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(REVIEW ARTICLE)

Pharmacological and pharmacognostical aspect of *Prosopis juliflora*: A review

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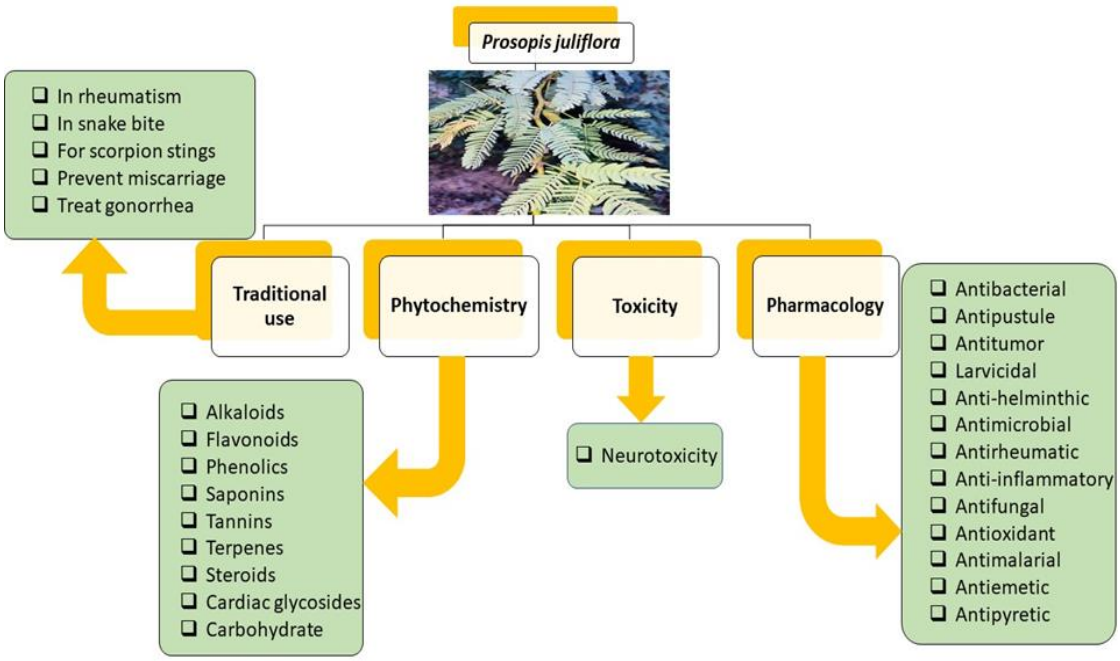
Abstract

Prosopis juliflora also called as mesquite or Velayati babul, found all over the world specially in semiarid and arid areas. It is a competitive weed and has been declared as noxious in several countries. WHO found that herbal medicines are used traditionally for the treatment of diseases, nearly 80% of the population utilize plants due to their less side effects and easy availability as compared to allopathic systems of medicine. *Prosopis juliflora* belongs to family Leguminosae and also has an effective role as traditional medicine. Every part of this species contains a large number of phytoconstituents mainly flavonoids, alkaloids, tannins, phenolics, terpenes and saponins. The plant possesses some pharmacological activity like antibacterial, anti-pustule, antitumor, larvicidal, anthelminthic, antimicrobial, anti-rheumatic, anti-inflammatory, antifungal, antioxidant, antimalarial activities. Despite of its various uses, it is a serious invasive weed and is cytotoxic in nature. Due to ingestion of *Prosopis juliflora* pods, a neurological disorder "Cara-torta" is most common in the ruminant animals like goats which directly affect mitochondria of nerve cell. So, this article is an aggregate of all the details and information of *Prosopis juliflora* plant published in different books and journals.

Keywords: Alkaloids; Cytotoxic; Invasive; Mesquite; Pharmacological activities; *Prosopis juliflora*



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1. Introduction

Prosopis juliflora is one of the most invasive species of India and the world, which belongs to the family Leguminosae and subfamily Mimosoideae and has 44 species across the world [1,2].Traditionally, *P. juliflora* is utilized for curing diarrhea, cold, dysentery, flu, inflammation, measles, hoarseness, sore throat and for the curing and healing of wounds [3]. Woods of *P. juliflora* species used as a source of charcoal and activated carbon and also in the manufacturing of paperboard and fiber for paper and hardboard industries. *P. juliflora* is also used as pods for animal feed and the flowers are used by bees for honey production [4,5,6]. It is a competitive weed and also called as a noxious weed in several countries because the tree dries out the soil and compete with every plant, especially grasses in the dry areas [1,7]. Drought tolerant genes have been identified in *P. juliflora* using expressed sequence tags and these genes are used as drought tolerance genes in various transgenic crops or plants [8]. Medicinal uses of *P. juliflora* have been demonstrated in many studies and the extracts of different parts of *P. juliflora* possess numerous pharmacological activities such as antimicrobial, antioxidant, antimalarial, larvicidal, insecticidal, antitumor, anthelmintic, antiemetic and cholinesterase inhibiting activity [9]. From ethnopharmacological studies, it was found that *P. juliflora* is used as an astringent, in rheumatism and as remedies against scorpion stings and snakes bite [10]. The plant is also a rich source of phytoconstituents, especially alkaloids, saponins and flavonoids. The pharmacological and biological activities signify the importance of this plant as a possible candidate for deriving phytomedicines [11].

2. Botanical information

Table 1 Taxonomical classification.

Kingdom	**Plantae**
Phylum	Angiosperms
Class	Dicot
Order	Fabales
Family	Leguminosae
Subfamily	Mimosoideae
Genus	*Prosopis*
Species	*Juliflora*

2.1. Synonym

Mimosa juliflora, Prosopis pallida, Prosopis inermis, Prosopis horrida [1].

2.2. Common Name

Honey Mesquite and Mesquite [12].

2.3. Geographical source

P. juliflora is a preserving and bionomic tree species found in semi-arid and arid places in the world. In India, it occurs throughout the area from Punjab to Tamil Nadu and from Gujrat to the dried region of Orissa. On earth, different species of *Prosopis* are found with differences in their physical, chemical and physiological properties. The states in India where this species mainly occur are: Andhra Pradesh, Karnataka, Rajasthan, Madhya Pradesh, Haryana, Maharashtra, Rajasthan, Tamil Nadu, Uttar Pradesh and Orissa.

2.4. Vernacular Names

Hindi - Velayati babul, Velayati Babool, Velayati khejra; Gujrati - Gando baval; Marathi – Velayati kikar; Marwari - angrezi bavaliya; Kannada - Bellari jali; Tamil - Velikaruvel, Velimullu [13].

2.5. Morphology

P. juliflora is either in the form of tree or shrub of various sizes. It is mostly xerophilous, spiny, armed and aculeate. The glands are present at the joint of leaflets and pinne. The legume is straw-yellow or brown in colour (8-29 cm long, 9-17 mm wide, 4-8 mm thick) after drying and straight with apex which is curved inward and sometimes falcate, compressed, linear, stipulate, rectangular to subquadrate. Plant has spines that are 0.5-5 cm long, not on every part, solitary or paired [14,15].

2.5.1. Tree form and size

Tree size and form vary from species to species and also depend on genetic and environmental influences. *P. juliflora* normally reaches a maximum height of 12 m, but can also reach up to 20 m under favorable condition.

2.5.2. Seeds

They are epigeous in germination. The cotyledons are fleshy and are first seed leaves that also exist after the first true leaves have formed, they are green or pale green in colour [15].

2.5.3. Wood

The woods of *P. juliflora* are diffusely porous in its gross structure and are (bark) pale brown in colour when present in dried form. At microscopic level *P. juliflora* contain fibers (48%), vessels (18%), rays (18%) and axial parenchyma (16%) [13].

2.5.4. Leaves

They are bipinnate in nature and have nodes, petiole and rachis (5-20 cm) long. The leaves are medium to large, 10-20 cm long. Leaflets are 8-18 mm long, either elliptic-oblong, linear- oblong or ovate in shape, with pointed apex. Glands are sessile with an apical pore, cuculiform and they are present at the junction of pinnae or the junction of leaflets [14].

2.5.5. Flowers

Flowers are long, spike like inflorescence known as racemes and are cylindrical in shape. They are yellow to yellow-white in colour. Inflorescences (9.5-16.5 cm) equal in length to the leaves, or slightly longer or slightly shorter with 237-344 number of flowers. Flowers are sterile, actinomorphic, pentamerous and hermaphrodite in nature. Inflorescence contains various parts like calyx, corolla, pistils, petals, stamen and pedicel [15].

2.5.6. Fruit

This species also belongs to the Leguminosae family because of the arrangement of different parts of fruit. The fruit is an indehiscent legume and has incurved apex, with or without parallel margins. The edges of the fruit have no parallel margins with 16-28 cm length, 14-18 mm width and 6-10 mm thickness. The pods which we called fruit are green in colour when immature and yellow when they are fully mature in nature. They are flattened to subquadrate in section and acuminate and stipitate, compressed to sub-compressed and sub- moniliform.

2.5.7. Thorns

Axillary spines are present which are divergent and geminate. They are straight, uni or multimodal, solitary and paired on different or solitary and paired on the same branch. Trees vary in the size and number of thorns, which either are absent or present or not on all branches [16].

2.6. Physiochemical properties

Different parameters such as ash value, moisture content of *P. juliflora* are 6.1±1.36% in green pods, 7.3±1.88% in dry pods, 4.8±1.02 in leaves, 8.9±1.19 in bark and 61.3±5.44 in green pods, 26.3±4.09 in dry pods, 56.0±6.38 in leaves, 35.0±4.99 in bark respectively [17].

3. Traditional use

Prosopis genus is used in the old days, for various activities and has a lot of biological, agricultural, chemical and medicinal uses. People use it for medicinal purposes in rheumatism, as remedies against snake bite and scorpion stings. Also, powdered flowers mixed with sugar are used by pregnant women for safety purposes in various regions. *P. juliflora* is also active against *Neisseria gonorrhoeae* which was isolated from symptomatic patients so used to treat gonorrhea.

Other *Prosopis* species are also used as diuretic and treat ocular and hepatic problems [18]. *Prosopis Africana* (leaves, bark twigs, roots) is used to treat dermatitis, bronchitis, tooth decay, malaria, stomach cramps and dysentery. In some areas, it is also used to treat sore throat, tooth decay and heal wounds and cuts [19]. *Prosopis farcta* in Iran is used traditionally for treating cardiac pain and angina pectoris [20]. *Prosopis cineraria* is used for curing earache, leprosy, dyspepsia, leukoderma, asthma, dysentery etc. [21].

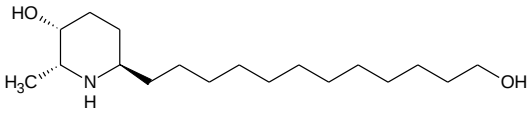
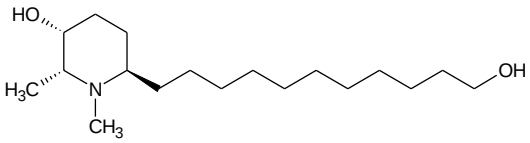
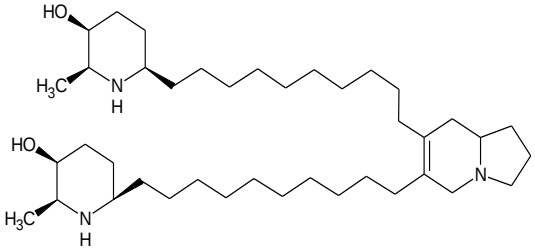
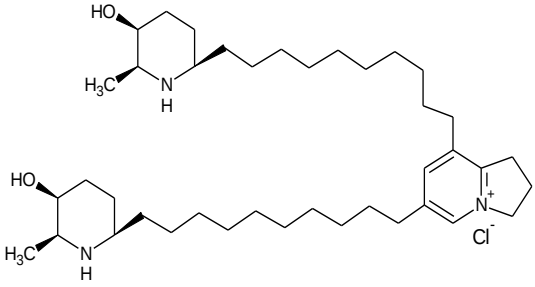
4. Phytochemistry

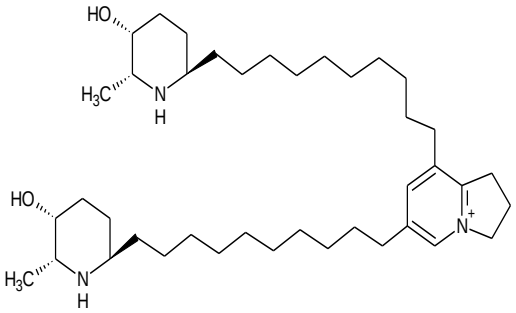
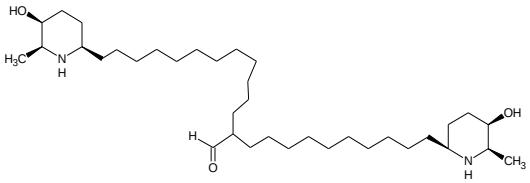
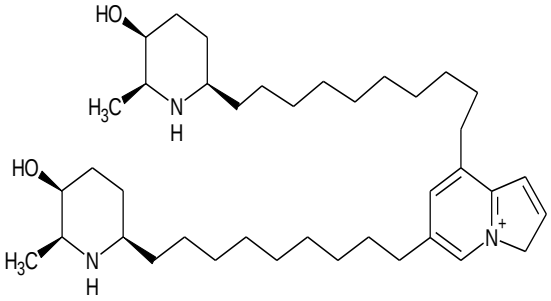
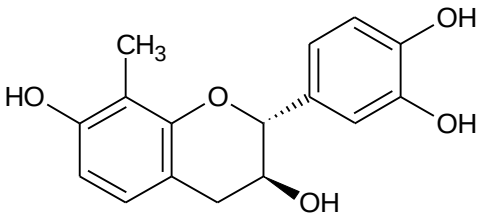
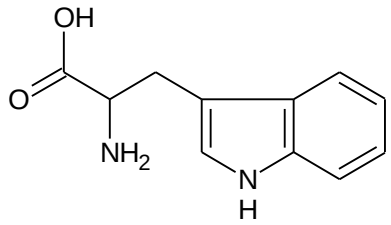
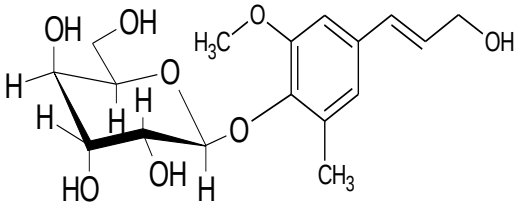
The air-dried leaves of *P. juliflora*, also known as Velayati Kikar were evaluated for phytoconstituents that are alkaloids, flavonoids, phenols, saponins and tannins [22]. Anti-bacterial, anticancer, anti-inflammatory and antiviral are some pharmacological activities shown only by alkaloids and saponin. *P. juliflora* or we can say it as mesquite, its different parts such as pods, flowers, leaves, stem and seeds contain a large class of metabolites. Pods and leaves contain a large amount of phytoconstituents as compared to other different parts of *P. juliflora* [3].

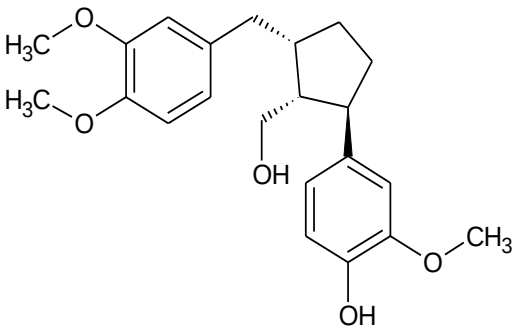
In the year 2012 Singh perform the phytochemical analysis on leaves, pod, flower, root and stem of *P. juliflora* and found the presence of various phytochemicals in varying concentrations in different parts. Phytochemical analysis revealed that the pods and leaf show the presence of alkaloids, steroids, terpenoids, flavonoids, tannins and phenolics. The flower extract shows the presence of alkaloids, steroids, terpenoids, flavonoids and phenolics. Also stem shows minimum concentration of compounds like phenolics, terpenes, flavonoids and steroids, while roots extracts show the presence of phenolics, tannins, flavonoids, steroids, alkaloids, terpenes and saponin. Phlobatannin and cardiac glycoside are absent in all parts of the plant, whereas saponin is only found in roots [23].

Extraction is the initial step of various phytochemical screening or for the isolation of phytoconstituents. Different solvents are used in increasing order of polarity for better extraction of all secondary metabolites i.e. petroleum ether, benzene, chloroform, ethyl-acetate, ethanol and water. Here, petroleum ether is least polar and water is most polar solvent [24].

Table 2 Chemical structure of various constituents in *Prosopis juliflora* with pharmacological activity

S. no.	Classification/ Compound	Compound	Biological activity	Ref.
1.	Alkaloid (Julifloridine)		Not specified	[25-26]
2.	N-methyl julifloridine		Not specified	[25-26]
3.	Juliprosopine		Anti-leishmanial Activity, Anti-dermatophytic activity, Antibacterial activity	[27-32]
4.	Juliprosine		Antibacterial agent, Antimalarial activity, Antifungal activity, DNA- binding activity	[31-33]

5.	Isojuliprosine		Antifungal activity	[27]
6.	Secojuliprosopinal		Plant growth inhibitor	[34]
7.	Juliprosinene		Antibacterial agent	[27]
8.	Flavanoid ((-)-Mesquitol)		Antioxidant	[35]
9.	Amino acid (L-tryptophan)		Plant growth inhibitor	[36]
10.	Glycoside (Syringin)		Plant growth inhibitor	[37]

11.	Enterolignan Precursor((-)-lariciresinol)		Plant growth inhibitor	[37]

The metabolites like shikimic acid metabolites ((-)-lariciresinol, phenylpropanoids) and piperidine alkaloids (secojuliprosopinal) from *P. juliflora* with allelopathic properties result from two major biosynthetic pathways i.e. shikimic acid pathway and acetic acid or polyketide metabolic pathway through the lysine amino acid pathway [38]. Leaves of *P. juliflora* contain a high number of alkaloids such as juliflorine, julifloricine, julifloridine, juliprosinene, juliprosine, juliprosopine and mesquitol24 and phenolic derivatives [39]. Some chemicals like syringin, (-)-lariciresinol, L-tryptophan, juliprosopine, juliprosine, and juliprosopinal are water soluble and released into its space through the leaves by rain water [40]. The chemical composition of all phytoconstituents and their concentration are not same in all parts but difference is noticed from parts to parts or organ to organ within the developmental cycle [41]. Bark of *P. juliflora* contains quercetin, 4,7-dimethylether, kaempferol 4-O-methylether, retusin, L-mannopyranoside which exhibit antifungal activity. It also contains 3-oxo-juliprosopine, secojuliprosopinal which shows anti-inflammatory activity. Different parts other than leaves and bark like pods, heartwood, flower, roots also contain some constituents which also have some biological activity [9].

Table 3 Plant metabolites (in gram) extracted by using various solvents from dry plant material [23].

Solvent → Plant part ↓	**Hexane**	**Chloroform**	**Acetone**	**Ethanol**	**Water**	**Total**
Leaf	1.31	2.85	0.96	5.63	4.97	15.72
Stem	0.82	1.51	0.68	3.08	2.48	7.92
Pod	1.05	2.23	0.72	5.55	5.84	15.30
Flower	0.95	2.62	0.77	5.04	4.30	13.68
Root	0.74	1.79	0.56	4.04	3.35	10.48

4.1. Wood

The woody biomass contains several constituents and can be classified into cellulose, hemicellulose, hemicellulose, lignin and extractives with levels 40-45%, 25-30%, 11-28% and 3-15% respectively [42].

4.2. Fruit

The pulp contains 56% of the total weight of the fruit. Sucrose (45%) is the very soluble constituent of pulp representing 90% of all soluble sugar present. Other reducing sugars also present that are glucose, fructose, inositol, raffinose and xylose etc [43,44].

4.3. Leaves

In leaves essential amino acid (AA) are maximum but low S-containing AA are present. Alkaloids, tannins, flavonoids, polyphenols and chemical constituents are also present. The constituents of the leaves can be classified into nitrogen free extract, basic extractives and mineral elements. Basic extractives present in the leaves are protein (26.3%), fiber (24.8%), extract (8.5%), ash (1.4%) and mineral elements such as micronutrients and macronutrients [45,46].

Table 4 Phytochemicals present in the extracts obtained from various parts of *P. juliflora* [23].

Plant parts → Phytochemicals ↓	Leaf	Pod	Flower	Stem	Root
Tannin	+	+	-	-	++
Phenolics	+++	+++	+++	+	++
Flavonoids	+++	++	+++	+	++
Cardiac glycosides	-	-	-	-	-
Alkaloids	++	+++	++	-	+
Terpenes	++	++	+	+	++
Steroids	+++	++	+	+	+
Saponin	-	-	-	-	+

"+" low concentration, "++" moderate concentration, "+++" high concentration, "- "absent

5. Pharmacological activity

P. juliflora showed antibacterial activity against strains of *E. coli, Staphylococcus aureus Klebsiella pneumoniae, Pseudomonas aeruginosa and Shigella sonnei* and other phytopathogenic agents [27]. Furthermore, investigated that Juliflorine possesses immuno- modulating activity when assayed in rabbits using Freund's complete adjuvant (FCA) containing Listeria hemolysin (antigen), administered intramuscularly in various concentration and dose dependent immune response was observed [47]. Choudhary *et al.,* demonstrated the acetylcholinesterase inhibitory potential in juliflorine alkaloid isolated from *P. juliflora* [48]. Also, pollen of juliflora species is an important source of flavonoids, which are considered as natural antioxidants [49]. The *in-vitro* antiplasmodial activity was studied in ethanolic extract of numerous south Indian medicinal plants against *Plasmodium falciparum* and found that flower, leaf and bark extracts of *P. juliflora* showed IC50 values of more than 100 µg/ml [50]. Due to its better antioxidant activity, it is also useful in controlling inflammatory diseases, cancer and diabetes [51].

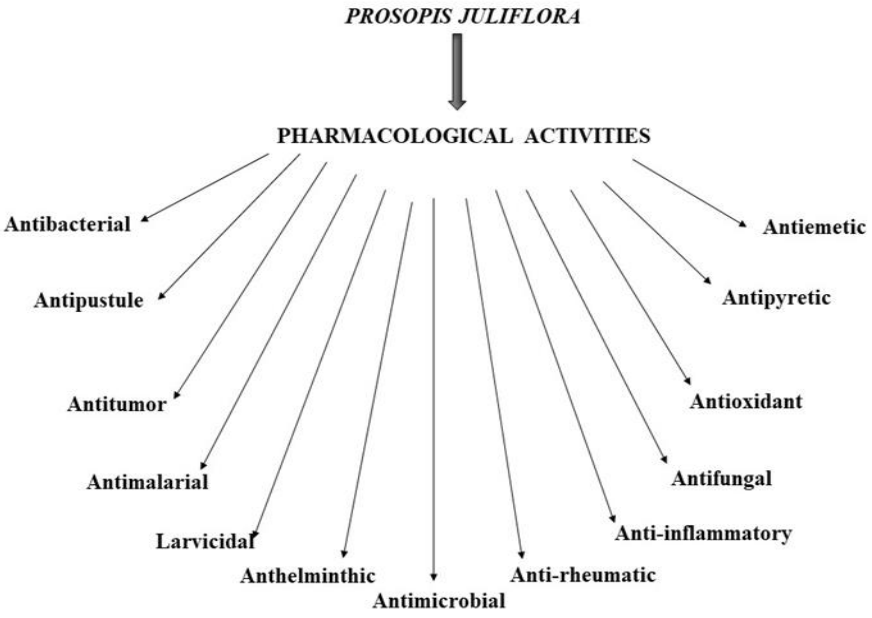


Figure 1 Pharmacological Activities of *P. juliflora*

5.1. Antibacterial activity

P. juliflora contains a large number of alkaloids in various parts that were tested for their antibacterial activity using disc diffusion technique on some gram-positive and gram-negative bacterial strains. The extract of leaves of *P. juliflora* showed better activity as compared to other plant parts. Klebsiella was found to more susceptible bacteria then Acinetobacter and Alcaligin [33]. Also, a dose-dependent inhibitory activitiy was observed in concentration range of 50 mg/ml to 300 mg/ml and results demonstrated that the extract showed good inhibitory activity against all the bacterial strains like *Pseudomonas aeruginosa, Escherichia coli, Staphylococcus epidermidis, Klebsiella pneumonia, M. luteus, S. aureus, Bacillus subtilis* and *Salmonella* typhimurium [52]. Similarly, well-diffusion test was carried out for *P. juliflora* methanolic extract on Gram-positive bacteria (*Staphylococcus aureus*, Bacillus sp. and Streptococcus sp.) and Gram-negative bacteria (*E. coli* and Klebsiella sp.) by Raghavendra *et al.* to study the inhibitory action of the extract on various bacteria. Widest zone of inhibition was showed by green leaves (22 and 19 mm zone of inhibition) as compared to dry leaves (22 and 19 mm zone of inhibition). The study findings concluded that gram-positive bacteria are more affected than gram-negative bacteria. Also, methanol extract of green leaves of *P. juliflora* was more effective as compared to dry leaves [24].

5.2. Antimalarial activity

Due to the development of resistance to some antimalarial drugs that are used to treat malaria and fever, numerous plants have been examined for *in-vitro* antiplasmodial activity which are used traditionally to treat malaria. According to a study by Simonsen *et al*., *P juliflora* ethanolic extracts from flower and fruit showed an IC50 value of 24 µg/ml and posses good antiplasmodial activity [53]. In another study, *in-vivo* antimalarial potential has also been evaluated in the formate salts of julifloridine and juliprosopine isolated *from P. juliflora* and compared with chloroquine. Juliprosopine was found to be more potent at 2 mg/kg as compared to chloroquine at 50 mg/kg [54].

5.3. Anti-tumor activity

Approximately 60 anticancer drugs were derived from different plants; mainly contain vinblastine, vincristine and vinorelbine which are sold in the market. Mani *et al*. studied *in vitro* anti-tumor potential in alkaloids present in leaves extract of *P. juliflora*. The extracts were assayed in different concentration (10 to 100 µg/ml) using MTT based cytotoxicity assay, which was done after 24, 48 and 72 hours exposure of T-cell leukemia (Molt-4) (1×106 cells/ml medium) and also assayed on mitogen-stimulated T-lymphocyte cultures derived from the venous blood of healthy volunteers. It was found that extract exhibits high toxicity towards the cancerous cells as compared to normal cells i.e. 72.65 % and 46.51 % cytotoxicity for cancerous and normal cells respectively. The study findings further demonstrated that cytotoxicity against T-cell leukemia depends on time and dose with a lack of genotoxicity [55].

5.4. Larvicidal activity

Yadav *et al.* evaluated extracts of different plants to facilitate the development of highly effective extract for mosquito control. Leaves of *P. juliflora*, *Malvastrum coromandelianum, Vernonia cinerea* and *Hyptis suaveolens* were collected and evaluated for larvicidal activity in different solvents like methanol, isopropanol, dimethyl sulfoxide, acetone and water. *Vernonia cinerea* in acetone showed maximum activity followed by *P. juliflora* in methanolic solution [56]. Also, in another study, acetone extract of *Vernonia cinerea* and isopropanol extract of *Callistemon viminalis* were found to be most effective against *Aedes albopictus* larva with LC50 value of 64.5 ppm 71.34 ppm respectively. *P. juliflora* acetone extract was also found to be effective oviposition-deterrent for the control of *Aedes albopictus* mosquito at 100 ppm [57].

5.5. Anthelmintic activity

A lot of animals in tropical regions are died due to nematode infection and synthetic anthelmintics are not capable of curing the infection. *P. juliflora* is a plant which is easily available in harsh environmental conditions and is fast growing and drought resistant. In the year 2011, Rechab *et al.* demonstrated anthelmintic activity in the ethanolic extract of both leaf and root of *P. juliflora* and further compared with standard drug Albendazole. Results showed that the ethanolic extract of leaves is more effective in anthelmintic activity than the roots extract whereas equally effective when compared with synthetic drug Albendazole. The presence of saponins, condensed tannins and alkaloids in the extract are the main causes of anthelmintic activity. Thus, these phytoconstituents can be a favorable source for veterinary drug development to cure nematode infection [58].

5.6. Antifungal activity

Antifungal potential in *P. juliflora* was investigated by Raghavendra *et al.* using poisoned food technique against fungus *Alternaria alternata* (cause brown spot of tobacco) in different solvents (petroleum ether, chloroform, benzene, ethanol,

methanol and aqueous). Methanol and ethanol extracts showed maximum antifungal property among all other solvent extracts. For isolation of alkaloids, methanol extract was further fractionated and compared with synthetic fungicides (blitox, captan, dithane M-45 and thiram) for antifungal activity at a minimum inhibitory concentration of 1000 ppm. The alkaloid extract at 1000 ppm showed better fungicidal activity and was effective at a low dose as compared to synthetic fungicides [59]. Dale, in his work studied that *P. juliflora* contain a majority of alkaloids with various biological activities that was active against a wide range of seed- borne fungi. Alkaloid extract of *P. juliflora* was amended with all the chemical fungicides at 1.5 g/L and 1 g/L. The combination of chemical fungicides amended with alkaloid extract showed highly significant antifungal activity compared to chemical fungicides tested alone at the particular dosage. Finally, the result recommended that the extract reduce the dose of chemical fungicides and increase the inhibition of seed mycoflora efficiently [60].

5.7. Antimicrobial activity

P. juliflora crude extracts, alkaloid-enriched fraction and isolated alkaloid was explained by dos santos *et al.* that was evaluated for antimicrobial potential by in-vitro methods. In 1999, Satish *et al.* described the potential use to combat microorganisms in crop plants and Caceres *et al.,* studied the treatment of gonorrhea by using tincture of *P. juliflora.* For that plant material was macerated in 50% alcohol and the tincture tested for in-vitro activity by measuring the inhibition zone. The leaf extract or tincture showed 9.6 mm of inhibition which was maximum and most active against *Neisseria gonorrhoeae* (Isolated from symptomatic patient) [61]. Besides the studies on microorganisms that affect humans, Satish et al. found that antibacterial property was only found in the aqueous extracts of *P. juliflora, Lawsonia inermis and Oxalis corniculata*. *P. juliflora* leaves have antibacterial activity against various Xanthomonas sp. (inhibition zone of 18-23 mm) comparable to bacterimycin and streptocycline and manage diseases in several crops [62]. In 2013, dos santos et al. described in-vitro antimicrobial activity to evaluate pods of *P. juliflora* as feed additives for ruminants which contain alkaloid enriched fraction for study. Chloroform extract of *P. juliflora* pods contains alkaloids which have in-vitro antimicrobial activity against *Micrococcus luteus* (MIC = 25 µg/ml), *Staphylococcus aureus* (MIC = 50 µg/ml) and *Streptococcus mutans* (MIC = 50 µg/ ml) and gas production have been evaluated with monensin as the positive control. The results showed that extract produces less gas during fermentation in ruminants as compared to monensin [32].

5.8. Antioxidant activity

It is observed that flavonoids and phenolic compounds are significantly important for describing antioxidant properties of various plant pollens. The compounds with phenolic hydroxy group have antioxidant property specially, the compounds with dihydroxy at 30th and 40th position of the B ring of flavonoid compounds [63]. *P. juliflora* honeybee collected pollen has higher antioxidant properties than *Amaranthus hybridus* pollen [64]. Antioxidant activity was seen by Prasad *et al.* in aqueous leaf extract of *P. juliflora* using rat liver enzymes. It was found that when the rats are fed-up with 5% aqueous extract, it showed protective activity against hepatotoxicity induced by *S.* aureus [65]. Furthermore, Sirmah *et al.* did an experiment to check whether *P. juliflora* extract (heartwood) could be used as a source of antioxidant compounds for food, cosmetics or for pharmaceutical application. Results concluded that presence of flavonoids (4-O-methyl-gallocatechin) and (-)-mesquitol as the main secondary metabolite in *P. juliflora* extract are a good source of anioxidant compound [35].

5.9. Antipyretic activity

Ethanolic extract *of P. juliflora* reveals the presence of major phytoconstituents like flavonoids, alkaloids, anthraquinones, quinines, tannins, Leucoanthocyanidin, and Ellagic acid glycosides, were tested for brewer's yeast induced hyperthermia in rats. The extract has been explored as potential and effective antipyretic activity at different tested dose level. Gopinath *et al.* utilized the extract of *P. juliflora* in two concentrations i.e. 250 and 300 mg/kg p.o. to study antipyretic action of *P. juliflora* and compared them with standard paracetamol (150 mg/kg p.o. in WFI). Rectal temperature was noted at 2,3,4 hours intervals and significant decrease in rectal temperature was observed indicating antipyretic poetical of *P. juliflora* [66].

5.10. Antiemetic activity

Ul Hasan *et al.* studied methanolic extract of leaves of *P. juliflora* and extract of some other plants (*Adenanthera pavonina, Peltophorum roxburghii, Prosopis cineraria)* for antiemetic activity and compared with chlorpromazine. Copper sulphate (50 mg/kg, p.o) was used as an emesis inducer in male chicks of four days age. The result was concluded by calculating mean decrease in number of retching in control, test and standard group. The decrease in emesis due to extracts of various plants (*Adenanthera pavonina, Peltophorum roxburghii, Prosopis cineraria and P. juliflora*) was compared with controls and the standard and it was found that among all extracts, *P. juliflora* showed maximum antiemetic activity of 76.64% and minimum by chlorpromazine that reduced retches by 32.71% [67].

5.11. Antipustule activity

Pimple eradication is the hot core and important task for research in the cosmetic sector. They occur due to growth of Staphylococcus species whose biomass swells and develops as a pimple. Acetone extract of *P. juliflora* have anti-pustule activity which inhibit staphylococcus sp. that was explained by using well diffusion method. Rajadurai et al., found the minimum inhibitory concentration of acetone extract of *P. juliflora* and it was 0.75 mg/ml. FTIR was done to confirm the functional group and growth curve analysis was done for the determination of inhibitory action of acetone extract. The extract when used with synthetic creams increase the anti-pustule activity because with the extract the activity was increased and chances of skin blackening, itching of skin and damage of tissue due to synthetic creams are decreased [68].

5.12. Antigiardial and Amoebicidal activity

Giardiasis is caused due to parasitic gastro-intestinal diseases and affected 200 million people globally. *Giardia lamblia* is considered as one of the main causatives means of diarrhoea in both children and adults. Leaves of *P. juliflora* that are extracted (Petroleum ether and methanol) were taken and tests were performed at different concentrations. The highest effective concentration of *P. juliflora* petroleum ether extract against *Giardia lamblia* was 1000 ppm with mortality of 78.91% after 72 hours and the same extract show lowest antigiardial activity in 24 hours with 1000 ppm concentration have mortality rate of 38.55 %. While 312.5 ppm of metronidazole was given 83.42% mortality after 72 hours. After malaria and schistosomiasis, *Entamoeba histolytica* stood at third position in the world in causing lethal infection. Although it is asymptomatic in nearly 90% of cases, the symptoms of amoebiasis are hemorrhagic colitis and amoebic liver abscess which affect 50 million people all over the world. The highest effective concentration of *P. juliflora* methanol extract against *Entamoeba histolytica* was 1000 ppm with mortality of 71.97% after 72 hours. While 125 ppm concentration in petroleum ether extract is the lowest antiamoebic concentration with 31.88 % mortality in 24 hours. Also, 312.5 ppm of metronidazole gave 78.01% mortality after 72 hours. It has been concluded by Garbi *et al.,* that the petroleum extract of *P. juliflora* leaves in both cases was better than the metronidazole which has been demonstrated to have side effects [69].

5.13. Cholinesterase inhibitory activity

Choudhary *et al.* investigated that *P. juliflora* contains alkaloids such as juliflorine which inhibit acetylcholinesterase and butyryl cholinesterase in non-competitive manner with IC50 value 0.42 and 0.12 µM and Ki values 0.4 and 0.1 µM respectively. It was also confirmed by molecular docking in which the alkaloid interacts with the active site of acetylcholinesterase and it also blocks calcium channels. It was confirmed by human neutrophils viability assay which make juliflorine as an interesting alkaloid for Alzheimer diseases. Juliflorine also showed dose dependent (30-500 µg/ml) spasmolytic and calcium channel blocking activity in isolated jejunum of rabbit [48].

5.14. Anti-inflammatory activity

The study was designed by Choudhary and Nagori, to phytochemically screen the anti-inflammatory potency of the ethanolic extract of *P. juliflora* leaves (100, 200 and 400 mg/kg) against carrageenan induced paw edema in rats. The phytochemical screening showed that flavonoids, saponins, carbohydrates, cardiac glycosides, tannins, and alkaloids are present in ethanolic extract of *P. juliflora* leaves. The oral median lethal dose (LD) of ethanolic extract was found to be 3807.9 mg/kg and > 5000 mg/kg in mice and rats respectively. The extract of *P. juliflora* shows highest activity at a dose of 400 mg/kg at which paw edema is attenuated. This study has been supported the traditional belief that *P. juliflora* used in the management of inflammations [70].

6. Toxicity studies

Toxicity refers to the harmful interaction between chemicals and biological systems. A toxicant is any substance that has harmful effects on a living system. *P. juliflora* or mesquite or algarroba parts are used by both animals as well as by human beings due to their beneficial effects. But sometimes due to consumption, intoxication is seen in animals, mainly in ruminant animals (in USA, Peru, Brazil). Mesquite is a very common plant in dry areas and easily available but the reports showed that it also causes animal poisoning due to the consumption of pods [71]. A disease known as "Cara-torta" is most common in the ruminant animals specially in goats and cattle. In this the lateral deviation of the head occurs due to cranial nerve dysfunction, degeneration and disappearance of neurons in the trigeminal motor nucleus which perform to keep food in the mouth during mastication. This disease occurs only in those animals which eat *P. juliflora* pods for 8 months or more [29,71]. Also, other clinical signs during rumination are seen like dysphagia, incoordination of chewing movements, atrophy, dysphagia and profuse salivation of the masseter muscle in animals, ruminal atony, anemia, submandibular edema and progressive weight loss [72]. All the symptoms result in degradation of brain flora like neuromuscular alteration, histologic lesions like spongiosis, gliosis, the loss of Nissl granules, fine

vacuolation of the perikaryon of neurons from trigeminal motor nuclei and finally which results in the degeneration and disappearance of neuronal cells in the trigeminal motor nucleus [72,73].

A toxicity study was performed by Silva et al. on *P. juliflora* plant which leads to the isolation, purification, identification of juliprosopina and juliprosinene from the mixture of alkaloids. The study shows that piperidine alkaloids show toxicity in laboratory animals because they act directly on neural cells causing intracellular impairments, principally to mitochondria. Neural cell cultures technique was used to understand the main cellular alterations seen in "cara torta" disease and the mechanism of action of piperidine alkaloids which is the main neurotoxic compound in *P. juliflora* leaves and pods. This study showed that autophagy shows protective mechanisms for neural cells against programmed cell death started by mitochondrial damage [74].

P. juliflora also induces glial cell activation, cytotoxicity and NO production and this was explained by using rat astrocyte culture medium. The culture was treated with the total alkaloid extract of *P. juliflora* leaves and its chromatographic fractions to understand the direct effect of these metabolites and the toxicity. LDH activity and MTT test was done to reveal that TAE and other alkaloids fractions in culture medium were cytotoxic to astrocytes or vice versa [75].

To understand neurotoxicity and mechanism of action of juliprosopine alkaloid in isolated mitochondria of rat, potential toxicity study of *P. juliflora* was done by Mailoi et al. evaluation of different concentration (5–25 μM) of extract revealed that juliprosine mostly affect the membrane potential of neuronal cells, stimulate respiration (10–25 μM) and also effect ATP production in high concentration (15 and 25 μM). The result explained that cell death, dysfunction of cell and neurotoxicity occur due to uncoupling of oxidative phosphorylation, which reduced ATP production in neuronal cells [76].

Mani et al., studied acute toxicity, in which animals were observed for toxicity for 72 hours by administering the *P. juliflora* extract orally at doses ranging from 50-500 mg/kg and there were no toxic symptoms seen below dose level of 200 mg/kg. Also, subacute toxicity study shows that there is no change in the parameters like hematological, biochemical, renal and liver function parameters when dose of 200 mg/kg were given for 30 days or more. All the parameters were same in experimental animals on 31st day when animals are sacrificed and blood and serum samples were analyzed for various biochemical parameters. These results showed that ethanolic extract of *P. juliflora* is nontoxic and the concentration was further used for long term in-vivo studies for various pharmacological activity [77].

7. Patents of *Prosopis juliflora*

S.No.	Patent number	Title	Date	Ref.
1	WO2019193109A1	Cosmetic composition comprising a polysaccharide, surfactants and fragments of one or more plants	10/10/2019	[78]
2	BR102012030155A2	Additive Based on alkaloid extract of mesquite pods (*Prosopis juliflora*) in feeds, using as ruminal fermentation modifier for the improvement of animal performance and mitigation of greenhouse gas emissions.	23/07/2013	[79]
3	BR102017006458-1 A2	Cosmetic compositions containing *Prosopis juliflora* extracts	30/10/2018	[80]
4	WO2007029271A2	Glutathione-s-transferase gene from *Prosopis juliflora* confers abiotic stress tolerance in plants	15/03/2007	[81]
5	WO2011009184A1	Use of *Prosopis juliflora* for producing a water- based, xanthan gum-like polysaccharide polymer	27/01/2011	[82]

6	US5,824,312	Sunscreen agents from natural sources	20/10/1998	[83]
7	BR 102016020554A2	Froze milk derivative using vegetable hemicellulose	02/05/2018	[84]
8	US 8,298,991 B2	Method for controlling undesired Mimosaceae vegetation	30/10/2012	[85]
9	4,849,337	Assaying allergen specific IgE levels with fluorogenic enzyme labeled antibody.	18/07/1989	[86]
10	US2898260A	Fiber board and process of making same from desert shrubs	04/08/1959	[87]
11	BRPI1107317A2	Food composition, nutritional bar, and food composition production process comprehending melipone pollen	12/12/2017	[88]
12	US 8,372,989 B2	Polypeptides and biosynthetic pathways for the production of Stereroisomers of monatin and its precursors	07/05/2013	[89]
13	US 2008/0138496 A1	Preparation of Smoke Extract	12/06/2008	[90]
14	WO 2009/021661 Al	Composition for the prophylaxis and treatment of osteoporosis	19/02/2009	[91]
15	WO 2012/112518 Al	Interfering RNAs that promote root growth	23/08/2012	[92]
16	BRPI1106864A2	Topical and oral photo-protective formulations containing Brazilian vegetable extracts and/or oils	19/07/2016	[93]

8. Conclusion

From the above review, it is concluded that *P. juliflora* contain various medicinal properties. It is used traditionally by people to complete their needs as mentioned in various literatures. *P. juliflora* has been proved to be effective as anthelmintic, antioxidant, antipyretic, cytotoxicity effect, antigiardial, amoebicidal, anti pustule activity and many more. It is versatile and widely applicable in the food, cosmetic, pharmaceutical, agricultural and renewable energy industries. It also provides benefit for the progress in several fields of science and technology. “Cara torta” is the diseases caused by excess eating of pods of *P. juliflora* is characterized by neuro-muscular alterations like emaciation, muscular atrophy of the masseter muscles, spongiosis, neuronal degeneration, and gliosis. Also, it was clear from literature that autophagy plays an important protective mechanism for neural cells against programmed cell death started by mitochondrial damage. The presence of bioactive metabolites in this plant can be used in development of new pharmaceuticals that address largely unmet therapeutic needs in our society.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest.

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