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PHYTOCHEMICAL AND PHYTOPHARMACOLOGICAL WOMB OF *CELASTRUS PANICULATUS* WILD.: AN OVERVIEW SINCE 1962-2021

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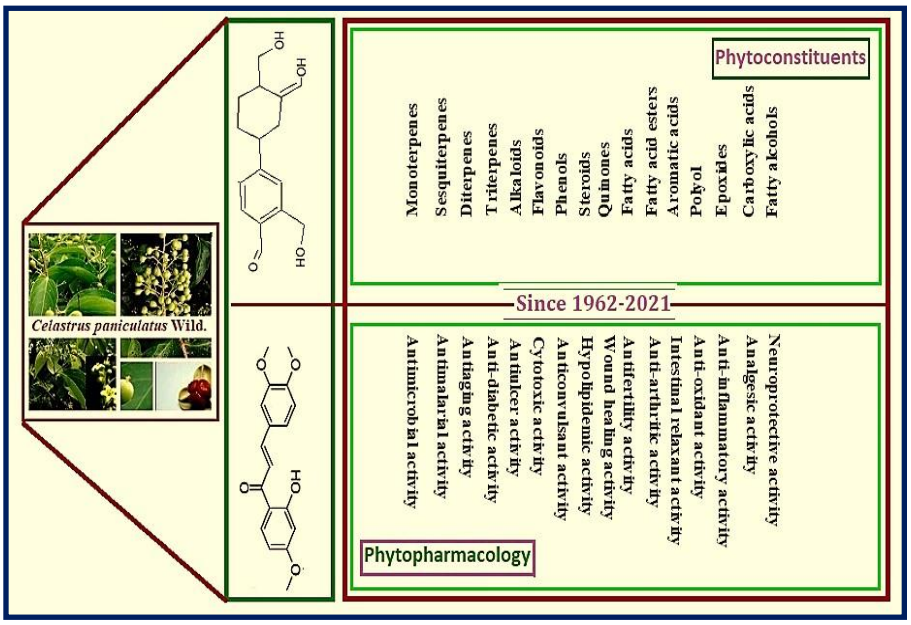
GRAPHICAL ABSTRACT



ABSTRACT

The multi-purpose medicinal plant, *Celastrus paniculatus* is widely used for a number of medicinal activities worldwide either as crude extracts or as pure compounds since the times unknown. This plant has proved for multiple pharmacological activities including cognition enhancing, neuroprotective, antipsychotic, anti-depressant, antibacterial, anti-arthritic, anti-malarial, analgesic, anti-inflammatory, anti-fertility, cardiovascular, locomotor, anxiolytic, wound healing activity, anti-spasmodic, hypolipidemic, anti-cancerous, antioxidant and iron-chelating activity with different extract as well as various phytoconstituents such as monoterpenes, sesquiterpenes esters, diterpenoids, triterpenoids, alkaloids, fatty acids, steroids, flavonoids, polyol, epoxides, polysaccharides and vitamin C of the plant. Instead of

searching for new bioactive compounds of medicinal plant origin continuously, it would be always better and time saving process to re-define the usage of bioactive scaffolds of multipurpose medicinal plant like *Celastrus paniculatus* against different human ailments. It indirectly states that usage of existing activity-biased phytoconstituents will also save billions of dollars' worth due to their chemical diversity and bioavailability. By keeping in view of relative importance of this plant, discussion has made in-detail on the reported phytochemistry, ethnopharmacological and phytopharmacological activities of *C. paniculatus* since 1962-2021.

KEYWORDS: *Celastrus paniculatus*, Phytoconstituents, Ethno/Phytopharmacological activities.

1. INTRODUCTION

In Ayurvedic history plants with medicinal activity have great importance for the healthof individuals. There are some bioactive substances which have medicinal value and produces definite physiological and pharmacological actions (Hill, 1952). Among wide range of medicinal plants, *Celastrus paniculatus* Willd. (Synonym: *Celastrus dependens* Wall) commonly known as jyotishmati, black oil plant, malkangni, climbing staff tree, intellect tree and staff tree belonging to the family Celastraceae is indigenous to Indian descent, but it grows rapidly in Australia, China, Malaysia, Cambodia, Taiwan, Indonesia, Laos, Myanmar, Nepal, Thailand, Vietnam as well as many islands in the Pacific Ocean (Singh et al., 1996; Bhanumathy et al., 2010). Common names of this plant include deng you teng (in Chinese); mal-kangani (in Hindi); jyotishmati (in Sanskrit); kilitheenipanji, cherupunnari and polulavam (in Malayalam); kariganne (in Kannada); valuluvai (in Tamil); skanguni (in Marathi); malkangni (in Gujrati); korsana (in Oriya); and Habbekilkil (in Urdu) (Mishra and John, 2020). This climbing shrub breeds all over India at heights up to 5900 ft from sea level (Tyler and Premila, 2012). *C. paniculatus* is an immense, everlasting, mounted, unarmed or unprotected shrub which involves 10 m height, with long, fragile and extended branches which are reddish brown in colour along with stem up to 23 cm diameter and sheltered with elongate pores. The leaves of this plant are simple, interchange, 6-10 by 3-6 cm, egg shaped, shortly acute, notched, usually cover all the base, irregular, rough and tough, hairless, rounded base rounded and 6-12 mm long petioles. This plant comprises the flowers which are yellowish or greenish white in colour, unisexual in pyramidal form of inflorescence where thecluster are loosely branched, finely pubscent pedicels are 5-15 cm long, sharp and small

bracts. Calyx lobes rounded, ciliated, 3 mm long petal. Male flowers are minute stamens inserted on margin of thin disc, short filament, oblonged petal about2 mm long, disk copular. Female flowers have sepals, sphere or ball shaped ovary which are having 3-lobed, edge of female flower disc is larger than male flower disc, anthers are small do not contain pollen. The diameter of Capsule 9-12 mm, sub-globular shape, bright yellow in colour, transversely folded into 3-valved, the valves are thoroughly distributed, remaining portion combined atthe base exposing seeds. It containing Seeds 3-6 seeds per capsule, solitary, seed pod is enclosed by orange-red aril. This species of this plant is highly assailable and endangered plant of western and eastern Ghats (Pattanaik et al., 2009; Rajasekharan and Ganeshan, 2002; Deodhar and Shinde, 2015). Medicinal activities of this plant are due to its phytoconstituents that are present such as alkaloids, tannins, terpenoids, fatty acids, steroids, flavonoids and other phenolic compounds (Kirtikar and Basu, 1984). *C. paniculatus* is used to treat a numberof ailments like flaming sensation, delivery before the purification of blood, which induces menstrual cycle and abortion (Lal and Singh, 2010). Pharmacological studies suggest that seed of *C. paniculatus* has many important properties including ani-arthritic, hypo-lipidemic, wound healing, failing heart, bronchiectasis, eczema, anti-inflammatory, amenia and dysmenorrhea (Kalaskar et al., 2012; Hemanth et al., 2014; Arora et al., 2014; Jing et al., 2013). Apart from this, oil obtained from seeds of this plant possess number of pharmacological activities such as analgesic (Ahmad et al., 1994), anti-malarial (Ayudhaya et al., 1987), anti- inflammatory (Dabral and Sharma, 1983), anti-bacterial (Patel and Trivedi,1962), anti- spermatogenic (Wangoo and Bidwai, 1988), etc. *C. paniculatus* seed oil showed memory improvement in rat (Karanth et al., 1981) and demonstrated useful effects in the psychiatric patients (Hakim, 1964). By understanding the medicinal importance of *C. paniculatus* this review article was planned to discuss pharmaceutical perspectives of *C. paniculatus* in detail.

2. METHODOLOGY

A comprehensive literature search was carried out on CP using different means of the scientific databases such as Google Scholar, http://www.ncbi.nlm.nih.gov/pubmed, Scopus, http://www.sciencedirect.com, http://www.libnet.ulg.ac.be/en/eresources/scifinder- scholar, Drug Bank (https://www. drugbank.ca/), Chem Bank (https://www.chemicalbank. com), and phytochemical interaction database until December 2021 to include up to date documented information in the present review. The search was limited to English language papers. For data

mining, the following MeSH words were used in the databases mentioned above: neuroprotection, prevention, natural product, phytoconstituents, natural products Alzheimer's, natural products brain, natural products Parkinson's, natural products motor behaviour disorders, *in vivo* and *in vitro* studies for prevention of nervous disorders, neurological disorders vs *Celastrus paniculatus*, Pharmacology of *Celastrus paniculatus*. A total of 249 articles obtained from all the sources. Out of 249, 198 articles were obtained from different scientific databases and 51 were from other sources. Among all the articles, 127 were finally selected for this review. In almost all cases, the original articles were obtained and therelevant data was extracted.

3. RESULTS

Out of the 127 studies identified, 12 studies (n=127) were focused on botanical description, propagative methods, and current scenario on usage of CP, 100 studies (n=127) were exclusively focused on ethnomedical, pharmacological, ethnopharmacological usage, ayurveda and traditional usage, and the rest 15 studies (n=127) were focused on identification bioactive secondary metabolites and their pharmacological potentialities against different kinds of human ailments respectively.

4. DISCUSSION

Apart from the taxonomical classification, eco-geographical features, the current review is majorly focused on two broad categories which include phytochemistry and ethnopharmacological/phytopharmacological benefits of CP, respectively. The obtained information has been briefly summarized in this paper with the following subheads.

4.1.Taxonomical classification

Kingdom: Plantae; Sub-kingdom: Tracheobionta; Super-division: Spermatophyta; Division: Magnoliophyta; Class: Magnoliopsida; Subclass: Rosidae; Order: Celastrales; Family: Celastraceae; Genus: Celastrus; Species: *C. paniculatus* (Mishra and John, 2020).

4.2.Topographical exposure

C. paniculatus grows in wide diversity of climatic conditions and ecosystems. The species of this plant occurs in tropical and subtropical regions of India (Andhra Pradesh, Karnatka, Gujarat, Uttar Pradesh, Madhya Pradesh, Punjab, and Himachal Pradesh), Australia, China, Cambodia, Malaysia, Maldives, Myanmar, Nepal, North America, Philippines, Sri Lanka, Taiwan, Thailand, Vietnam and also in the Pacific Islands. This plant is globally distributed

from South Asia to Australia (The PLANTS Database, 2021; Nayar and Shashtry, 1987; Mishra and John, 2020).

Table 1: List of the complete phytoconstituents identified till now (in total) of *C. paniculatus.*

Monoterpenes05	Sesquiterpenes44	Diterpenes03
Triterpenes09	Alkaloids06	Flavonoids02
Phenols02	Steroids02	Quinones02
Fatty acids11	Fatty alcohols03	Fatty esters06
Polyol01	Epoxides01	Carboxylic acids04
Aromatic acids01	Polysaccharides01	

4.3.Phytochemical profile

The complete phytochemistry profile (bioactive compounds identified since 1962-2021) of *C. paniculatus* is presented in Table 1. Different types of active constituents identified from different parts of plant, type of solvents, morphological activity and their medicinal uses were also properly determined (Kumar and Gupta, 2002; Gurumurthy et al., 2008; Mekari et al., 2009; Zohera et al., 2010).

Table 2: Phytoconstituents present in various parts of *C. paniculatus*.

Class	Phytoconstituents and Reference
Monoterpenes	Linalool; Nerol acetate; α-Terpinyl acetate; Isopulegol; *trans*-Carveol (**Arora et al., 2014**)
Sesquiterpenest	1,9-Dibenzoyloxy-6-cinnamoyloxy-4-hydroxydihydro-β-agarofuran; 1,8,15-Triacetoxy-9-bezoyloxy-4 hydroxydihydro-β- agarofuran; 1,9-Dibezoyloxy-2-acetoxy-6-cinnamoyloxy-4-hydroxydihydro-β agarofuran; 1α-Acetoxy-6β,9α-dibenzoyloxy-8α-cinnamoyloxy-4β hydroxydihydro-β-agarofuran; 1α,6β,9β-Tribenzoyloxy-4β-hydroxydihydro-β-agarofuran; 1α,2α,6β,15-Tet raacetoxy-9α-benzoyloxy-4β,8β- dihydroxydihydro-β-agarofuran; 1α,6β, 8β, 15-Tetraacetoxy-9α-benzoyloxy-4β-hydroxy dihydro-β- agarofuran; 1α,8β-Di acetoxy-6β,9β-dibenzoyloxy-4β-hydroxydihydro-β-agarofuran; 1α, 9β-Diben zoyloxy- 4β-hydroxydihydro-β-agarofuran; 1α,9β-Dibenzoyloxy-6β-acetoxy-8α,4β dihydro xydihydro-β-agarofuran; 1α-Acetoxy-6β,9β-dibenzoyloxy-8α,4β dihydroxydihydro-β-agarofuran. (**Sasikumar et al., 2018**)
	1α,6β,8β-Triacetoxy-9β-benzoyloxydihydro-β-agarofuran; 1α,6β,8α-Triacet oxy-9α-benzoyloxydihy dro-β-agarofuran; 1α,6β,8β,14-Tetraacetoxy-9α-ben zoyloxydihydro-β-agarofuran; Malkanguniol; Malkangunin. (**Sharma et al., 2020**)
	trans- β-Copaene. (**Ali et al., 2020**)
	Iscomene; *allo*-Aromadendrene; α-Selinene; α-Calacorene; Valerenal; Spathulenol; Globulol; Viri diflorol; *trans*-Longipinocarveol; Cubenol; α-Cadinol; Epiglobulol; Bicyclogermacrene; β-Panasinsene; γ-Muurolene;

	Callicarpenal; Sclareolide; Deoxyqinghaosu; Deoxyqinghaosu. (**Arora et al., 2014**)
	Angulatueoid C. (**Younus et al., 2013**)
	Orbiculin A, D, E, F, H, I; Celastrol. (**Jin et al., 2002**)
	Eudalene. (**Rana & Das et al., 2017**)
Diterpenes	Andrographolide; Phytone; Isophytol. (**Arora et al., 2014**)
Triterpenes	Lupeol. (**Sharma et al., 2014**)
	Pristimerin; Paniculatadiol; Zeylasterone; Zeylasteral. (**Sharma et al., 2020**)
	β-Amyrin. (**Ali et al., 2020**)
	Squalene; Cycloartenol acetate. (**Arora et al., 2014**)
	Olean-12-ene-3β,29-diol. (**Younus et al., 2013**)
Alkaloids	Paniculatine; Celapanin; Celapanigin. (**Sharma et al., 2020**)
	Celastrine. (**Ali et al., 2020**)
	Maymyrsine. (**Arora et al., 2014**)
	Celapagin. (**Younus et al., 2013**)
Flavonoids	Paniculatin. (**Dwivedi & Mayure, 2018**)
	3-(3,4-dimethoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one. (**Chintha & Wudayagiri 2021)**
Phenols	Butylated hydroxytoluene; 1,4-Benzenediol. (**Rana & Das et al., 2017**)
Steroids	β-Sitosterol. (**Dwivedi & Maurya, 2018**)
	Carpesterol benzoate. (**Arora et al., 2014**)
Quinones	2,6-Di-*tert*-butyl-pbenzoquinone. (**Rana & Das, 2017**)
Fatty acids	Oleic acid; Linoleic acid; Linolenic acid. (**Sharma et al., 2020**)
	Palmitic acid; Phytol. (**Ali et al., 2020**)
	Erucic acid. (**Arora et al., 2014**)
	Stearic acid; Lignoceric acid. (**Younus et al., 2013**)
	Myristic acid; Eicosenoic acid; 11-Eicosenoic acid. (**Rana & Das, 2017**)
Fatty alcohols	1-Triacontanol. (**Sharma et al., 2020**)
	Tetracasanol. (**Dwivedi & Maurya, 2018**)
	Heahydrofarnesol. (**Arora et al., 2014**)
Polyol	Dulcitol. (**Sharma et al., 2020**)
Fatty acid esters	Dipalmitoylglycerol; Glycerol-1-linoleio-2-oleo-3-stearate. (**Ali et al., 2020**)
	Oxalic acid hexadecyl isohexyl ester; Valericacid, 3-pentadecyl ester; Palmitaldehyde diallyl acetal; Phytol acetate. (**Arora et al., 2014**)
Vitamins	Vitamin C. (**Sharma et al., 2020**)
Epoxides	Humulene epoxide II. (**Arora et al., 2014**)
Carboxylic acids	Aceticacid; Formicacid. (**Ali et al., 2020**)
	Malonic acid. (**Arora et al., 2014**)
	Cinnamic acid. (**Rana & Das, 2017**)
Aromatic acids	Benzoicacid. (**Sharma et al., 2020**)
Polysaccharides	2-Benzoyl-3,4-diacetyl-d-galactosan. (**Arora et al., 2014**)

Diverse class of phytoconstituents were reported in various parts of *C. paniculatus* including terpenes, alkaloids, steroids, fatty acids, flavonoids, fatty alcohols, fatty acid esters, alkyl halides (myristyl chloride), hydrocarbons, carboxylic acids, epoxides, benzoic acid and vitamin C. Celastrus seeds when extracted with aqueous reagent show the effect of tannins

and reducing sugars (Jain, 1963). Petroleum ether extract of seed when saponified gave palmitic acid and sterol fraction (Warsi, 1940). Methanolic extract when saponified yielded sesquiterpenes, polyalcohols (polyalcohols A-D) and makanguniol as major constituents (Den Hertog Jr, 1974). The methanolic extract of soluble segment of *C. paniculatus* seed yielded1α,6β,8-triacetoxy-9α- benzoyloxydihydro-β-agarofuran, angulatueoid C and 1α,6β,8β,14-tetra-acetoxy-9α- benzoyloxydihydro-β-agarofuran (Borbone et al., 2007). The seed of this plant yielded 52% oil of its weight in which mainly sesquiterpene alkaloids were isolated (such as celapanin, celapanigin and celapagin). The major triglyceride components present were palmito-oleo- palmitin (6.8%), palmito-diolein (14.7%), palmito-oleo-linolein (7.0%), stereo-diolein (6.1%), triolein (8.0%) and dioleo-linolein (7.6%) (Sengupta et al., 1987). Seeds of this plant contain various constituents such as celastrine, celapagine, celapanigine and celapanine (Basu and Pabrai, 1946; Lu et al., 2006; Patel et al., 1995). The methyl alcohol extract of soluble segment of *C. paniculatus* seed yielded 1α, 6β, 8-triacetoxy-9α-benzoyloxydihydro-β-agarofuran, angulatueoid C and 1α, 6β, 8β,14-tetraacetoxy-9α-benzoyloxydihydro-β-agarofuran (Patel et al., 1995). The fruit of this plant when extracted with petroleum ether reported the presence of steroids, alkaloids, terpenoids and saponins (Mukherjee and Ray, 1980; Harish et al., 2008). Chemical structures of various phytoconstituents reported in *C. paniculatus* are presented in Table 2.

4.4.Traditional intervention

This plant is one of the best nervine tonics used in the indigenous system of medicine. The expressed seed oil upon administration with ghee (ghrita) is used to initiate intelligence with enhanced mental performance. Two drops of seed oil of this plant are used to enhance memory power as nasal drops for a week. Synergistic effects were obtained with one spoon of seed oil and eight spoons of clarified butter (obtained from buffalo's milk) that in turn proven to be renowned intellect enhancer when applied on the head for an hour (Sujana et al., 2012). The powder of flowers, fruits, leaves, and seeds is advised on routine basis to treat ailments of centralnervous system and to advance brilliance. Seed powder mixed with water, is administered via oral route for the treatment of nervous system disorders. The seed essence, prescribed as a nervine tonic, is utilized in headache, melancholia and somnolence. Jyotishmati oil is prescribed in neurasthenia. Seed oil possesses anti-oxidant, depressant, anxiolytic and anticonvulsant properties (Deodhar and Shinde, 2015; Dwivedi and Maurya, 2018). Seed oil which promoted intellectual memory was proved beneficial for the treatment of mentally retarded children (Kirtikar and Basu, 1984). It also helps in vitamin B1

deficiency disease Beri-Beri when used in conjugation with cloves, nutmeg and benzoin (Younus, 2015; Nalini et al., 1995).

4.5. Pharmacological profiles

In Ayurvedic medicine, the plant has remained as one of the significant medicinal plant that shows pharmacological activity. The biological activity of seed oil depends on route of drug administration (IP, IV, or orally) and dose of extract in selective animals having drug induced toxicity as shown in Table 3.

Table 3: Pharmacological activities of *C. paniculatus* seed oil.

Animalused	Drug model	Dose ofextract	Pharmacological Activity	Ref.
Albino rats	Amphetamine	35 to 70 mg/kg	Reduced hyperactivity	Sheth et al., 1963
Wistar rats Swiss mice	Sodiumnitrate	Rat (350-1050 mg/kg) Mice (500-1500 mg/kg)	Nootropic effect	Bhanumathy etal., 2010
Albino rats	Carrageenan	500 mg/kg	Anti- inflammatory	Ind. Her. Pharm.1999
Young adultrats	Scopolamine	Chronic (50,200,400 mg/kg) Acute (200 mg/kg)	Cognitiveenhancing property	Gattu et al., 1997
Mice	Hexobarbitone	200 mg/kg	Tranquilizingeffect	Sheth et al., 1963
Swiss albino rats	Chlorpromazine, Phenothiazine	0.2 ml	antipsychoticactivity	Bidwai et al., 1987
Male Wistar rats	Natural remedies	400 and 600 mg/kg	Anti-anxiety, depressant activity	Bhagya et al., 2016
Sprague-Dawley rats	Glutamate	0.01-1.0 µg/ml	Neuronal activity	Godkar et al., 2004
Sprague-Dawley rats	Hydrogen peroxide	0.001-1.0 µg/ml	Neuronal activity	Godkar et al., 2003
Wistar rats	Buspirone and diazepam	1-1.5 g/kg	Anxiolytic activity	Rajkumar etal., 2007

4.6. Neuropharmacological activities

Malakanguni (*C. paniculatus*) was known as a famous indigenous tranquillizing drug in the literature (Sheth et al., 1963; Gaitonde et al., 1957). Various central nervous system activities of this plant were reported including memory enhancement, neuronal protection, antidepressant, and antioxidant activity. Biochemical investigations showed a significant rise in lipid and protein matter in brain of the albino rats upon treating them with crude oil obtained seeds (45 days post-treatment) of the plant (Bidwai et al., 1987). Mentat (BR-16A),

herbal product containing various herbs including *C. paniculatus* (100 mg/kg) in combination with piracetam (100 mg/kg) caused the statistically significant nootropic effect in normal and in rats with cognitive defects (Bhattacharya, 1994). Celastrus oil expressed from the seeds was found to lower the contents of monoamines (norepinephrine, dopamine and serotonin) and their metabolites in the central nervous system of albino rats significantly (Nalini et al., 1995). Oral administration of oil (gavage) (50, 200, or 400 mg/kg) for 14 days completely reversed the content of scopolamine (0.5 mg/kg)-induced task performance deficit by causingacute blockade of central muscarinic receptor in adult rats (Khare, 2004). Aqueous extract of seeds (200 mg/kg for 14 days) manifested a remarkable amelioration in learning and memory in the shuttle-box and step-through criterion in male Wister rats and stimulated a significant fall in levels of malondialdehyde with simultaneous rise of glutathione and catalase (200 and 300 mg/kg) (Kumar and Gupta, 2002). It exhibited free radical scavenging capacity in a dose dependent manner for 1,1-diphenyl-2-picryl-hydrazyl radical and also accounted for superoxide- generated protocols (*in vitro* conditions). They were also found to protect cultured neuronal cells in the forebrain from H_2O_2-induced oxidative injuries (increased catalase activity and malondialdehyde levels were decreased significantly) (Godkar et al., 2003). Aqueous extract of seed showed significant neuroprotective effect in primary neuronal cell cultures of forebrain against glutamate impelled neuronal damage. The extract expressively significantly and reversibly stopped inhibited the whole-cell fluctuations generated by N- methyl-D-aspartate (in electrophysiological studies) (Godkar et al., 2004). Seed oil and twoof the alcoholic extracts attenuated hydrogen peroxide and glutamate-induced injury in a dose dependent manner in embryonic neuronal cells present in forebrain of rat. When administered together they were found to protect nerve cells against H_2O_2 derived virulence because of their antioxidant efficacy and their tendency to cause production of antioxidant enzymes (Godkar et al., 2006). Celastrus oil, when tested in two concentrations (1 and 1.5 g/kg), revealed notable anxiolytic effect and failed to cause any sort of resilience. The non-soporific behaviour and reversal of buspirone caused activity (in open field exploration) accounted for the serotonergic pathway explaining the anxiolytic effect (Rajkumar et al., 2007). Water extract of seeds significantly retained learning capacity in elevated plus maze and passive avoidance test in rat (350 and 1050 mg/kg) and mice (500 and 1500 mg/kg) in reference to piracetam (100 mg/kg). They were reported to possess dose-dependent cholinergic actions as evidenced by estimation of acetyl cholinesterase enzyme in brain cells of rat, thereby found to improve memory performance (Bhanumathy et

al., 2010). Jyothismati oil extracted from *C. paniculatus* seeds exhibited high efficacy in decreasing immobilization stress in animals (experimentally induced acute and chronic immobilization). The oil raised the concentration of the antioxidant enzymes and restored their levels markedly in the acute and chronic immobilized groups, respectively (Lekha et al., 2010). The extract prepared in methanol using entire plant lowered the initiation time and prolonged the duration of sleepingin the mice. The extract (200 mg/kg and 400 mg/kg) lessened the count of fostering and steps significantly in Staircase test (Atigari et al., 2012). Seed oil of the plant prevented the onset of chronic aluminium induced cortico-hippocampal neurodegeneration and overall oxidative stress in neurobehavioral, biochemical and histological investigations (Chakrabarty et al., 2012). Ethanolic extract of seeds (2 g/kg body weight) was administrated by oral route for 16 days in 20 months old albino rats and the outcomes were compared with 3 months, 12 months and 20 months old ones (concentration of trace elements). In case of Cu a decline in content in early aged control (0.240 µg/ml) and age control (0.115 µg/ml) groups whereas an increase in treated ones (0.124 µg/ml) was noticed. Young control consisted of 0.683 µg/ml Zn in cerebellum and age control groups displayed peak concentrations of Zn 0.954 µg/ml whereas rats treated with *C. paniculatus* conveyed the minimal of Zn (0.457 µg/ml) in cerebellum. Young one had 0.066 µg/ml Mn amounts that got significantly declined in early age control (0.022 µg/ml) followed the significant increase in age control (0.087 µg/ml). Young control had the highest Co content (0.084 µg/ml) followed by decrease in early age control (0.83 µg/ml) and age control (0.006 µg/ml). Treated animals showed an increase in Co content (0.032 µg/ml) (Saini et al., 2012). Pre-treatment of rats ($AlCl_3$ promoted neurotoxicity) with alcoholic extract of seeds (200 mg/kg body weight) escalated the antioxidant and potential of membrane associated enzymes and lessened that of marker ones predominantly in referenceto aluminium induced groups. Pre-exposure with the alcoholic seed extract showed downfall in deterioration of an impaired DNA by aluminium. Aluminium induction also affected tissuerelated alterations in cortical cells of cerebrum in the cerebral cortex, cerebellum and hippocampus of rat brain that in turn were reversed by pre-treatment with the extract (Sumathi et al., 2013). Supply of seed extract (50 mg/kg body weight) increased the duration of exercise up to two-fold in forced swimming test and also controlled the concentration of serum biochemical markers including glucose, blood urea nitrogen, creatine kinase, lactate dehydrogenase and tissue biochemical markers such as glycogen, lactic acid, superoxide dismutase, catalase and lipid peroxidation. Exercise induced muscular dystrophy and DNA disunion were restored by the extract

and it further facilitated the exercise moved display of metabolic and oxidative stress markers such as AMPK, Glut-4, PDK4, VEGF, PGC-1α, MCT-1, MCT-4, SOD, CAT and HSP-70 as proven through western blot (Kandikattu et al., 2014). Seed oil (50, 100 and 200 mg/kg body weight given for 14 days) showed antidepressant effects in Swiss young albino mice subjected to long term non-predictable weak stress. The oil significantly lowered the rate of non-motility of both groups in forced swim model. The oil also by passed the stress caused decreased sucrose preference, indicating its significant ability comparable to the reference drug, fluoxetine (20 mg/kg). The oil also lowered the actions of monoamine oxidase-A along with reduction in malondialdehyde concentration in both the groups hence averted the stress-induced reduction in glutathione amounts and catalase activities. It also remarkably diminished the raised concentrations of plasma nitrite and corticosterone (Valecha and Dhingra, 2014). Seed oil was tested for its fruitful outcomes affecting the retention capacity as assessed by mixing it in equimolar proportions with pure ghee when given by oral route in mice (200 mg/kg/day) using Piracetam as standard memory enhancer drug and scopolamine as an amnestic agent. Mice receiving oil showed the significant improvement in learning capacity as compared to the scopolamine group and hence could be advanced as a possible treatment for dementia (Raut et al., 2015). Nerve protection effects of oil were evaluated on stress-associated cognitive abnormalities. Strained rats showed impaired performance in radial arm and T-maze tasks compared to normal ones. Treatment with oil improved their responses too in both the models mentioned above. In addition, anxiolytic activity was pronounced remarkably in stress induced anxiety (Bhagya et al., 2016). The antidepressant effect of seed oil (50, 100and 200 mg/kg) was evaluated in non-stressed Swiss young albino mice using tail suspension and forced swim test. A notable fall in duration of immobility was observed in comparison to those of fluoxetine (Standard drug). ED_{50} value of the oil in both the models was mentioned to be 17.38 and 31.62 mg/kg, respectively. The oil significantly inhibited brain monoamine oxidase-A activity and caused decreased plasma corticosterone levels (Valecha and Dhingra, 2016). Learning and memory enhancing capacities of the *C. paniculatus* extract were testedin scopolamine induced dementia in rats using T-maze apparatus and compared with donepezil. Aqueous extract of *C. paniculatus* confirmed an increased memory performance in reference to scopolamine group (Bohra and Maheshwary, 2017). Ethanolic extract showed protective action for 3-nitropropionic acid induced Huntington's disease and associated symptoms in Wistar male rats. Treated groups reflected a notable advancement in behavioral changes in rats

accompanied by reduction in oxidative stress when compared to animals treated with 3-nitropropionic acid. Out of different extract tested, water-based fractions at 18 mg/kg confirmed almost complete reversal of 3-nitropropionic acid induced behavioral patterns and biochemical changes (Malik et al., 2017). Investigations conducted against methyl mercury caused nerve toxicity in the cerebellum of male Wister rats revealed an increased mitochondrial electron transport chain activity, lessened release of cytochrome C and higher rate caspase 3 mRNA expressions upon treatment the subject with *C. paniculatus* ethanolic extract. In the aorta, methylmercury-imposed oxidative stress, changein fatty acid compositions and endothelial unfolding were enhanced by this plant (Sumathi et al., 2018). In a study conducted on five herbal extracts methanolic extract of *C. paniculatus* (malkagni) seeds demonstrated the *in vitro* anti-acetylcholinesterase (19.17% inhibition at 100 µM concentration) with IC_{50} of 2773.39 µg/mL (Balkrishna et al., 2019). Behavioral and neuroprotective potential of *C. paniculatus* seed oil was evaluated on hippocampus of the brain in kainic acid initiated neurodegenerative ailments in albino Wister rats. The kainic acid caused Alzheimer has presented outstanding conversions in usual behaviours. The erythrocyte count, number of platelets, haemoglobin concentration has manifested a significant rise whereas on contrary WBC count has shown a remarkable decline inamounts. A significant decrease in the serum cortisol and cholinesterase levels were also exhibited by experimental groups treated with seed oil as a mark of neuroprotection (Pujari et al., 2019). The methanolic extract exhibited neuroprotective effect in *Caenorhabditis elegans* models of Parkinson's disease (BZ555 and NL5901 strains). It showed protection against 1- methyl-4-phenylpyridinium iodide-induced dopaminergic neurodegeneration in *Caenorhabditis elegans* BZ555 strain. This extract inhibited the aggregation of heterologously expressed human α-synuclein in the NL5901 strain (Anjaneyulu et al., 2020). A new flavonoid compound, 3-(3,4- dimethoxyphenyl)-1-(4-methoxyphenyl)prop-2-en-1-one isolated from seeds showed significant neuroprotective effect against ketamine-induced cognitive deficits in rats. Ketamine affected cholinergic variations in different parts of brain were retained to normal levels after treating with this compound on par with clozapine (standard drug) (Chintha et al., 2021). The neuroprotective potential of this compound was further assessed for ketamine-induced schizophrenia in relation to cholinergic bio-transformations under *in vivo* and *in silico* techniques. The reduction in glutamine concentrations, glutamate dehydrogenase levels, glutamine synthetase and glutaminase in different cerebral parts in rat pointed towards lowered oxidative deamination followed by low rate of conversion of

glutamate towards glutamine. Pre-exposure with the plant extract resulted in a 'U' turn changes in glutamate transformations and retained the normal glutamatergic neurotransmission akin to clozapine. Further the compound displayed strong interaction and exhibited the highest binding energies against selected NMDA receptors with the lowest retardation constant than the reference drug (Venkataramaiah et al., 2021). In the latest research studies, the neuroprotective efficiency of the compound was checked against ketamine-induced schizophrenia in particularly relating to catecholaminergic metabolism. Ketamine-induced schizophrenia resulted in significant increase in concentration of biogenic amines (epinephrine, nor epinephrine dopamine and serotonin) and monoamine oxidase activity that in turn were restored to normal during the treatment with the compound akin to clozapine. In addition, the compound has exhibited maximum affinity score against all the biogenic amine receptors (i.e., D1, D2, D3, D4 dopamine receptors and 5-HT2A serotonin receptor) with lowest retarding constant values in comparison to the standard drug, clozapine (Venkataramaiah et al., 2021a). This bioactive compound was also evaluated in PC 12 cell lines *in vitro* against ketamine induced cell death. This compound increased around 80% cell viability, down- regulated cell destruction; decreased intracellular reactive oxygen species (ROS) caused free radical harm, and up-regulated cell survival capability (Venkataramaiah et al., 2021b). An investigation into possible toxic effects was conducted with polar and semi polar compounds isolated from the fractionated seed oils in animal models. Upon injecting the fractionated extracts temporary adverse effects including fatty liver, degeneration of hepatic cells and impairment of proximal tubular cells in the kidney were reported in rats (Bidwai et al., 1990).

4.7. Antimicrobial activity

Antibacterial activity of *C. paniculatus* was reported in 1962 (Patel and Trivedi, 1962) and 1990 (Pandya et al., 1990). Seed oil obtained was reported to have antimicrobial properties (Parch et al., 2003). Saponins obtained from seed (methanolic extract) showed moderate activity for oral ones, *Streptococcus salivarius* and *Lactobacillus acidophilus* (zone of inhibition: 11 and 10 mm, respectively) (Jyothi and Seshagiri, 2012). In an investigationusing the disc diffusion method, the water and methanolic extracts of leaves exhibited potent effects against *Bacillus cereus*, *Staphylococcus aureus* MTCC, *Shigella flexneri* and *Vibrio cholerae* (with zone of inhibition ≥ 12 mm and minimum inhibitory concentration below 1 mg/mL) (Panda et al., 2016). In a study, six medicinal plants were tested for anti-quorum sensing activity using bio monitor strain of *Chromobacterium violaceum* CV12472. Outcomes of test

confirmed the efficacy extract as it retarded the expansion of tested species (Ganesh and Rai, 2017). Silver nanoparticles with *C. paniculatus* seed coat exudates were prepared and their bactericidal as well as biofilm inhibition effects were evaluated. Nano-silver strongly inhibited the bacterial growth, resulting in minimum inhibitory concentration values of 40 µg/ml and 60 µg/ml against *Escherichia coli* and *Bacillus subtilis*, respectively. There was destruction in biofilm formation after treatment with nano-silver (Moola et al., 2019). In an investigation to identify natural lead compound against molecular targets playing role in regulation of biofilm synthesis in *Pseudomonas aeruginosa* (resistant against most of the last resort antibiotics), celastrol (a constituents of *C. paniculatus*) affected better binding capacities with response regulator Gac A (binding free energy = -7.2 kcal/mol) relative to attachment of meropenem and its target (binding free energy = -6.2 kcal/mol) in docking studies. Gac A-celastrol complex confirmed conformational stability throughout the MD simulation process (Skariyachan et al., 2020). In a random trial conducted on 28 plants from south India possessing therapeutic activity when tested for their potential against mycotoxins produced by six fungi, aqueous extract of seeds found to significantly inhibit *Trichophyton rubrum* (Vonshak et al., 2003). Copper nano-particles prepared using leaves extract (via eco-friendly green synthesis) demonstrated good antifungal activity against plant pathogenic fungal strain *Fusarium oxysporium* (76.29 maximum mycelia inhibition *in vitro*) (Mali et al., 2020).

4.8. Anti-inflammatory and analgesic activity

Methanolic extract of flowers exhibited significant analgesic potential in tail immersion model and affected swelling in carrageenan induced paw oedema in rats as compared to aspirin (Ahmad et al., 1994). Seed oil obtained from the plant (methanolic and ethanolic extracts) displayed potent anti-inflammatory activity (Parcha et al., 2003). The same demonstrated significant inhibition (70% at 500 mg/kg body weight) in albino rats using carrageenan caused hind paw oedema compared to diclofenac sodium (79% inhibition at 50 mg/kg body weight) (Parimala et al., 2009). The methanolic, ethyl acetate and petroleumether extracts of leaves provided notable relief in pain in acetic acid induced writhing test in Swiss albino mice. Potency was observed as highest in methanolic ones preceded by other two fractions (Debnath et al., 2012). Aqueous, methanolic and chloroform seed extracts were assessed for anti-inflammatory activity via lipoxygenase inhibition assay where among three of them water extract confirmed significant anti-inflammatory activity (Arora et al., 2014). Alcoholic extract of *C. paniculatus* seeds were evaluated for the antinociceptive behaviour in

swiss albino mice by using tail immersion (30.16% at 1000 mg/kg), hot plate (6.23 increase in paw licking time compared to control, i.e., 3.20) and acetic-acid-induced writhing (58.8% inhibition in writhing) tests; and for anti-inflammatory activity in carrageenan-induced acute plantar model of inflammation in Wistar rats (significantly reduced paw oedema at 3 and 4 hours when compared to control animals) (Kulkarni et al., 2015). Extract obtained from plant seed oil inhibited imiquimod-induced psoriasis-like dermatitis in mice model (Arora et al., 2016).

4.9. Antioxidant activity

Dose related clearance of free radicals were seen which provided protection against DNA disunion provided remarkable shielding for H_2O_2 caused damage and also affected impairment of DNA in human non-immortalized fibroblasts (Russo et al., 2001). The polar and non-polar seed extracts exhibited moderate potential in a dose related manner and possessed flavonoids and phenolic compounds. In 1,1-diphenyl-2-picryl-hydrazil radical scavenging test, ethyl acetate extract exhibited the minimum IC_{50} value (585.58 µg/ml) in reference to ascorbic acid. In nitric oxide scavenging test IC_{50} value was reported to be 122.99 µg/ml, 320.54 µg/ml, 601.81 µg/ml and 206.37 µg/ml respectively for water, methanol, ethyl acetate and petroleum ether extracts compared to ascorbic acid (IC_{50} = 6.83 µg/ml) (Zohera et al., 2010). The crude methanolic extract seeds along with its organic fractions were screened for antioxidant and anti- Alzheimer potential. The ethyl acetate fraction of the crude methanolic extract showed the maximum activity with a IC_{50} value of 25.92 mg/ml in 1,1-diphenyl-2-picryl-hydrazil radical scavenging test (IC_{50} = 25.92 µg/ml) and authentic peroxynitrite system (IC_{50} = 15.79 µg/ml). Ethyl acetate fraction also showed significant inhibition against the total reactive oxygen species (ROS) generation comparable to that of standard Trolox (IC_{50} = 16.79 µg/ml). Mentioned fractions executed statistically important cholinesterase inhibitory effects (IC_{50} values in the range 134.7-562.1 µg/ml)(Alama et al., 2011). Antioxidant efficacy of all extracts were assessed in 2,2-diphenyl-1-picrylhydrazyl radical scavenging assay, similar to capacity equivalent to trolox and antioxidant power assay by reducing ferric. Among all chloroform extract were found to exert significant antioxidant effect containing highest phenolic content (Arora et al., 2014). Anti-oxidant and anti-apoptotic activities of seed extract were tested in tertiary butyl hydro peroxide (t-BHP) caused myopathy in mice. Cell were able to survive at 50 µg/ml accountingfor 70% protection as evidenced by 3-(4,5-dimethylthiazol-2-yl)-2,5-

diphenyltetrazolium bromide cell survival procedure. The extract confirmed its potential via restoration of mitochondrial membrane and diminished the production of reactive oxygen species and decreased lipid per oxidation. Pre-treatment with the extract also controlled the responsible markers including superoxide dismutase and catalase amount facilitated by protein expression. Anti-apoptotic responses by regulation of cytochrome-C and thermal shock protein-70 expression were seen too that resulted in 43% inhibition of DNA distortion in muscle cell against t-BHP (Kumar et al., 2015).

4.10. Intestinal relaxant activity

Dose related easiness is measured in the rat ileum upon administration of methanolic extract of seeds (IC_{50} value of 0.24 µg/mL). Out of four fractions (n-hexane, CCl_4, $CHCl_3$, n-butanol) obtained from methanolic extract, only carbon tetrachloride fraction produced the significant effect (IC_{50} value of 1.9 ng/mL). Sesquiterpene esters isolated from the carbon tetrachloride fraction produced 7.27-30.6% relaxant effect at 1 µg/mL concentration (Borrelli et al., 2004). Methanolic seed extract showed potent myogenic and Ca^{2+} dependent relaxant effect on isolated rat and human ileum (IC_{50} value of 0.26 µg/mL for human). The extract also executed a tetrodotoxin and omega-conotoxin-resistant repulsive action on the motility of ileum (IC_{50} value of 0.26 µg/mL) (Borrelli et al., 2009).

4.11. Anti-arthritic activity

Petroleum ether and alcoholic extracts of seeds showed anti-arthritic effect in Freund's adjuvant arthritis in Wister albino rats upon oral administration. The lost body mass was also regained after treating the animals with petroleum ether, alcoholic extracts accompanied by decrease in secondary lesions and a significant reduction in paw volume (Patil and Suryavanshi, 2007). Petroleum ether fraction obtained from seeds showed anti-arthritic effect induced Sprague-Dawley rats. This extract significantly alleviated arthritic progression as measured by parameters including paw oedema, arthritic measurement, immune organ indexes, hyperalgesic responses and weight of body and the mentioned determinants were found to be directly co- related with significant reduction in inflammatory markers including cytokines, oxidant stress and cellular enzyme levels. Outcomes from different investigations suggested the potential role of the plant could be due to its ability to affect osteogenesis, suppression of immune system, regulation of cytokines and to scavenge free radicals and (Kothavade et al., 2015).

4.12. Antifertility activity

Extract obtained from *C. paniculatus* seeds demonstrated anti-spermatogenic potential when tested in the testis of albino rats (Wangoo and Bidwai, 1988). Oily extract obtained from seeds of this plant showed vacuolization, reduction in germ cells and cessation of spermatogenesis (Bidwai et al., 1990a).

4.13. Antimalarial activity

Preparations from the plant have been found to be useful in cure of malaria and management of febrile illness since ancient times as part of traditional practices of Thailand. Fractions of the chloroform extract prepared from the root bark of this plant showed maximum activity under *in vitro* assay. Isolation and characterization of chloroform fraction yielded a bioactive compound identified as a quinonoid triterpene, pristimerin which showed significant antimalarial effect *in vitro* against multidrug resistant strains of *Plasmodium falciparum*, and wasfound to be comparatively less active than the conventional anti-malarial drug (Pavanandt et al., 1989).

4.14. Wound healing property

Lupeol, from petroleum ether extract of the leaves of this plant when incorporated in concentration of 8 mg/ml of 0.2% sodium alginate gel exhibited rapid healing of abrasive surfaces in external and internal cut surfaces and dead space wound models in adult albino rats. Treated groups responded significantly (17.83) compared to the standard nitrofurazone containing ointment (18.33). The comparative docking of the isolated constituent, lupeol (inhibition constant=1.38×10^{-7}) and standard drug nitrofurazone (1.35×10^{-4}) with glycogen synthase kinase 3-β protein also added to the efficacy of this constituent (Harish et al., 2008).

4.15. Angiotensin converting enzyme (ACE) inhibition

In an investigation on the Indian medicinal plants, aqueous extract of *C. paniculatus* showed 50% reduction of ACE and the same could be further utilized for further development of the antihypertensive agents (Somanadhan et al., 1999).

4.16. Hypolipidemic activity

Methanolic extract (65 mg/kg body) confirmed the hypolipidemic activity in rats fed with diet laden with high fat. This extract potently decreased plasma total cholesterol, triglycerides and low-density lipoprotein however raised the concentrations of high-density lipoproteins. The enzymatic rates of reactions for β-hydroxy β-methylglutaryl-CoA (HMG-CoA) reductase

enzyme, glucose-6-phosphate dehydrogenase and malate dehydrogenase got slower down. Lesser of cholesterol was found to get deposit in the aorta of the treated groups in comparisonto the non-treated ones (Patil et al., 2010).

4.17. Anticonvulsant activity

Petroleum ether and ethanol extracts of seeds showed statistically significant response against maximal electroshock and PTZ induced convulsions in the mice. 90% of the animals treated with petroleum ether extract (600 mg/kg body weight) survived in maximal electroshock and in induced seizures, respectively (Yadav et al., 2011).

4.18. Cytotoxic activity

(1α,2α,8β,9β)-1,8-Bis(acetyloxy)-2,9-bis(benzoyloxy)-14-hydroxy-β-dihydroagarofuran, a β-dihydroagarofuranoid sesquiterpene isolated from this plant suppressed the feasibility of MCF-7 cancer cells mammary glands (IC_{50}=17μM) attributable to apoptosis. Western blot analysis confirmed its ability to combine with broad range of signaling effectors in context to continuity and progression of cell cycle further added by increased synthesis of reactive oxygen species (ROS) in flow cytometry analysis in response to the isolated compound (Weng et al.,2013).

4.19. Antiulcer activity

The seed oil of the plant showed the efficacy by reducing number of ulcers as well as by maintaining the integrity of gastric mucosa in the dose at (200 mg/kg and 400 mg/kg in pylorus- ligated and ethanol and indomethacin-induced ulcers models employing ranitidine(40 mg/kg) as reference drug. The results obtained proved the effectiveness of oil in all the models by inhibiting the gastric secretions thus reducing total amount of gastric juice and caused the raise in pH of stomach The protective effect of indomethacin can be jointly responsible for desired suppression of biological markers including proinflammatory cytokines along with escalated concentrations of TNF-α, IL-6, and IL-10. Ethanol-induced ulcers were significantly treated by seed oil by causing reduction in malondialdehyde levels accompanied by enhancing superoxide dismutase (SOD) and catalase activities (Palle et al., 2018).

4.20. Cardiovascular

Somanadhan *et al.* in his finding regarding cardiovascular effects, it was observed the gradual fall of cardiac output, marked increased in the pulse pressure and inhibition of angiotensin-

converting enzyme in the animal model of cat administered with seed oil as emulsion and aqueous extract of CP at a dose of 50-100 mg/kg.

4.21. Cosmetic applications

Seed oil of the plant after incorporation into 2-hydroxypropyl-β-cyclodextrin cavities was subjected for evaluation of biological activity, physicochemical stability and dermal permeation of the inclusion complex. In the skin-penetration study the inclusion complex serum dosage contained the maximum aggregated amount of oleic acid in the entire layer andexhibited a rapid outflow through receptor fluid, after six hours, of 32.75µg/cm² and 1.02 µg/cm²/h, respectivelyin comparison to other formulations hence directing towards the usageof inclusion complex for the further development of cosmetics formulations (Ruksiriwanichet al., 2018).

4.22. Alpha-glucosidase inhibitory activity

Catalytic action of α-glucosidase was found to be inhibited by the sesquiterpenoids named dihydro-β-agarofurans obtained from seed extract of this plant with IC_{50} values in the range 35.60-45.84 µM. Molecular docking studies of these compounds with protein 3A4A supported α-glucosidase inhibitory activities of these isolated compounds (Sasikumar et al., 2018).

4.23. Antiaging activity

In one of the studies the dihydro-β-agarofuran-enriched fraction of seeds along with their three derivatives isolated from this plant showed significant elevation in mean survival timeof the nematode *Caenorhabditis elegans* by 23%, 16%, 18%, and 17%, respectively incomparisonto control group (Fu et al., 2020).

4.24. Patent literature

Different compositions of *C. paniculatus* were patented and some of them are listed in Table 4.

Table 4: List of various types of *C. paniculatus* compositions reported in patent literatures.

Patent No. and Office	Outcome	Company/ Applicant and year	Reference
AU2002246308 Australia	Herbal product for treatmentofattention deficit ailments	Dalmia Centre for Research and Development-2002	Murali,2002
WO2003068251 WIPO	Herbal product for treatmentof attention deficit ailments	Dalmia Centre for Research and Development-2330	Murali,2003
IN0370/DEL/2005 India	for treating early ejaculationand sexual problems	Y. Shrivastavand A. Shrivastav-2006	Shrivastav and Shrivastav,2005
CN101830960 China	Procedure for synthesis of celastrine	Suzhou Paiteng Biopharmaceutical Technology-2010	Wang et al., 2010
IN1546/DEL/2010 India	Product for treating alopecia	Synkrom Healthcare Pvt. Ltd.-2012	Raizada, 2012
IN1150/DEL/2012 India	Topical herbal product for treatment of psoriasis	D. K. Sadh-2012	Sadh, 2012
US20140322198 USA	Product having vicenin-2 memory enhancement	Amino Up Chemical Co. Ltd.-2014	Buchwald-Werner, 2014
IN201611021396 China	Collaborative product for therapy of gout	L. K. Sharma-2016	Sharma, 2016
CN106389805 China	Ayurvedic products as massage oil	C. Zhiwei-2017	Zhiwei, 2017
CN106490695 China	Herbal product for treatmentof reproductive ailments	Shaanxi Hanzhong Qinhui Biomedical Technology-2017	Mingjie, 2017
IN201721015049 India	Product for rheumatic arthritis, pain and cold	V. Mishra-2017	Mishra, 2017
WO2019016717 WIPO	Sleep persuading formulation	V. Naharwar and J. V. Thakkar-2019	Naharwar, 2019
IN202011020939 India	Herbal product for OCI	Dev Sanskriti Vishwavidyalaya-2020	Patel, 2020
IN201921013567 India	Product for pain	V. S. Tarate-2020	Tarate, 2020

5. Current scenario

With reference to the Indian context, which is a native for a maximum number of medicinal plants, more than 70% of the population use herbal drugs for their health. Among those *C. paniculatus* is being used as a major component in many numbers of pharmaceutical formulations because of its versatile properties. Although *C. paniculatus* possess great pharmaceutical values, the indiscriminate overexploitation of this plant to meet growing

demand made this plant close to threatened status, and listed as vulnerable and endangered medicinal plant. Hence, a remedial measure to be taken to maintain the species sustainability to derive in- depth therapeutic modalities regarding the mentioned properties above.

6. CONCLUSION

Based on the in-detailed discussion on phytoconstituents and phytopharmacological profile of *C. paniculatus*, it is concluded that *C. paniculatus* has wide range of medicinal activities. The major note-worthy thing of this plant is all the identified phytoconstituents were exhibited significantly high content of activity against the respective pharmacological modality when they tested. Besides, no pharmacoresistance, idiosyncratic, neurotoxic reactions were exhibited by the compounds during supplemented with induced drug and administered alone. Till today, a total of 103 phytoactive constituents were identified in different parts of *C. paniculatus* such as Root, bark, leaves, fruits, and flowers by several researchers all are proven as strong bioactive scaffolds. The multifaceted versatility of the *C. paniculatus* observed by many of the researchers from 1962 to 2021 against different kinds of pharmacological activities revealed its efficacy and effectiveness in a multi-purpose manner. Hence, I conclude that with no-doubt the *C. paniculatus* will be definitely reach too much bigger stage in terms of pharmacological application in a short period and the phytoconstituents will also stand as core molecules for the synthesis of analogues of biopharmaceutical concern/synthetic/safe drugs and we can deliberately rely on it.

7. Conflict of interest

The author declares no conflict of interest.

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