The Pharmacognostic profile and therapeutic potential of the wonder tree, Prosopis cineraria: A Review

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The 'king of the desert', commonly known as Khejri (*Prosopis cineraria)* grows predominantly in dry and arid regions, performs a vital role in preserving the ecosystem. All the parts of the plant are used for numerous medicinal purposes. Leaves of *P. cineraria,* commonly called as "Loong", are formed into paste and applied on blisters, boils, mouth ulcers in livestock[1]. *P. cineraria* (the king of desert) has an extensive deep-root system and it is often considered as an aridity-loving tree because it possesses an ability to withstand drought and adverse climatic conditions. Its tap root system can penetrate vertically to more than 20 m hence, *P. cineraria* is popularly referred to as the "wonder tree" [2].
It is a multipurpose tree owing to the fact that all the parts of *P. cineraria* are useful for medicinal purposes and hence, it is referred as "kalpvriksha" in the ancient literature of India [3]. *Prosopis cineraria* is an evergreen, small to moderate sized thorny tree. It has slender branches with conical thorns and dark-green coloured leaves which are bipinnately compound. This tree is a legume and has the ability to fix atmospheric nitrogen thereby, plays a remarkable role in enhancing soil fertility and promotes the growth of other surrounding trees[4].

1.1 DISTRIBUTION

The wonder tree, *Prosopis cineraria*, is predominantly found in arid areas of Indian subcontinent, including India, Iran, Afghanistan, Saudi Arabia, Pakistan, Oman, UAE and Yemen. In India, it is native to the several parts of Rajasthan, Uttar Pradesh, Gujarat, Haryana and Tamil Nadu [5].

1.2 TAXONOMIC CLASSIFICATION

Kingdom: Plantae
Order : Fables
Family: Fabaceae
Genus: Prosopis
Species : cineraria

VERNACULAR NAMES

Table 1.1: Representation of Vernacular names of *Prosopis cineraria.*

Arabic	Ghaf
Bengali	Shami
Gujarati	Khijado, Sumri, Semru, Sami, Karma
Hindi	Banni, Chonksa, Shami, Khejiri, Janti, Sangria, Jand, Chaunkra
Sanskrit	Jhind, Jhand
Tamil	Perumbay, Vanni, Jambu
Urdu	Jandi, Thand, Kandi

TRADE NAMES

Jand, kandi, khejri.

1.3 BOTANICAL DESCRIPTION

The experimental plant, *Prosopis cineraria*, has the following salient features [1,6-7].

- It is an evergreen tree.
- The bark of the tree is thick and rough gray with very deep fissures (Figure 2.6).
- The branches of the medicinal plant are slender, glabrous and with compressed, straight and scattered prickles of 3-4 cm length.
- Flowers of the plant are in the form of axillary spikes.
- The flowers posses yellow corolla and thereby, attract huge number of insects and various other wild bees.
- The tree has 'bipinnately compound leaves' which are alternate in their arrangement (Figure 2.6).
- The leaflets are in the pairs of 15–18, and they have oblong shape with an entire margin and the petiole is normally 0.5–4 cm long.
- The average size of the leaves of the tree is 2.5 cm (in length) and 1 cm (in breadth).
- The freshly procured leaves of the tree are usually green in colour, odourless and bitter in taste.

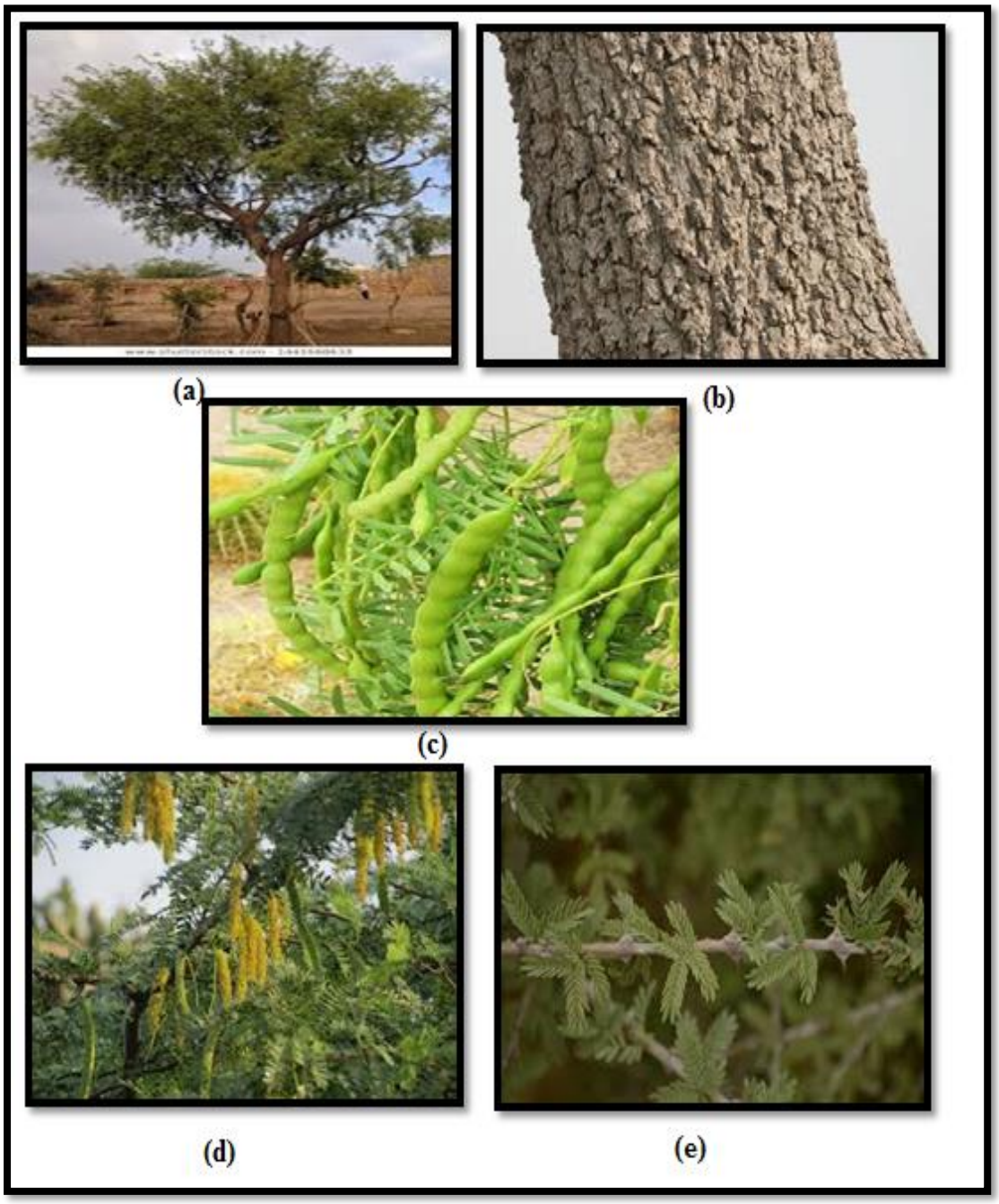

Figure 1.1: Different parts of *Prosopis cineraria* [The tree of *Prosopis cineraria* (a); Stem-Bark (b); Pods (c): Flowers (d); Leaves (e)].

1.4 PHYTOCHEMISTRY OF PROSOPIS CINERARIA: A POTENTIAL HERB

Prosopis cineraria is a store-house of numerous active chemical entities that possess nutritional value and play a pivotal role in the treatment of many serious diseases. Numerous chemical entities are present in several parts of the experimental

plant, *Prosopis cineraria* are mentioned below:

Table 1.2: Representation of phytochemicals derived from different parts of the plant.

Part of the Plant-*Prosopis cineraria*	Phytochemicals
Flowers	Patuletin glycoside patulitrin Sitosterol Spicigerine Prosogerin A and Prosogerin B (Flavone derivatives)[8-9]
Leaves	Steroids- campesterol, cholestrol, sitosterol and stigmasterol Actacosanol Piperidine alkaloid 'spicigerine' Hentriacontane Methyl docosanoate[10-11]
Seeds	Prosogerin C Prosogerin D Prosogerin E Gallic Acid Patuletin Patulitrin Luteolin Rutin[12-13]
Dried Pods	3-benzyl-2-hydroxy-urs-12-en-28-oic acid Maslinic acid 3-glucoside Linoleic acid Prosphylline[14]
Bark	Hexacosan-25-on-l –ol, a new keto alcohol along with ombuin and a triterpenoid glycoside Vitamin K1 n-octacosyl acetate-the long chain "aliphatic acid" Presence of glucose, rhamnose, sucrose and starch has also been reported[15]

1.5 THERAPEUTIC PROPERTIES OF 'THE WONDER TREE'

P. cineraria (the king of desert) has an extensive deep-root system and it is often considered as an aridity-loving tree because it possesses an ability to withstand drought and adverse climatic conditions. Its tap root system can penetrate vertically to more than 20 m hence, it is also popularly referred to as the "wonder tree" [16]. *Prosopis cineraria* has therapeutic importance and it is used for curing serious diseases and possess important activities like anti-fungal, anthelmintic, anti-cancer, anti-bacterial, anti-viral, anti-hyperglycaemic, anti-hyperlipidemic, anti-oxidative [17].

Flowers of *P. cineraria* are orally administered in order to prevent miscarriage. Bark of *P. cineraria*, has been utilized in the cure of various serious ailments such as asthma, leprosy, wandering of mind, fever, dyspepsia, dysentery, rheumatism, muscle tremors, bronchitis, piles, leucoderma [18-19]. Dried pods of the plant have a vital role in the treatment of protein calorie malnutrition (PCM) and deficiency of calcium and iron in blood [20]. The leaflets of the plant are rich in nutritive value and the smoke of leaves is considered as a remedy to cure eye-troubles [11].

Leaves of *P. cineraria*, commonly called as 'Loong', are formed into paste and applied on blisters, boils, mouth ulcers in livestock [1]. Phytochemical screening of the leaflets unravelled the presence of phenolic acid derivatives and hydrocarbons [11,21]. The studies carried out on the extracts of leaves of *P. cineraria* reported their antihyperglycemic, antihyperlipidemic and antioxidative potential [17]. The alkaloids present in the extracts of *P. cineraria* showed remarkable anti-bacterial potential against gram-positive and gram-negative bacterial species comparable to the commonly used antibiotics like penicillin, streptomycin and tetracycline [22]. The leaves of the plant were collected to study their prominent antimicrobial compounds. The research study highlighted the potential utilization of this plant leaves as antimicrobial agents. Dried leaves were extracted with aqueous ethanol. Antimicrobial activity tests were performed for the extracts and fractions obtained by preparative TLC. Tannins constitute the major compounds in the plant extracts. The leaves revealed the significant antimicrobial activity and highlighted its potential for the treatment of infectious diseases. The developed TLC solvent system may further be applied on column chromatographic separation of pure active compounds from *P. cineraria* [23].

In search of safe and effective therapeutic agents as an alternative to synthetic chemotherapeutics for the treatment of leukaemia, the research work was conducted to isolate and identify the active compounds from the leaves of *P. cineraria*. Dose and time-dependent cytotoxicity of the isolated compounds were studied against leukaemia cells and

their anticancer mechanism such as cell wall damage, nuclear damage, ROS and NO generation, SOD level, LDH release and lipid peroxidation were investigated. Based on anti-proliferative activity, the isolated phytocompound vitexin from *P. cineraria* could be developed as a natural drug for treating leukaemia [24].

The study demonstrated that an ethanol extract of *Prosopis cineraria* pods can reduce serum cholesterol when fed to hypercholesterolemic rabbits. The extract also reduced the level of atheromatous plague in the aorta. Notably, the extract can improve antioxidant enzyme activity and inhibits HMG-Co reductase activity. Therefore, the use of an ethanolic extract of *Prosopis cineraria* pods could be further investigated as an alternative therapeutic agent to statins and other drugs, but one that does not have adverse side effects for the treatment of cardiovascular diseases [25]. The studies conducted on the stem-bark demonstrated the antihyperglycemic, antihyperlipidemic and antioxidative properties [26]. It is also considered to possess laxative and abortifacient properties [18]. The bark of this plant provides relief in case of scorpion sting [27].

Anti-inflammatory activity has been exhibited by the water-soluble extract obtained from the residue of methanolic extract of *P. cineraria* [27,28]. Flowers have anti-diabetic potential and their powder is used to prevent miscarriage. Patulitrin, a cytotoxic principle has been isolated from the flowers of *P. cineraria* [8]. The gum of the tree is highly nutritive and used at the time of delivery by pregnant women. The pods of the plant are commonly known as 'sangar' or 'sangri' and have high nutritive value. Pods of *P. cineraria* are considered astringent by people of Punjab and they are highly nutritive hence, their consumption helps in curing mineral deficiency [20]. Studies conducted on the pods showed their 'LPO, COX-1 and COX-2' enzyme inhibitory activities [29].

The study was planned to explore the biological properties (antioxidant, antibacterial and lipoxygenase) and phytochemical investigation of extracts of stem, leaf and bark. Results showed that the plant has significant antioxidative potential and it is active against lipoxygenase enzyme. Antibacterial potential of the plant extracts was shown against- *Escherichia coli*, *Salmonella typhi*, *Pseudomonas aeroginosa*, *Bacillus subtilis*, *Staphylococcus aureus* and presence of various bio-active constituents like alkaloids, glycosides, flavonoids, saponins, tannins, steroids and terpenoids was detected [30]. The hydro-alcoholic extracts of plant parts like leaf and stem-bark of *P. cineraria* were investigated by trypan blue exclusion method and MTT assay to explore the cytotoxic effects against human cancer cell lines such as HeLa and MCF-7. Hence, it was postulated that the plant extracts of the plant possess potent anticancer activity [31].

` The extract (methanolic) obtained from the stem-bark of *P. cineraria* was evaluated for hepatoprotective activity and the study revealed that the extract rendered protection to the hepatic cells against carbon tetrachloride induced hepatotoxicity [32]. Numerous phytoconstituents like tannins, steroids, flavone derivatives (namely Prosogerin A, B, C & E), Rutin, Patulitrin, Luteolin, Patuletin, alkaloids etc. have been isolated from various parts of this medicinal plant [33]. Two new compounds methyl 5-tridecyloctadec-4-enoate and nonacosan-8-one, together with three known compounds (lupeol, β-sitosterol and stigmasterol) were isolated from chloroform fraction of *P. cineraria* stem bark. The chloroform fraction of stem bark was investigated in STZ-stimulated experimental diabetic rats, at doses of 50 and 100 mg/kg b.w. for 21 days. A marked reduction in blood glucose levels, glycosylated haemoglobin was observed, and it was also able to restore body weight, liver glycogen content and serum insulin level in diabetic rats, in a dose-dependent manner. Furthermore, a decrease in serum lipid profile and elevation in HDL after administration of the chloroform fraction was found, revealing that chloroform fraction has potential to protect from "diabetes-associated" complications [34].

1.6 PHARMACOLOGICAL ACTIVITIES OF *PROSOPIS CINERARIA*

1.6.1 Anti-bacterial Activity

Stem-bark extracts (aqueous and methanolic) of *Prosopis cineraria* exhibited antibacterial potential at 250 µg/ml in comparison with Ciprofloxacin (Standard at 100mg/ml) against eight bacterial strains- *Streptomyces griseus*, *Salmonella typhi*, *Bacillus subtilis*, *Bacillus Lintus*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Staphylococcus albus*, *Escherichia coli*. Significant potent action of methanolic extract of the plant has been analyzed against all pathogens. It was postulated that flavonoids and tannins contribute and render the antibacterial activity to *Prosopis cineraria*. Antimicrobial potential of different extracts of dried unripe pods of *P. cineraria* was investigated by using the method- Agar well diffusion. However, negligible activity was reported by petroleum ether extract [35].

1.6.2 Anti-hyperglycaemic Activity

Prosopis cineraria has significant capacity in lowering the levels of blood sugar. Numerous studies were investigated and on the basis of the research study it has been postulated that the reduction in body weight and elevation in blood sugar level in diabetic rats were normalized when the extract of *Prosopis cineraria* was administered. *Prosopis* extracts presumably restore the survival of the β cells of the islets of langerhans and thereby, blood sugar level is lowered down by generating an "insulinogenic effect." The reduction in body weight is prominently because of heightened glucose uptake in muscles which results in preventing tissue loss [36]. Hydro-alcoholic extract (50%) of *P. cineraria* stem bark was researched for its "anti-hyperglycaemic activity" by using Alloxan induced Hyperglycaemia Model. The research study was conducted by administering orally plant extract at the dose of 300 mg/kg body weight to hyperglycaemic mice once in a day for 45 days. It was reported that the fasting blood glucose level was lowered down by 27.3%, in comparison to that of standard glibenclamide which rendered 49.3% decline and the content of liver glycogen was significantly elevated in comparison to the control group. Loss of body weight in experimental mice was managed (significantly) in comparison to control group. Reduced concentration of non-enzymatic antioxidants and activity of antioxidant enzymes were also restored by drug administration, thereby, curing the oxidative damage in the cells of experimental animals and hence pointing out the anti-diabetic and antioxidant activity of the extract [26].

1.6.3 Analgesic Activity

Ethanol, ethyl-acetate, Petroleum ether extracts of stem bark were prepared (by soxhlet apparatus). Among the studied extracts-ethanolic extract was studied to possess significant analgesic activity when evaluated by using Eddy's hot plate model at a dosage of 300 mg/kg body weight in rats. Petroleum ether extract showed a significant antipyretic activity using Brewer's yeast induced hyperpyrexia model at same dose [37]. Analgesic activity of aqueous extract of leaves by using glacial acetic acid (GAA) induced writhing test model was investigated. The analgesic activity of the extract exhibited at a dose of 200 mg/kg body weight of Swiss albino mice was found to be significant in comparison to control. The leaf extract analyzed by using Brewer's yeast induced hyperpyrexia model demonstrated a significant antipyretic activity at the dose of 200 mg/kg body weight [38].

1.6.4 Anti-convulsant Activity

Prosopis cineraria stem bark was evaluated against maximal electro shock (MES) and Pentylenetetrazole (PTZ) induced convulsions in Swiss albino mice to study anticonvulsant activity. It was unravelled that the methanolic extract suppressed hind-limb tonic extensions (HLTE), those induced by MES and a protective effect in PTZ-induced seizures in a dosage dependent manner was exhibited. Methanolic extract of the wonder tree, *Prosopis cineraria*, at doses of 200 and 400 mg/kg and standard Phenytoin (25 mg/kg) have shown significant decline in duration of convulsions [39].

1.6.5 Anti-oxidant Activity

Elucidation of anti-oxidant activity of different extracts of the leaves of *Prosopis cineraria*, scavenging capability of the plant extracts for radicals like DPPH, hydrogen peroxide, hydroxyl, superoxide, nitric oxide and ABTS were performed. It was revealed that the leaves extract of *P. cineraria* which is a storehouse of numerous compounds that are capable of donating hydrogen to a free radical for the removal of odd electron which is detrimental for radical's reactivity. Six extracts of leaves of *P. cineraria* were analyzed and among them ethyl acetate and methanolic extracts showed maximum scavenging activity followed by chloroform and aqueous extracts [40].

1.6.6 Apoptotic Activity

Methanolic extract of the leaves of the wonder tree, *P. cineraria*, was analyzed in non cancerous cell line HBL 100 and breast cancer cell line MCF -7. Various staining techniques were adopted namely, ethidium bromide, Giemsa, Propidium iodide and Hoechst both in cancerous and noncancerous cell line. The plant extract rendered a steep elevation in apoptotic ratio in cancer cell line in contrast to HBL 100. This study unravelled that *P. cineraria* leaves possess the ability to inhibit the proliferation of MCF-7 breast cancer cells by involving apoptosis or programmed cell death. *P. cineraria* is a promising anti-cancer agent in treatment of cancer [41].

1.6.7 Anti-tumor Activity

Extract of leaves and bark (hydro-ethanolic) of *P. cineraria* were examined for anti-tumor activity against Ehrlich ascites carcinoma tumor model. Both the extracts of the plant at doses of 200 and 400 mg/kg body weight exhibited significant antitumor activity [42]. The extract (methanolic) of leaves of *P. cineraria* was investigated for ameliorative potential against *N*-nitrosodiethylamine (DEN, at dose of 200 mg/kg) induced experimental liver tumours developed in male Wistar rats. Treatment with DEN has elevated the lipid peroxidation (LPO) levels in mitochondria and weight of the liver which was reduced by the treatment of extract (200 and 400 mg/kg) in dose-dependent manner. Levels of CAT, SOD, GPx and GSH increased in comparison to animals having liver tumours. The study revealed that extract of *P. cineraria* may attribute its curative activity by modulating the levels of lipid peroxidation and activating antioxidant defence system [43].

1.7 PROSPECTIVE OF PHYTO-THERAPEUTIC APPLICATION OF *PROSOPIS CINERARIA*

In recent years it has been witnessed, that the research for drugs derived from plants has increased tremendously, due to the growing usage of plant-based medicines and their worldwide increasing popularity. The available research data on *Prosopis cineraria* provides sufficient experimental support for the clinical development of *P. cineraria*, a potential herb, as adjuvant therapy. Thus, given the literature reports, *Prosopis* has positive impact on the human diet and general health. In this sense, the present review provides an in-depth overview of the literature data regarding *Prosopis* plant's chemical composition, pharmacological and food applications, covering from pre-clinical data to upcoming clinical studies.

The analysis of the literature reports markedly highlights the promising beneficial health effects of *Prosopis cineraria*, given the advances reached with concerns to their biological activities. The multiple pre-clinical studies conducted so far clearly emphasize the use of *Prosopis* as a rich source of extremely useful phytochemicals, particularly phenolic compounds. In addition, clinical studies are extremely scarce to effectively support the pharmacological effects of *P. cineraria*. On the other hand, despite their traditional uses, toxicological reports available advice for more in-depth studies on this matter to improve the overall knowledge, safety windows, quality and widespread use of the plant. Thus, more in-depth pre-clinical studies are needed to further support and confirm the effective biological effects of *Prosopis* with scientific evidence.

P. cineraria successfully fulfil the criteria and can be considered for the development of plant-based medicines due to its potent therapeutic potential, and also its easy availability. Many researchers have attempted to draw the attention

towards this beneficial tree for the development of phytomedicines. The pharmacological activities of *P. cineraria* could be associated, towards a possibility of its incorporation into the present healthcare system.

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