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## An overview of *Prosopis Juliflora's* pharmacologic aspects

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### Abstract

Throughout the globe, *Prosopis Juliflora* (*P. Juliflora*), sometimes known as Velayati babul or mesquite, is common, especially in dry and desert regions, is common, especially in dry and desert regions, a poisonous weed which is currently classified as invasive in various nations. The herb has anti-inflammatory properties, antibacterial, antifungal, anti-pustule, antimalarial, antitumor, antioxidant, larvicidal, anthelmintic, antimicrobial, and anti-rheumatic properties. Considering its many uses, it's a dangerous invading species that is carcinogenic in nature. Ingestion of pods of *P. Juliflora* causes a brain disorder known as "Cara-torta" in ruminant species such as goats, which impacts on the mitochondria of nerve cells.

**Keywords:** *Prosopis juliflora*, pharmacological activity, invasive weed, cytotoxic, cara-torta, ruminant animals

### 1. Introduction

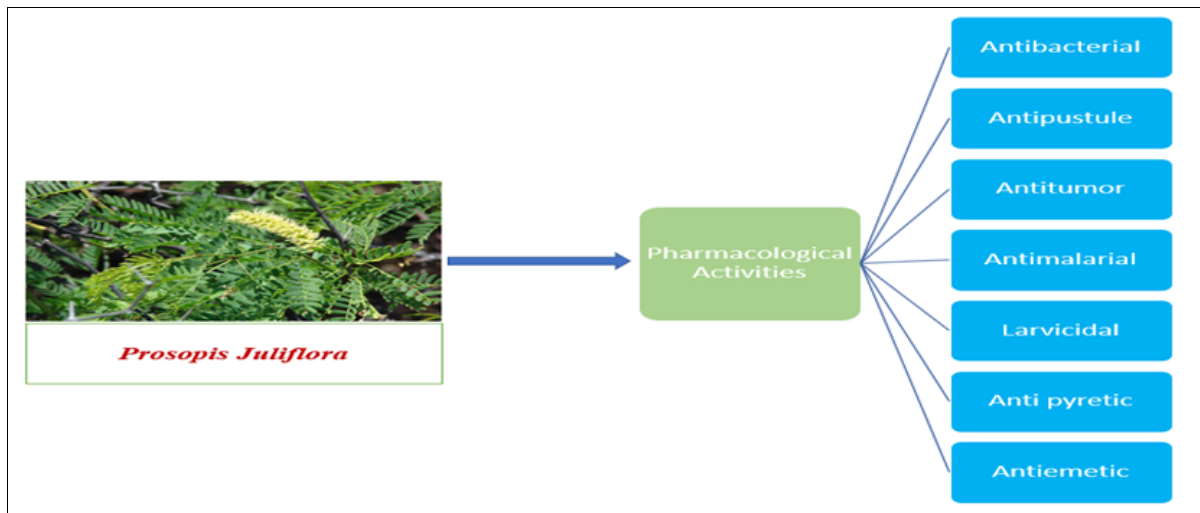
*Prosopis Juliflora* (*P. Juliflora*), a species of the Leguminosae family and the Mimosoideae subfamily, contains 44 species worldwide, constitutes the most prevalent widespread plants in India throughout the world [1, 2]. A number of investigations have shown that *P. Juliflora* has medicinal properties, and herbal extracts from different plant parts having antibacterial, antioxidant, anthelmintic properties, antimalarial, larvicidal, antiemetic, insecticidal, antitumor, and cholinesterase enzyme hindering action [3]. According to ethnopharmacological investigations, while using *P. Juliflora* as a remedy for scorpion stings and snake bites, an astringent and in arthritic conditions [4]. The species is also high in plant-based constituents including flavonoids, saponins and alkaloids. The toxicological and agricultural actions of this plant indicate its importance as possibilities for the production of botanical medicines [5].

### 2. Pharmacological impact

There was evidence of antibacterial activity in *P. Juliflora* against *Pseudomonas aeruginosa*, *E. coli*, *Klebsiella pneumoniae*, *Shigella sonnei*, *Staphylococcus aureus* and other phytopathogenic organisms [6, 7]. Moreover, Juliflorine was found to have immunomodulatory effect when tested employing Freund's complete adjuvant (FCA) containing *Listeria hemolysin* (antigen) in rabbits and delivered through the muscle in various concentrations [8]. It has been established that the acetylcholinesterase shows inhibitory effect of *P. Juliflora* from Juliflorine alkaloid [9]. Pollen from species of juliflora, good sources of flavonoids, the natural antioxidants [10]. *In vitro* antiplasmodial efficacy of various south Indian plants used as medicine against *Plasmodium falciparum* was examined in ethanolic extracts, and bark, leaf, and flower extracts of *P. Juliflora* revealed IC50 values of over one hundred g/ml [11]. It is also effective in treating inflammatory illnesses, cancer, and diabetes due to its higher antioxidant activity.

#### 2.1. Antibacterial activity

Using the method of disc diffusion, the large amount of alkaloids present in *P. Juliflora's* various parts were examined for their potential to have antibiotic impacts on both gram-negative and gram-positive bacterial strains.



**Fig 1:** Aspects of Pharmacological Activities of *P. Juliflora*

In comparison with various portions of the plant, *P. Juliflora* leaves' liquid extract showed greater activity. Klebsiella was discovered being the most vulnerable to Acinetobacter species and Alcaligin<sup>[12]</sup>. Likewise, a dose-related inhibiting activity was noticed in concentration in order range of 50mg/ml to 300mg/ml and the findings displayed beneficial inhibitory effects using the extract of leaf contradictory to each strains of bacteria such as Bacillus subtilis, M. luteus, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus epidermidis, Klebsiella pneumonia, Staphylococcus Aureus, Salmonella Typhimurium<sup>[13]</sup>. A well-diffusion test on Gram-negative bacteria (Klebsiella sp. Escherichia coli) & Gram-positive bacteria (*Streptococcus* sp., *Bacillus* sp., *Staphylococcus aureus*) was performed to have research the extract's inhibitory effect on various bacteria. Green leaves are having a wider region of inhibitory effect (22 and 19 mm zone of inhibitory effect) than dry leaves (22 and 19 mm zone of inhibitory effect)<sup>[14]</sup>. Resulting, gram-positive bacteria have been more damaged than gram-negative bacteria. In addition, extract of *P. Juliflora* green leaves using methanol as solvent was more successful than dried leaves<sup>[15]</sup>.

## 2.2. Antipustule activity

Eradication of pimples is a prominent topic and an important issue in cosmetic research. They occur because to the multiplication of Staphylococcus species, whose density expands and transforms into a pimple. The well diffusion method indicated that the anti-pustule effectiveness of *P. Juliflora* extract in acetone inhibits staphylococcus sp. *P. Juliflora* using acetone as solvent having minimal suppressive dosage measured was 0.75 milligram per milliliter. FTIR was employed in validating the functional group, and growth curve analyses were performed to verify the inhibitory impact of the acetone extract. Whenever combining with synthetic creams, the extract enhances anti-pustule action since its efficacy is raised and the possibilities of skin blackening, irritation, and tissue damage caused by synthetic creams are reduced<sup>[16]</sup>.

## 2.3. Anti-tumor activity

Roughly 60 anticancer medicines manufactured from various plants are presently found in market, with primarily vinblastine, vincristine, and vinorelbine. It is being investigated, the anti-tumor effects of alkaloids found in *P.*

*Juliflora*'s leaves extract *in vitro*. The herbal extracts were investigated in various concentrations (10 to 100 g/ml) via an MTT-based cellular toxicity assay after 24, 48, and seventy two hrs of being exposed to T-cell leukaemia (Molt-4) (1106 cells/ml medium) and also on mitogen-stimulated T-lymphocyte cultures obtained from healthy volunteers' venous blood. It was discovered that the substance used is highly hazardous to cancerous cells while comparing with normal cells, with 46.51% and 72.65% cytotoxicity for normal & cancerous cells, respectively. The outcomes of the investigation additionally indicated that cytotoxicity against T-cell leukaemia is time and dose dependent, without any genotoxicity<sup>[17]</sup>.

## 2.4 Antimalarial activity

Because of the disclosure of tolerance to various antimalarial medicines utilised for treating malaria and fever, numerous plants have been examined experimentally for antiplasmodial activity that were previously employed to heal malaria. It has been recorded that extracts of *P. Juliflora* containing ethanol from fruit and flower had an IC50 value of 24 g/ml and have significant antiplasmodial activity<sup>[18]</sup>. Another investigation assessed the *in-vivo* antimalarial activities of the formate salts of juliprosopine and julifloridine isolated from *P. Juliflora* to chloroquine. Juliprosopine was discovered to be the most effective at 2mg/kg than chloroquine at 50mg/kg<sup>[19]</sup>.

## 2.5. Larvicidal activity

An investigation performed using tested extracts from various trees resulting in generating an extremely successful extract for prevention of mosquitoes. *Hyptis suaveolen*, *Malvastrum coromandelianum*, *P. Juliflora*, and *Vernonia cinerea* leaves were gathered and tested for larvicidal effectiveness in isopropanol, dimethyl sulfoxide, acetone, methanol, and water. *Vernonia cinerea* had the highest growth rate in acetone, followed by *P. Juliflora* in methanol<sup>[20]</sup>. A further investigation indicated that isopropanol extracts of *Callistemon viminalis* and *Vernonia cinerea* extract using acetone as solvent and were the most successful over *Aedes albopictus* larva, having LC50 values of 64.5 ppm and 71.34 ppm, respectively. Extract of *P. Juliflora* containing acetone as solvent has been displayed being an efficient oviposition-deterrent for prevention of *Aedes albopictus* mosquitos over 100 ppm<sup>[21]</sup>.

## 2.6. Antipyretic activity

Brewer's yeast-induced hyperthermia employed with mice was experimented using an extract made from ethanol of *P. Juliflora*, which showed the existence of important phytoconstituents like alkaloids, flavonoids, anthraquinones, tannins, quines Leucoanthocyanidin, and ellagic acid glycosides. At various examined dose levels, the extract's medicinal potential and useful antipyretic action has been investigated. To evaluate *P. Juliflora*'s antipyretic activity, comparison between two extract at two concentrations, 250 & 300 milligram per kilogram per oral, was done contrasting with normal paracetamol (150 milligram per kilogram per oral in WFI). The temperature of rectum had monitored every one hour upto 4 hours starting from 2 hours, and a significant drop in rectum temperature had seen, demonstrating *P. Juliflora*'s antipyretic properties.

## 2.7. Antiemetic activity

The antiemetic activity of *P. Juliflora* leaves extract using methanol as solvent & extracts of other plants (*Peltophorum roxburghii*, *Adenantha pavonina*, *Prosopis cineraria*) were examined against chlorpromazine. Copper sulphate (50 milligram per kilogram per oral) had utilised to produce emesis in four-day-old male chicks. The conclusion was reached by analysing the average reduction in some of grumbling in the test, control, and standard groups. The reducing effect of emesis caused by extracts of various plants (*Prosopis cineraria*, *Adenantha pavonina*, *P. Juliflora*, *Peltophorum roxburghii*.) was compared between the standard and controls, & that was discovered that *P. Juliflora* had the highest antiemesis activity, i.e., 76.64% and the lowest by chlorpromazine, reduction of retches by 32.71 percent.

## 2.8. Antifungal activity

*P. Juliflora*'s antifungal activity has been examined in several solvents such as chloroform, methanol, aqueous solvent, benzene, petroleum ether, and ethanol over the fungus *Alternaria alternata* (cause of brown stain of tobacco). Amongst every solvent extracts, methanolic & ethanolic extracts demonstrated the greatest antifungal activity [22]. Extract of methanol was extensively fragmented and tested for antifungal activity over fungicides those are synthetic nature (dithane M-45, blitoxnd, thiram, and captan,) at a minimal inhibitory concentration of hundred parts per million. When contrasted with synthetic fungicides, the alkaloid extract demonstrated superior fungicidal activity at hundred parts per million and was efficacious at low doses. It is being observed that the *P. Juliflora* has alkaloids in a huge number with distinct biological functions that are effective over an extensive variety of seed-borne fungus. At 1.5g/L and 1g/L concentrations, all the chemical-based fungicides mixed with the *P. Juliflora* alkaloid extract. While contrasting with the fungicide chemicals that were evaluated individually at same dose, a combining fungicides altered with alkaloidal extract demonstrated significantly substantial antifungal efficacy. Finally, resulting the extract minimise the quantity of synthetic fungicides while effectively inhibiting seed mycoflora [23].

## 2.9. Antimicrobial activity

Evaluation was done by using *P. Juliflora*'s crude extract, alkaloids-enriched fraction, and extracted alkaloids were

tested for the antibacterial properties using *in-vitro* methods. It is having possible application to battle microbes in agricultural plants and in treating gonorrhoea using *P. Juliflora* tincture has been explored. Maceration of the extract of the plant had been done with 50% alcohol for that purpose, and the tincture was examined for *in-vitro* activity through determining the area of inhibition. The tincture or leaf extract inhibited *Neisseria gonorrhoeae* (isolating from a sick patient) with a maximal and greatest inhibition of 9.6 mm [24]. Antibacterial property has been discovered using aqueous *P. Juliflora*, *Oxalis corniculata*, and *Lawsonia inermis* extracts, additionally investigations on microbes that affect individuals. *P. Juliflora* leaf exhibits antibacterial efficacy across a type of *Xanthomonas* species (inhibition zone of 18-23 mm), equivalent to bacterimycin and streptomycin, and are employed as treating infectious disease in a variety of crops [25]. In 2013, *in-vitro* antibacterial activities of the *P. Juliflora*'s pod was discovered as additives to feed for ruminants containing an alkaloid-enriched fraction. *P. Juliflora* pod chloroform extract includes alkaloids alongside *in vitro* antimicrobial activity contrary to *M. luteus* (MIC = 25 g/ml), *Staphylococcus aureus* (MIC = 50 g/ml), and *Streptococcus mutans* (MIC = 50 g/ml), & used as a positive standard, gas production has been considered with monensin. The outcomes determined that the less gas was created using the extract during ruminant ferment than monensin [26].

## 2.10. Antioxidant activity

It has been discovered that flavonoids and phenolic chemicals play a vital role in characterising the antioxidant activities of diverse plant pollens. Flavonoids containing phenolic hydroxy groups, particularly those possessing dihydroxy at the 30th and 40th positions of the B ring of elements that contains flavonoid, possess antioxidant properties [27]. Pollens gathered by *P. Juliflora* honeybees had better antioxidant qualities than pollen collected by *Amaranthus hybridus* [28]. *P. Juliflora*'s antioxidant activity has been discovered in leaf extract using aqueous solvents utilising rat liver enzymes. It was discovered that feeding rats 5% aqueous extract demonstrated protective activities over *S. aureus*-induced hepatotoxicity [29]. Likewise, an experimentation on *P. Juliflora* extract (heartwood) has been conducted which could be employed as an origin having antioxidant chemicals in cosmetics, food, or pharmaceuticals. The high range of (-)-mesquitol and flavonoids (4-Omethyl-gallocatechin) as the predominant secondary metabolite in extract of *P. Juliflora*, source of antioxidant substance, as per the results [30].

## 2.11. Anti-inflammatory activity

An investigation was planned to phytochemically test the anti-inflammatory activities of extracts of *P. Juliflora* leaf (100, 200, and 400mg/kg) using ethanol as solvent against carrageenan-induced paw edoema in rats. The phytochemical analysis revealed the extraction of *P. Juliflora* leaves using ethanol saponins, alkaloids, flavonoids, carbohydrates, tannins, and cardiac glycosides. In rats and mice, the oral mean lethal dosage (LD) of extracts using ethanol as solvent were documented to be 3807.9mg/kg and > 5000mg/kg, respectively. *P. Juliflora*'s extract having the greatest effectiveness with a dose of 400mg/kg, reduces paw edoema. This investigation backs up the conventional opinion that *P. Juliflora* is being useful

in the treating irritations [45].

### 2.12. Antigiardial and Amoebicidal activity

Giardiasis is a pathogenic gastro-intestinal infection that affects 200 million subjects worldwide. *Giardia lamblia* constitutes the most common causes of diarrhoea in adults and kids also. Leaf of *P. Juliflora* have been extracted using methanol & Petroleum ether as solvent and experiments were performed at various doses. At hundred parts per million, *P. Juliflora* petroleum ether extract displayed the greatest beneficial concentration over *Giardia lamblia*, having a mortality rate of 78.91 percent after seventy two hrs, & the identical extract displayed the least antiigiardial effectiveness after 24 hours, with a death rate of 38.55%. After 72 hours, while administering with 312.5 ppm metronidazole 83.42% of the patients died. *Entamoeba histolytica* was the third-highest fatal pathogen across the world, after malaria and schistosomiasis. Though approximately 90% of cases are unnoticed, the primary signs of amoebiasis are hemorrhagic colitis and amoebic liver abscess, which impact 50 million people across the world. The optimal conc. of *P. Juliflora* extract using methanol in turns of solvent over *Entamoeba histolytica* was thousand parts per million, with a 72-hour fatality rate of 71.97%. While the least antiamoebic conc. in extract using petroleum ether as solvent is 125 ppm, with 31.88% mortality in 24 hours. After completion of 72 hrs, additionally, 312.5 ppm metronidazole caused 78.01% mortality. It is being determined that *P. Juliflora* leaf extract using petroleum performed superior in both instances than metronidazole, which is being displayed to cause negative effects [32].

### 2.13. Cholinesterase inhibitory activity

With IC<sub>50</sub> concentrations of 0.42 and 0.12 M and KI concentrations of 0.4 and 0.1 M, it has been reported that *P. Juliflora* containing alkaloids like juliflorine which is having blocking activity in butyryl cholinesterase & acetylcholine esterase in a non-competitive manner. It was supported by molecular docking, which disclosed that the alkaloid interacts with the active site of acetylcholinesterase and disables calcium channels. Human neutrophil vitality assay supported it, making juliflorine a potential alkaloid for treating Alzheimer's disease. Juliflorine also demonstrated influencing by dose spasmolytic and calcium channel blocking action by isolating rabbit jejunum.

### 2.14. Anthelmintic activity

Many animals belonging to tropical areas passed away because of nematode, disease, and synthetic anthelmintics are incapable of healing the condition. *P. Juliflora* grows quickly and is tolerant of droughts, making it ideal for tough environments. In 2011, anthelmintic effect in an extract made with ethanol of each leaves & root of *P. Juliflora* is being displayed while contrasting it to the conventional treatment Albendazole. The outputs disclosed that the extract of leaf using ethanol is more efficient than the roots extract as anthelmintic action, but it is equally successful in comparison to the synthetic medicine Albendazole [33]. The main sources of anthelmintic effectiveness of extract are condensed tannins, saponins, and alkaloids. Resulting that, these plant-derived compounds might be an optimistic origin for veterinary pharmaceutical development to treat infection with nematodes [34].

### 3. Toxicity studies

Toxicity is termed as the damaging interactions of substances with biological systems. A toxicant is any material which has a negative impact on a living organism. Because of the beneficial effects that *P. Juliflora*, mesquite, and algarroba components are employed by individuals, & animals. However, poisoning is being reported in animals, mostly ruminant species (in US, Peru, and Brazil). Mesquite is a popular and readily accessible plant in dry locations, however reports reveal that it additionally leads to animal toxicity due to eating the pods [35]. The medical condition "Caratorta" is most prevalent in ruminant species such as goats and cattle. The medial deflection of the head develops as a outcome of cranial nerve degeneration, malfunction, & neuron absence in the trigeminal motor nucleus, which performs the role of keeping food in the mouth during mastication. This disease exclusively affects animals that have eaten *P. Juliflora* pods for minimum 8 months [36]. Other clinical indications noticed during rumination include dysphagia, incoordination of chewing movements, masseter muscle atrophy, dysphagia, and copious salivation in animals, ruminal atony, anaemia, submandibular edoema, and gradual weight loss [37]. All of the indications cause brain flora destruction such as neuromuscular modification, histologic tumours such as fine vacuolation of the perikaryon of neurons from trigeminal motor nuclei, gliosis, spongiosis, the loss of Nissl granules, & finally the deterioration and the vanishing of neuronal cells within the principal trigeminal nucleus [38].

A toxicity investigation was performed on the *P. Juliflora* plant, which terminated in the separation, extraction, and recognition of juliprosinene and juliprosopina using a combination of alkaloids. As the outcomes, piperidine alkaloids are harmful in animal studies as they impact immediately on neural cells, producing intracellular abnormalities, particularly to mitochondria. This neural cell culture method was employed to examine key cellular abnormalities exhibited with "cara torta" conditions along with the strategy of operation of the most valuable neurotoxic chemicals and piperidine alkaloids, found in *P. Juliflora* pods and leaves. This study found that autophagy that protects brain cells from programmable cell death caused by mitochondrial injury [39].

Using rat astrocyte culture medium, *P. Juliflora* also causes activation of glial cell, toxicity in cells, & NO production. To investigate the direct effect of those elements and their toxicity, the culture treating in a total alkaloid extract of leaf of *P. Juliflora* & its chromatographic fractions. Other alkaloid fractions and culture medium containing TAE were reported to be cytotoxic towards astrocytes using LDH activity and MTT tests [40].

A possible toxicity investigation regarding *P. Juliflora* was performed to be capable of better comprehend the neurotoxicity and mode of effectiveness of juliprosopine alkaloid by isolating rat mitochondria. The study of various conc. of extract (5-25 µm) demonstrated that juliprosine primarily affects the potential in the membrane of neuronal cells, stimulates respiratory (10-25 µm), and has an influence on ATP synthesis in high concentrations (15 and 25 µm) [41]. The outcomes disclosed that the cell mortality, cell malfunction, and neurodegeneration occur because of the oxidative phosphorylation uncoupling, which reduces ATP generation in neural cells [42]. Acute toxicities were investigated by administering orally the *P. Juliflora*

extraction at particular doses ranging between 50-500mg/kg for 72 hours, and no toxic effects were detected below the dose of two hundred milligram per kilogram. Furthermore, subacute toxicity study displayed, when a single dose of two hundred milligram per kilogram is administered upto 30 days or more, no alteration is there in variables such as biochemical, haematological, liver, and renal, function parameters. On the 31st day, once the animals had been killed and blood and serum samples were analysed for several biochemical variables, every parameters in the experimental animals were exactly the same <sup>[43]</sup>. These observations revealed that the ethanolic extraction of *P. Juliflora* is harmless, and its concentration was then used in for a long time in-vivo experiments for diverse pharmacological purposes <sup>[44]</sup>.

#### 4. Conclusion

*P. Juliflora* possesses a level of medicinal properties. It has been determined that, *P. Juliflora*, for being useful for a variety of conditions, including anthelmintic, antioxidant, antipyretic, cytotoxic, anti-angiogenic, amoebicidal, and antipustule activity. It also helps the technology development and science across a fixed range of fields. Overindulgence of *P. Juliflora* pod causes "cara torta" condition, which is distinguished by neuro-muscular irregularities such emaciation, muscular atrophy of the masseter muscles, spongiosis, neuronal degeneration, and gliosis. Additionally, research shows that autophagy is a required defence mechanism for brain cells against programmed cell death brought on by mitochondrial damage.

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#### 6. Conflict of Interest

The authors claim that there are no contested subsidies.

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