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CELASTRUS PANICULATUS; MEDICINAL AND PHARMACOLOGICAL PROPERTIES: A REVIEW

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ABSTRACT

Celastrus paniculatus Wild. mentioned in Ayurveda as 'Tree of life', a plant belonging to family Celastraceae was in use from time immemorial to treat brain related disorders and to enhance learning and memory. The Jyotishmati oil extracted from the seeds of *C. paniculatus* is known to have effect on Central Nervous System. *C. paniculatus* shows many activities along with main activity i.e memory enhancing effect. Its reported activities are antiviral, antibacterial, insecticidal, anti-inflammatory, antispermatogenic, sedative, anti-fatigue and analgesic, hipolipidemic. It is arthralagenic, antirhumatic, aphrodisiac, emetic, laxative, nervine tonic. Plant is widely used for its medicinal properties, mainly to extract the seed oil, the seeds of plants are harvested indiscriminately from wild as well as cultivars. Hence species is highly vulnerable and it is highly endangered plant of Western and Eastern Ghats. The article is review of medicinal and pharmacological properties of *Celastrus paniculatus*.

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INTRODUCTION

Celastrus paniculatus Wild. mentioned in Ayurveda as 'Tree of life', a plant belonging to family Celastraceae was in use from time immemorial to treat brain related disorders and to enhance learning and memory. The Jyotishmati oil extracted from the seeds of *C. paniculatus* is known to have effect on Central Nervous System. It is native of Indian continent, but is known to grow wildly in Australia, China, Taiwan, Cambodia, Indonesia, Laos, Malaysia, Myanmar, and Nepal, Thailand, Vietnam as well as many of the pacific islands (Singh *et al.*, 1996). A large, deciduous, climbing unarmed shrub attaining a height of 10 m, with long slender elongating branches which are reddish brown with stem up to 23 cm in diameter and covered with elongate lenticles. Leaves are simple, alternate, 6-10 by 3-6 cm. ovate or obovate, shortly acuminate, crenate-serrate in upper part, usually entire near base, crenulate, coriaceous, glabrous, base rounded or acute, petioles 6-12 mm long. Inflorescence is paniculate. Flowers yellowish or greenish white, unisexual in terminal pyramidal panicles, 5-15 cm long, pedicels pubescent, bracts small and lanceolate. Calyx pubescent outside; lobes semi-orbicular, ciliate; petals 3mm long, oblong, rounded at apex. Male flowers: stamens inserted on margin of disc, filament short; anthers oblong about 2 mm

long; rudimentary ovary small, subconical slightly 3-toothed at apex. Female flowers: ovary globose, narrowed into a short stout style, glabrous stigma large 3-lobed; stamens inserted on the edge of disc which is larger than disc in male flowers, anthers small without pollen, ovate, acute or subtriangular, less than 1mm long. Capsule 9-12 mm in diameter, subglobose, bright yellow, transversely wrinkled, 3-valved, the valves spreading after dehiscing, remaining united at the base exposing seeds. Seeds 1-6, often solitary, completely enveloped in scarlet, fleshy aril. Through our literature research it was observed that plant is widely used for its medicinal properties, mainly to extract the seed oil, the seeds of plants are harvested indiscriminately from wild as well as cultivars. Hence species is highly vulnerable (Rajashekharan *et al.*, 2002) and it is highly endangered plant of Western and Eastern Ghats (Pattanaik *et al.*, 2009).

Medicinal uses

Plant parts used- Root, stem, leaves, fruits, seeds.

Roots

The roots of *C. paniculatus* are used as poultice to cure headache. Crushed roots are used in pneumonia. The roots are used to cure excessive pain during menstruation and to induce fertility (Ramanna, 2005; Chopra and Khanna, 2007). The root

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is prescribed for dysentery, diarrhoea and fever. The powdered root bark of *C. paniculatus* is used in treatment of malaria (Old Style Doctor Association, 1964). Decoction of root is given internally as a brain tonic for depression swooning, as laxative for cleaning digestive system (Warrier *et al.*, 2001). The root bark is abortifacient, depurative and brain tonic (Panda, 1994; Sheath, 2005). Powdered root is useful in treatment of tumor (Parotta, 2001). In central India, root or root bark paste is applied on forehead in children to cure boils. The long root of *C. paniculatus* and Piper longam L. made into paste, is given twice a day against leucorrhoea and spermatorrhoea (Sahu, 2010). The root powder of *C. paniculatus* is given to treat rheumatism (Nath and Khatri, 2010). The powdered root or root bark is taken with cow milk once a day for a month to cure leucorrhoea (Shukla *et al.*, 2010).

Stem

Northeast folk medicine practitioners prescribe stems of *C. paniculatus* as lactagogue. The stem is used for treating diarrhoea, dysentery (Katchrinnee *et al.*, 1989).

Leaves

The leaves of *C. paniculatus* are used as poultice to cure headache. Leaf sap is good antidote for opium poisoning (Panda, 1994). Dried leaves of *C. paniculatus* are recommended for inducing menstruation. The leaves are prescribed internally as purgative (Warrier *et al.*, 2001). The leaves are also used for the treatment of dysentery, diarrhoea and fever (Katchrinnee *et al.*, 1989). Poultice of the paste of *C. paniculatus* leaves and roots is applied in headache. The mixed powder of leaves, fruits and flowers, seeds is taken regularly to cure mental disorders and increase mental power. Boiled leaves are applied externally on swellings and fractures (Chopra and Khanna, 2007).

Fruit and seeds

Codified literature of Himachal Pradesh confirms that fruit juice is used as cardiogenic. Paste of the fruit mixed with warmed mustard oil when applied externally is good for scalp. Shade dried fruit is ground into fine powder and sieved. 2-3 teaspoons of powder is taken to destroy intestinal worms (Tiwari *et al.*, 2010). The seed decoction is prescribed as brain tonic, is used in headache, depression swooning and as a laxative. Sushruta prescribed oil of seeds internally in neurological disorders, urinary infections, skin affections, intestinal parasites and externally for wound healing (Warrier *et al.*, 2001). Jyotishmati oil is prescribed in neurasthenia, hemiplegia, Bells palsy, lumbago and gout (Khare, 2002). Seed oil possesses anti-oxidant properties. It prevents fatigue and increases appetite (George *et al.*, 2010).

Oil (3 drops) mixed with egg yolk is given to patient orally with water for acidity/gas. Oil is applied on infected areas of skin. Decoction of seed of *C. paniculatus* is used to treat rheumatism (Nath and Khatri, 2010). The seed oil is extracted and applied externally to keep body warmth in winter season. It is also applied to relieve pain and for proper circulation of blood in body. Seed oil is massaged on the part affected by gout and rheumatism upto the complete cure (Singh *et al.*,

2010). The crushed seeds of *C. paniculatus* in ointments are applied externally on the wound (Chitravadivu *et al.*, 2009). Seed powder of *C. paniculatus*, mixed with water is taken orally to treat nervous disorders (Karruppusamy, 2007). *C. paniculatus* oil is used in the treatment of joint pain (Kamble *et al.*, 2010). Oil extracted from boiled seeds is applied on the paralysed parts in morning; evening and 2 ml. oil is taken orally. It is bitter, thermogenic, digestive, laxative, emetic, expectorant, appetizer, aphrodisiac, cardiogenic, anti-inflammatory, and diuretic, emmenagogue, diaphoretic, febrifuge and tonic. It is used in vitiated conditions of Vata, Kapha and used in abdominal disorders, leprosy, paralysis, skin diseases, cephalgia, arthralgia, fever, nephropathy, amenorrhoea, dysmenorrhoea. It stimulates intellect and sharpens the memory. The seed oil is used in beriberi sores (Panda, 1994; Sheath, 2005).

Proven activities

The oil obtained from the seeds of the plant *C. paniculatus* produced sedation in the rats in a dose of 1 gm/kg when given intramuscularly. On intraperitoneal administration, the same dose of oil produced sedation but the effect was not so marked. The oil showed anticonvulsant activity in rats. The oil (as emulsion in between 80 and water) at a dose of 50-100 mg/kg produced a gradual fall in the blood pressure of cats. At a dose of 200 mg/kg, the oil produced a fall in cardiac output bradycardia and a marked increase in pulse pressure on isolated heart lung preparation (Gaitonde, 1957). The anti-convulsion activity of seed oil was examined against leptazole, picrotoxin and strychnine-induced convulsions in rats. It increased strychnine convulsions and reduced leptazole toxicity. It produced calming effect in injected rats, potentiated pentobarbitone sedation and exerted antispasmodic activity with respect to acetylcholine but did not significantly affect the amphetamine toxicity (Shroff *et al.*, 1959).

The aqueous extract of *C. paniculatus* seed showed potent antibacterial activity against *Bacillus cereus*, *Klebsiella pneumoniae*, *Proteus morgani*, *Proteus vulgaris*, *Salmonella marcescens*, *Salmonella typhosa*, *Salmonella paratyphi A*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus lutea*, *Staphylococcus aureus* but was found inactive against *Bacillus subtilis* and *Salmonella paratyphi B*. (Patel *et al.*, 1962 and Pandya *et al.*, 1990). An active fraction, designated as Mal III/A was isolated from the CP seed oil. It produced a tranquillizing effect on rats, mice, monkeys and cats in a dose of 200 mg/kg. It potentiated the effect of hexobarbitone and produced hypothermia in mice. The fraction also decreased spontaneous motor activity, amphetamine-induced hyperactivity, orientation hyperactivity and oxygen consumption in mice (Sheth *et al.*, 1963). A fraction of the chloroform extract of the root bark of *C. paniculatus* showed the highest antimalarial activity.

A quinonoid triterpene, pristimerin was identified as active principle. However, pristimerin when tested in vitro against various multidrug resistant isolates of *P. falciparum* was less active than conventional antimalarial drugs tested (Katchrinnee *et al.*, 1989 and Chopra, 1956). Biochemical, histochemical and histological studies of the effect of an oily extractive from the seeds of *C. paniculatus* were done on the

testis and liver of adult rats. The testis of treated animals showed vacuolization, germ cell depletion and arrest of spermatogenesis. The liver revealed focal necrosis in animals receiving 0.2 ml i.p every day for 30 days, but in 45 days post treatment those lesions were absent. Intermediate repair and regenerative changes were apparent in 30 days post treatment. These results indicated that *Celastrus* oil may have useful anti-fertility effects and that the degenerative changes seen in the liver are reversible with time (Bidwai *et al.*, 1990). Administration of 50% ethanolic seed extract at 500 mg/kg from day 1 to 120 to hyperlipidaemic rabbits, prevented accumulation of cholesterol and triglycerides in liver and aorta and regressed atheromatous plaques of ascending thoracic and abdominal aorta. The serum cholesterol and LDL-cholesterol levels were reduced by 60.10 and 71.70%, respectively. Increased faecal excretion of cholesterol was observed suggesting that modulation of adsorption was affected (Mathur *et al.*, 1993).

Flowers of *C. paniculatus* and whole plant of *Tecomella undulata* were extracted individually in absolute methanol. Using hot water tail immersion test in mice and carrageenan induced pedal edema in rats; both extracts were tested for their oral analgesic and anti-inflammatory potentials. Results showed that *C. paniculatus* had both analgesic and anti-inflammatory activities (Ahmad *et al.*, 1994). Silmilar anti-inflammatory activity study by carrageenan induced hind paw edema method on the albino rats was done by Sudha *et al.*, (2009) proving that *C. paniculatus* shows considerable anti-inflammatory activity. As the effects of an indigenous drug, oil extracted from the seeds of *C. paniculatus* on learning and memory in a two compartment passive avoidance task was studied in albino rats. The effects on the contents of norepinephrine (NE), dopalamine (DA) and Serotonin (5-HT) in the brain and on the level of their metabolites both in the brain and urine were assessed.

Studies have shown that *Celastrus* oil has ability to increase the intelligence of mentally retarded children. It is concluded that *Celastrus* oil has beneficial effect on the learning and memory process in mentally retarded children (Karanth, 1986). Significant improvement was observed in the retention ability of the drug treated rats compound with the saline administrated controls. The contents of NE, DA and 5-HT and their metabolites in the brain were significantly decreased in the drug treated group. The urinary metabolite level was also significantly decreased except for total 3-methoxy-4-hydroxyphenyl glycol. This indicates that, *C. paniculatus* oil causes an overall decrease in tumor of all the three central monoamines and implicates the involvement of these processes (Nalini *et al.*, 1995).

The study investigated the effect of the seed oil of *C. paniculatus* on the 6 day performance of young adult rats in a navigational memory task-the Morris water maze. Chronic oral (gavage) daily treatment with *C. paniculatus* (50, 200 or 400 mg/kg) for 14 days completely reversed the scopolamine (0.5mg/kg)-induced task performance deficit. *C. paniculatus* did not alter the scopolamine-induced increase in locomotor activity (Gattu *et al.*, 1997). Controlled clinical trial reported efficacy of *C. paniculatus* in cases of depressive illness (Baranwal *et al.*, 2001). One study reported the use of

malkanguni with other indigenous drugs in the treatment of depression (Hakim, 1964). *C. paniculatus* is one of the Indian medicinal plants having a remarkable reputation as a factor of health care among the indigenous medicinal practitioner. The free radical scavenging capacity of methanolic extracts was investigated from *C. paniculatus* and the effect of DNA cleavage induced by H₂O₂, UV/photolysis. The extract showed a dose dependent free radical scavenging capacity and a protective effect on DNA cleavage (Russo *et al.*, 2001).

The aqueous, methanolic, chloroform and petroleum ether extracts of seeds of *C. paniculatus* were investigated for their effect on cognitive functions in rat. Only the aqueous seed extracts (200 mg/kg body wt. for 14 days), showed an improvement in learning and memory in both shuttle box and step through paradigms. The further experiments were conducted using the aqueous extract of 100, 200 and 300 mg/kg body wt. doses in different paradigms of cognition. All three doses of aqueous extract increased the number of avoidance in shuttle box and step through latency in step through apparatus, but no significant difference was observed between the doses tested. Among the 3 doses tested, only 200 and 300 mg/kg body wt. stimulated a significant increase in level of glutathione and catalase, which indicate the *C. paniculatus* seed has cognitive properties and antioxidant effect might be involved (Kumar *et al.*, 2002). Twenty-eight south Indian medicinal plants were screened for their anti-fungal activity against six species of fungi (*Trichophyton mentagrophytes*, *T. rubrum*, *T. soudanense*, *Candida albicans*, *Torulopsis glabrata*, and *Candida krusei*).

Three plant species extracts, *C. paniculatus*, *Eriodendron anfractuosum* and *Ficus glomerata* showed inhibitory activity against 6 species of fungi (Vonshak *et al.*, 2003). The petroleum ether extract of seeds was evaluated for antianxiety activity using behavioral disinhibition model of anxiety in rats. It showed significant inhibition of punishment related and reward related suppression of operant behavior in rats, at dose level of 3.2 g/kg/day for 5 days (Jadhav *et al.*, 2003). The seed oil obtained from *C. paniculatus* has been used in Ayurvedic medicine for the treatment of several complaints including intestinal disorders. The muscle relaxing activity of *C. paniculatus* has been studied in vitro on isolated preparations of rat intestine. *C. paniculatus* seed extract (0.001/100 microgm/ml) produced a conc/related relaxation of the rat ileum [IC (50) (95% C.I), 0.24, (0.13/0.45) mg/ml]. Among the 4 fractions, (n-hexane, CCl₄, CHCl₃, n-BuOH) obtained from the methanolic extracts of *C. paniculatus*, only the CCl₄ fraction (0.01/10,000 mg/ml) induced a significant relaxation of the intestinal muscle [IC (50) (95% C.I): 1.9 (1.38/2.87) mg/ml] (Borelli *et al.*, 2009). Pre-treatment of neuronal cells with *C. paniculatus* seed oil significantly attenuated glutamate-induced neuronal death. *C. paniculatus* seed significantly and reversibly inhibited whole cell currents activated by N-methyl D-aspartate.

The results suggest that CP-WSE protected neuronal cells against glutamate induced toxicity by modulating glutamate receptor function (Praful *et al.*, 2004). The CCl₄ fraction from the methanolic extract of *C. paniculatus* (0.01-10,000 mg/ml) induced a significant relaxation of the intestinal muscle [IC (50) (95% CI): 1.9(1.38-2.87) mg/ml]. Three new

sesquiterpene polyol esters isolated from the CCl_4 fraction at the concentration of 1 microgm/ml produced a relaxant effect of $30.6 \pm 12.2\%$, $26.9 \pm 4.7\%$, $7.27 \pm 1.7\%$ respectively (Sang *et al.*, 2005). Seed oil of *C. paniculatus* has been reported to improve memory and the methanolic extract (ME) of *C. paniculatus* was shown to exhibit free/radical scavenging properties and anti-oxidant effects in human non/immortalized fibroblasts. *C. paniculatus* oil and 2 extracts, an ethanolic (EE), methanolic (ME); ethanolic extract showed dose lesser degree than observed for ME. Oxidative stress involves the generation of free radicals and free radical scavenging is one of the mechanisms of neuroprotection. Pretreatment of neuronal cells with *C. paniculatus* Oil (CPO) dose, dependently attenuated H_2O_2 induced neuronal death. CPO, ME and EE protected neuronal cells against H_2O_2 induced toxicity in part by virtue of their antioxidant properties and their ability to induce antioxidant enzymes.

CPO, which exhibited the least antioxidant properties, was the most effective in protecting neuronal cells against H_2O_2 and glutamate induced toxicities (Godkar *et al.*, 2006). The anti-arthritis effect of oral administration of petroleum ether, alcoholic extracts of *C. paniculatus* seed on Freund's adjuvant arthritis has been studied in Wistar albino rats, the body weight loss that was found during the arthritis condition was corrected on treatment with petroleum ether, alcoholic extracts of *C. paniculatus* seed. The swelling of the paw during the secondary lesions was also markedly reduced. Hematological parameters like haemoglobin content, total WBC count, ESR and RBC were also estimated. The results indicated that seed of *C. paniculatus* is endowed with anti-arthritis activity (Patil and Suryavanshi, 2007). The *Celastrus* oil, extracted from seeds of *C. paniculatus* tested at 2 dose levels (1 and 1.5 g/kg) in rats exhibited significant anxiolytic activity and did not produce tolerance. The non-sedative nature and reversal of anxiolytic property of 5-HT_{1A} partial agonist buspirone in the open field test point to the serotonergic mechanism underlying the anxiolysis (Rajkumar *et al.*, 2007).

A triterpene compound lupeol isolated from petroleum ether extract of leaves of *C. paniculatus* was screened for wound healing activity (8 mg/ml of 0.2% sodium alginate gel) by excision, incision and dead space wound models on Swiss albino rats (175-225 g). In lupeol treated groups wound healing activity was more significant than the standard skin ointment nitrofurazone. Epithelialization of the incision wound was faster with a high rate of wound contraction as compared with the control group. In dead space wound model the weight of the granulation tissue of the lupeol treated animal was increased indicating increase of collagenation and absence of monocytes (Harish *et al.*, 2008). *C. paniculatus* seed aqueous extract was administered orally in two different doses to rats (350 and 1050 mg/kg) and to mice (500 and 1500 mg/kg). Chemical hypoxia was induced by subcutaneous administration of sodium nitrite (35 mg/kg) immediately after acquisition training. In elevated plus maze and sodium nitrite induced amnesia model, *C. paniculatus* extract has showed statistically significant improvement in memory process when compared to piracetam (Bhanumathy *et al.*, 2010). The *C. paniculatus* is one of the important ayurvedic medicinal plants and its seed oil is important as memory enhancer and intellect promoter. The antioxidant rich *C. paniculatus* seed oil was

found to be efficient against immobilization stress induced in the groups of animals. It was more pronounced in the case of animals receiving chronic immobilization stress, the reversal of the conditions was recorded within 24 hours and the effects were dose dependent, increase in the dosage increased the activity (George *et al.*, 2010).

The antifungal activity of methanolic crude extracts *Acorus calamus*, *Tinospora cordifolia* and *C. paniculatus* were investigated against *Alternaria solani*, *Curvularia lunata*, *Fusarium* sp. *Bipolaris* sp. and *Helminthosporium* sp. At different concentrations (1000, 2000, 3000, 4000 and 5000 $\mu\text{g/ml}$) *C. paniculatus* showed better activity against *A. solani* and *Helminthosporium* at 5000 $\mu\text{g/ml}$. At 5000 $\mu\text{g/ml}$ all the three crude extracts showed least activity against *C. lunata* and *Fusarium* sp. HPLC of the crude extracts of medicinal plants showed six different phenolic acids (Benzoic acid, Cinnamic acid, Caffeic acid, Ferulic acid, Gallic acid and Tannic acid) present in varying amount (Singh *et al.*, 2010). Hypercholesterolemia was induced by feeding the animals with high fat diet. Oral administration of methanolic seed extract (50%) of *Celastrus paniculatus* at the optimized dose of 65 mg/kg body weight, substantially reduced the plasma total cholesterol, triglycerides and LDL cholesterol in comparison with induced hypercholesterolemic animal group and the results were comparable with the standard hypocholesterolemic drug and almost similar to the control group. Atherogenic index and liver weight of treated animals also showed significant decrease compared to the hypercholesterolemic animals.

It substantially increased the HDL cholesterol level as compared to control group. A significant increase in the activities of lipoprotein lipase and plasma LCAT enhanced hepatic bile acid synthesis and thereby, increased degradation of cholesterol to neutral sterols. Furthermore, the activities of HMG-CoA reductase, glucose 6-phosphate dehydrogenase and malate dehydrogenase were significantly reduced. Histological studies showed less cholesterol deposits in the aorta of animals fed with seed extract of *C. paniculatus* compared to the induced hypercholesterolemic animals not given *C. paniculatus* (Patil *et al.*, 2010). The crude methanolic extract of the seeds of *C. paniculatus* along with its organic soluble fractions were tested for their possible antioxidant and anti-alzheimer (AD) activity by Badrul and Ekramul (2011). The extracts showed prominent DPPH free radical scavenging activity, inhibiting activity of authentic peroxynitrite (ONOO-) and inhibition of total reactive oxygen species (ROS) generation.

In DPPH radical scavenging assay, the EtOAc fraction showed the highest activity with IC₅₀ value of 25.92 ± 1.02 $\mu\text{g/ml}$ whereas aqueous fractions had no activity at all within the tested concentration. Scavenging of the authentic ONOO-system, all extract/fractions showed good activity and among them, EtOAc fraction had the highest activity with a IC₅₀ value of 15.79 ± 0.18 $\mu\text{g/ml}$. EtOAc fraction also showed significant ($p < 0.001$) inhibitory activity against the total ROS generation which was almost similar with that of the positive control Trolox (IC₅₀ 16.79 ± 0.19 $\mu\text{g/ml}$). All extract/fractions exhibited statistically significant ($p < 0.001$) cholinesterases (ChEs) inhibitory effects with IC₅₀ values ranging between

134.7- 227.5 µg/ml for AChE and 209.6-562.1 µg/ml for BChE.

Current status

The above information proves that *C. paniculatus* truly is 'Elixir of life.' Naturally in no. of the pharmaceutical medicines it is used as major component. Hence it is in great demand in pharmaceutical industry. The current market price of seeds of *C. paniculatus* (2010-2011) across Mumbai is Rs. 2000/kg in wholesale market and at local ayurvedic shops the price is around Rs.4000 to 5000/kg. Thus the seeds possess great economic and pharmaceutical value. But indiscriminate over exploitation from natural sources to meet the growing demand by pharmaceutical industry coupled with low seed viability, lack of vegetative propagation methods and insufficient attempts for replenishment of wild stock of this medicinally important species have contributed to its threatened status. It is listed as 'vulnerable and endangered' medicinal plant (Warrier *et al.*, 2001). So realizing the threat of extinction and to meet the growing need, the special attention is required towards conservation and propagation of this plant by scientific efforts.

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