of authentic proxy nitrite and total reactive oxygen species. The chloroform extract showed a moderate and aqueous extract had no activity in DPPH method.

In vitro antioxidant activity of ethanolic extract of *Celastrus paniculatus* leaves was evaluated by Sharma and Shrivastava, 2013 by reducing power assay. In this method, there was an increase in absorbance of the reaction mixture, which may be due to the active constituents present in the *Celastrus paniculatus* leaves extract and total phenolic content present was 125.6 mg/gm equivalent to gallic acid in 1 mg/ml of the extract [47].

Celastrus paniculatus fruit seed oil showed good antioxidant activity when performed by the DPPH method by Ramadan, 2019.

Antibacterial activity

Harish et al., 2007 reported that ethanolic extract higher than 100µg and the isolated, purified constituent celapanin higher than 50µg per 100µl of *Celastrus paniculatus* leaves exhibited a better zone of inhibition when screened by agar well diffusion method against Staphylococcus aureus (gram-positive bacteria). Against Pseudomonas aeruginosa and Klebsiella pneumonia (gram-negative bacteria) ethanolic extract and celapanin showed reasonable activity compared to the standard drug Ciprofloxacin (50µg/100µl). The dissimilarity in the activity may be due to



differences in the cell wall because in gram-positive bacteria, the cell wall is a single layer while in gram-negative bacteria, it is multi-layered [48].

Hypolipidemic Effect

Hypolipidemic effect of *Celastrus paniculatus* seeds was evaluated by Patil and coworkers, 2010 by extracting seeds with methanol and then testing the dose of 65 mg/kg in experimentally induced hyper cholesterolemia rats orally. Results showed that *Celastrus paniculatus* decreased the total plasma cholesterol, triglyceride and Lowdensity lipoprotein (LDL) level comparable to standard hypo cholestrolemic drug and induced hyper cholestrolemic rats. There was an increase in High-density lipoprotein (HDL) cholesterol level, lipoprotein lipase activity and less deposit of cholesterol in aorta of rats that were fed with seed extract.

Antifungal Activity

Singh *et al.*, 2010 investigated the antifungal activity of methanolic extract of roots and aerial parts of three plants, namely *Acorus calamus, Tinospora cordifolia and Celastrus paniculatus* against *Curvularia lunata, Fusarium, Bipaloris* and *Helminthosporium* species [49]. They used the doses of 1000, 2000, 3000, 4000 and 5000μg/ml. The result showed that *Celastrus paniculatus* at the dose of 5000μg/ml had better activity against *Celastrus lunate* and *Fusarium*.

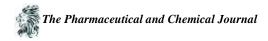
Antifungal potential of *Celastrus paniculatus* mother plant leaves and *in vitro* raised clones was also investigated by using chloroform and methanolic extracts against *Phytophthora capsici* and *Rhizoctonia solani* by *Sasidharan and Elyas*, 2019 [50]. Growth of fungi and its percentage was checked on the dextrose agar medium. The brine shrimp lethality assay was done to check the cytotoxicity of extracts of *Celastrus paniculatus* leaves. After experimentation, it was clear that the methanolic extract of both mother plant and *in vitro* raised clones showed 100 percent of inhibition of *Phytophthora capsici* while chloroform extract of mother plant had very less activity and *in vitro* propagated plants showed 40 percent of inhibition and against *solani*, the methanolic extract showed maximum activity and chloroform extract showed 77.77% and 86.66% respectively.

Neuromodulating effects

Sumathi *et al.*, 2013 investigated the alcoholic seed extract of *Celastrus paniculatus* (ASECP) to prevent aluminium induced neurotoxicity in the cerebral cortex and the cerebellum of the rat brain. They gave the aluminium chlorideat a dose of 4.2 mg/kg/day i. p. for 4 w to male albino rat. Experimental rats were given two different doses of 200 and 400 mg/kg/day orally of *Celastrus paniculatus* seed extract 1hr prior to the aluminium chloride administration for 4 w. At the end, results showed that aluminium administration significantly decreased the level of glutathione and the activities of superoxide dismustase, glutathione peroxidase, Na⁺/K⁺ATPase, Ca²⁺ATPase and Mg²⁺ATPase and increased the activities of alkaline phosphatase, acid phophatase, alanine transaminase and aspartate aminotransferase in all the brain regions when compared with control rats. Aluminium induction also caused histopathological changes in the cerebral cortex and cerebellum of rat brain, which was reverted by pretreatment with ASECP. The result clearly indicates the potential of the seed extract of *Celastrus paniculatus* prevents the damage inflicted by aluminum on rat brain regions [51].

Iron chelating activity

Nakhva and colleagues, 2015 evaluated that the methanolic extract of seeds of *Celastrus paniculatus* for *in vitro* iron-chelating activity by using various reagents like ferrous sulphate, potassium thiocynate and desferrioxamine ⁵². Further, *in vivo* activity was also done that decreased the serum iron level in the test group as compared to the disease treated control group. SGPT, SGOT and Creatinine levels were reduced as compared to iron overloaded rats. So the methanolic seed extract can be used to treat thalassemia and hemochromatosis.



Anti-arthritic activity

Kothavade *et al.*, 2015 used the petroleum ether extract of *Celastrus paniculatus* seeds to study the anti-arthritic effect in adjuvant- induced arthritis in rats [53]. After evaluation of arthritis score, paw volume, body weight, climbing ability and thymus and spleen index, it was clear that *Celastrus paniculatus* seed extract alleviated all these parameters that were due to suppression of overproduction of inflammatory cytokines, cellular enzymes. It also restored the decreased level of superoxide dismustase, catalase and glutathione. The results suggested that the anti-arthritic effect may be due to cytokine regulation, immune-suppressive effects, and bone protective activities. *In vitro* anti-arthritic activity of *Celastrus paniculatus* was also studied by Thangaraj [54].

Antidepressant-like activity

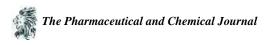
Behavioral and biochemical evidences for antidepressant-like activity was evaluated by Valecha and Dhingra, 2016 by using the seed oil of *Celastrus paniculatus* [55]. Seed oil at the dose of 50, 100 and 200 mg/kg and the drug fluoxetine were given to mice for fourteen days. On the fourteen days after the drug administration tail suspension test and force swim test were performed that showed decrease in an immobility period of mice and plasma corticosterone level and inhibition of monoamine oxidase-A activity, thus responsible for the antidepressant-like activity.

Conclusion

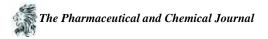
Celastrus paniculatus is a well-known plant in Indian traditional medicine with different medicinal uses and negligible side effects. In this review, we concluded traditional uses, ethnobotanical study, organoleptic characters, chemical constituents and pharmacological uses in a descriptive manner. Best use of seeds of drugs with memory-enhancing activity or as nervine tonic. Other traditional uses are as sedative, tranquilizer, in paralysis, rheumatism, leprosy, bacterial infection and as wound healing agents. Literature review showed that most of the reported activities like anti-arthritic, antioxidant, hypo lipidemic, iron chelating, nootropic and cognitive enhancement activity are by different extracts of *Celastrus paniculatus* seeds which may be due to celapanin, celapagine, celapanigine, β -amyrin, β -sitosterol, stigmaserol, malkanguinol, malkangunin and paniculatadiol. Only a few activities are reported with the use of leaves, roots and flower extract. So there is a need to explore the other parts of *Celastrus paniculatus* also for the beneficial effects as they also contain active constituents like n- triacontanol, pristimerin, benzoic acid, quinine and golden yellow oil, zeylasterol, zeylasterone, celastrol, phenolic triterpenoids and tannins. This review will be useful as the scientific story of *Celastrus paniculatus*.

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