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A review on *Pithecellobium dulce*: A potential medicinal tree

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Abstract
Pithecellobium dulce a plant of many uses which has versatile role in traditional system of medicine. Several studies are being conducted regarding the efficacy of whole plant or its parts for treatment of different diseases and aliments. The active compound of the plant includes flavonoids, sterols, tannins, triterpenoids etc. The health promoting properties due to the presence of proteins, carbohydrates, steroids etc. and diseases preventing properties such as antioxidant, antifungal, antiviral, antibacterial, anti-diabetic, diastolic, diuretic, anthlmintic effects antipyretic, anti-inflammatory, hypoglycemic and sedative activities which has been investigated and verified by modern scientific research. The various properties of therapeutic properties of *Pithecellobium dulce* have been discussed in the present paper.

Keywords: *Pithecellobium dulce*, therapeutic properties, anticonvulsant, cardio protective, antiulcerogenic.

Introduction
Pithecellobium dulce, native to the Pacific Coast and adjacent highlands of Mexico, Central America and Northern South America, is a small to medium sized, evergreen, spiny tree grows up to 18 m height and is cultivated throughout the plains of India and in the Andamans. The generic name refers to the curly pod that mimics an ape's earring (pithekosellobium) and the species name "dulce" refers to the sweet pod. *Pithecellobium dulce* is the only species among 100-200 species in the genus and has become widespread outside its origin (Duke *et al.*, 1981) [1]. The plant is well known for its edible fruits and they have been consumed for various ailments in a traditional manner. The fruits are linear, curved legumes (pods) that range in length from 10 to 13 cm. usually, single pod contains 10 seeds; pods are irregular in shape and flattened, set in spirals of 1 to 3 whorls and strangled between the seeds (lomentaceous). Seeds are black and shiny with 1 cm in diameter hanging in the pods by a red funicle. The pod is dehiscent on both sides (Orwa *et al*., 2009) [2].

Common names
- Arab : Showkat Madras
- Bengali : Dekhani babul
- Chinese : Niu ti dou
- English : Quamachil, Madras thorn, manila tamarind
- French : Campeche (New Caledonia), Cassie de Manille,
- German : Camambilarinde
- Greek : Pithekos ellobion
- Hindi : Vilayati babul, Vilayati imli, Jangle jalebi
- Japanese : Huamuche, Guamuche
- Javanese : Asem londo, Asam belanda
- Kannada : Seeme hunase
- Philippines : Camachile
- Sanskrit : Kodukkaapuli
- Spanish : Guamuchil, Guama americano, Quamachil
- Tamil : Kodukkaapuli
- Thai : Makham-khong,makham-tha
- Vietnamese : Me Keo, Keo Tay, Me nuoc, Gang Tay.


The chemical composition of *Pithecellobium dulce* is highly complex containing many basic biological active compounds. The different parts of the herb such as leaves, barks, fruits, seeds and root are known to posses therapeutic and have been used by traditional practitioners.

Ethnomedicinal uses: Various parts of *Pithecellobium dulce* are used for ethnomedicinal use

- **Leaves**: leaves of *P. dulce* extract mainly contain major components identified which include cyclitol, dulcitol, octacosanol, α-spinasterol, kaempferol-3-rhamnoside, quercetin and afzelin (Zapesochnaya *et al.*, 1980) [3]. The literature survey suggests that the leaves of the plant used traditionally for treating leprosy, intestinal disorders, peptic ulcer, and toothache, ear ache, emollient, abortifacient and larvicidal in folk medicines (Megala and Geetha, 2010) [4]. The leaves of *P. dulce* when applied as a plaster can allay pain of venereal sores and relieve convulsions and when taken with salt can cure indigestion, but can also produce abortion (Sunarjono and Coronel, 1991) [5].
- **Fruit**: Fruit of *Pithecellobium dulce* are rich with nutritional and medicinal value. The fruits are consumed as a food in many parts of India, because of its sweet taste and medicinal property. Phyto constituents analyzed for the fruits using gas chromatography and mass spectrometer revealed that the fruit contained ten compounds *viz*., (1) 2, 5, 6-trimethyl 1, 3-oxathiane, (2) trans-3-methyl-2-N-propylthiophane, (3) 2-carboxaldehyde-5-(hydroxymethyl), (4) D-pinitol, (5) heptacosanoic acid, (6) hexadecanoic acid, (7) tetracosanol, (8) 22-tricosenoic acid, (9) methyl-2-hydroxy icosanoate and (10) stigmasterol (Preethi and Saral, 2014) [6]. Traditionally the fruit was evidenced its use in treating gastrointestinal disorders such as peptic ulcer (Megala and Devaraju, 2015) [7].
- **Seeds**: Seeds of plant contains 13 free amino acids out of which 5 (valine, histidine, threonine, leucine) are essential amino acids varies from 0.46 to 4.69%. This seed protein is rich in amino acids tyrosine (4.7) and leucine (2.4) in mg/100 gm of defatted seed powder (Singhal, 2014) **[8]**. In the recent study has indicated that methanolic extract of *Pithecellobium dulce* seeds proved beneficial in the treatment of diabetes and associated complications. Hence, due to this reason traditionally it was used treat diabetics mellitus patients (Nagamothi *et al*., 2015) **[9]**.
- **Peel:** The fruit peel of the plant has been used for the control of diabetes by the local people of the northwest region of Tamil nadu, India. Some people chew raw fruit peel or drink its decoction in water to control blood sugar. But there is no scientific evidence. Researches, hitherto carried on the fruit peel, have reported only for its antibacterial, antioxidant and wound healing potential (Sukantha *et al*., 2011; 2014) **[10-11]**. But later, on isolation of secondary metabolites from *Pithecellobium dulce* fruit peel revealed that it contains stigmasterol, sitosterol, quercetin and pinitol which proved be the extract is viable drug target for diabetes mellitus (Sukantha *et al*., 2015) **[12]**.
- **Tree:** The *Pithecellobium dulce* tree, as a whole is reported to be active against venereal diseases, the decoction also being given as enema and studies revealed that the phytochemical analysis of crude extract of bark the contained alkaloids, anthraquinones, tannins, terpenoids and sterol exhibiting significant antimicrobial activity, and thus confirming the traditional therapeutic claims of this plant (Nehra *et al*., 2014) **[13]**. The bark of the plant is reported to be used as an astringent for dysentery, febrifuge and is useful in dermatitis, eye inflammation and posses antivenomous activity (Pithayanukul *et al*., 2005; Kumari, 2017) [14-15].
- **Roots:** Scientific studies on roots of the *Pithecellobium dulce* tree are limited but, traditionally the roots were used in treating dysentery. In Haiti, root and bark decoctions are taken orally against diarrhea and in Guiana, root bark used for dysentery and as febrifuge (Orwa *et al*., 2009; Kamatsile, 2014) **[2, 16]**.

Considering the above facts it is thought to be worthful to explore the possibility of beneficial effects and to review the therapeutic pharmacological actions of *Pithecellobium dulce*.

Therapeutically properties of *Pithecellobium dulce*

All parts of the *Pithecellobium dulce* elaborate a vast array of biologically active compounds and have been demonstrated to exhibit antidiabetic, locomotor, free radical scavenging, protease inhibitor, anti-inflammatory, anti-bacterial, anti-dysentery, anti-mycobacterial, anti-convulsant, anti-ulcer, anti-diarrheal, anti-fungal and anti-oxidative properties (Sukantha *et al*., 2011; Megala and Geetha, 2010; Manna *et al*., 2011; Mule *et al*., 2016) **[10, 4, 17-18]**.

Anti-inflammatory activities

Anti-inflammatory refers to the property of a substance or treatment that reduces inflammation or swelling. (Kalavani *et al*., 2016) **[19]** reported that the ethanloic extract of *Pithecellobium dulce* showed the presence of secondary metabolites such as alkaloids, flavonoids, glycosides, phenols, steroids, tannins, terpenoids and saponins had showed increase in response percentage of inhibition of protein denaturation and HRBC membrane stabilization when compared to the standard drug "Aspirin" of about 62.80 and 59.25% respectively. Ethanolic and aqueous leaf extracts of *P. dulce* were studied for its anti-inflammatory activity using carrageenan–induced paw edema in rats. Both extracts showed significant anti-inflammatory activity by lowering paw volume at the tested dose level. The aqueous extract showed more activity than the ethanol extract which was comparable to diclofenac sodium, a standard anti-inflammatory drug (Sugumaran *et al*., 2009) [20].

Antibacterial activities

Ethyl acetate of *Pithecellobium dulce* fruit peel was found to be effective against *S. epidermis*, *E. coli, K. pneumonia, S. aureus, E. faecalis, P. aeruginosa and P. putida*, while the methanolic extract was active against *K. pneumonia, S. aureus and P. putisda*. The aqueous extract was found to be effective against *K. pneumonia* and *S. aureus* only, while petroleum ether extract was active only against *P. Putida*. The results also indicated that the peel extracts, particularly the methanolic, ethyl acetate and aqueous extracts, exhibit the

ability to quench DPPH radical, suggesting that the extracts are good antioxidants with radical (Sukantha *et al*., 2011) [10]. The *P. dulce* pod pulp extract revealed that the effective inhibitory activity against Gram-positive bacteria, *Bacillus subtilis* and Gram negative bacteria, *Klebsiella pneumonia*. *B. subtilis* showed a larger diameter of clearance than that of other Gram positive bacteria. Similarly, extract showed a maximum zone of clearance in the Gram negative bacteria, *K. pneumoniae* than that of other Gram negative bacteria (Pradeepa *et al*., 2014) [21].

Antioxidant activities

Oxidative stress has been identified as the root cause of the development and progression of several diseases. Indeed plants containing secondary metabolites such as phenolic compounds have been reported to possess strong antioxidant activity of *P. dulce* leaf extract prepared in different solvents (acetone, methanol, and water) was evaluated for its antioxidant activity by analysis of phenolic content, FRAP, DPPH, and nitric oxide radical scavenging activity assays. The results showed that the presence of phenoic content (alkaloids, terpenoids, phlobatannins, coumarins, tannins, and flavoniods) in the extract but higher content was found in methonic extract. IC_{50} value for FRAP, DPPH, Nitric oxide radical scavenging assay for acetone (72.17, 13.70, 50.7), methanol (49.77, 74.89, 35.7) and water extract (91.5, 67.41, 81.80) were reported authenticating the antioxidant activities and antifungal activity (Kumari., 2017) [15]. Methanol and 70% acetone extracts of wood bark and leaves of *P. dulce* were evaluated for antioxidant activity nd results revelaved that the wood bark and leaves of the plant are the significant source of total antioxidant activity with good content of total phenolic and flavoind content. It is also found to be a good iron. Thus concluded that the plant might be helpful in preventing the progress of various oxidative stresses (Shankar, 2014) **[22]**.

Anti-diabetic activities

(Praveen *et al*., 2010) [23] studied that in alloxan treated rats, there was significant increase in blood glucose, cholesterol and triglyceride levels. Oral treatment with 200 mg/kg.b.wt and 400 mg/kg.b.wt of hydro alcoholic extract of bark of *Pithecellobium dulce* significantly reduced the blood glucose, cholesterol and triglyceride when compared to the standard glibenclamide. Hence the antidiabitc activity may be due to this presence of phytoconstituents like sterols, alkaloids, glycosides, saponins, tannins, carbohydrates, proteins, phenolic compounds and flavonoids in alcoholic extract of bark of *P. dulce*. Oral administration of *P. dulce* fruit extract (300 mg/kg b.w. /day) to diabetic rats for 30 days significantly reduced the levels of blood glucose, glycosylated hemoglobin, urea and creatinine. The altered levels of serum aminotransferases and alkaline phosphatase were normalized upon treatment with the fruit extract it also observed that the decrease in the levels of plasma protein, plasma insulin and hemoglobin in the diabetic rats were elevated to near normal. The level of glycogen content was improved upon treatment with the extract. Hence the results of the study showed that the fruit extract is nontoxic and possess anti-diabetic nature (Pradeepa *et al.,* 2013) [24].

Antimicrobial activities

The silver nano particles prepared biologically from the plant *Pithecellobium dulce* developed sensitivity against the microbial strains *E. coli, S. aureus, P. aeuruginosa* and *C. albicans* showed the highest sensitivity among the different concentrations used (Lakshmi *et al*., 2014) [25]. (Kumar *et al*., 2013) [26] studied antimicrobial activity of leaf of *P. dulce* against twenty pathogenic microorganisms. Leaf extracts of *P. dulce* were prepared in distilled water and organic solvents. Agar well diffusion technique was used to assess the antimicrobial activity of leaf extracts against five Gram-positive (*Bacillus subtilis, E. faecalis, M. luteus, S. aureus and S. epidermidis*), seven Gram-negative (*Aeromonas hydrophila, A. faecalis, E. aerogenes, E. coli, K. pneumoniae, P. aeruginosa and S. typhimurium*) bacteria and eight fungi (*A. flavus, A. niger, A. oryzae, A. terreus, A. alternata, Alternaria brasicola, A. solani and A. vitis*). The extracts showed variable inhibition zone (ranging between 7 to 27 mm) against most of the tested microbes. Solvent extracts were found to be more effective than the aqueous extract. The most susceptible microorganism was *E. faecalis* exhibiting a zone of inhibition of 27 mm. The lowest MIC values were obtained against *E. faecalis*, indicating the susceptibility of the strain for all the extracts. The results of the study indicated that the *P. dulce* extracts possess bioactive compounds having antimicrobial properties.

Anticonvulsant activities

Epilepsy is characterized by recurrence of seizures associated with loss or disturbance of consciousness, usually but not always with characteristic body movements (convulsion) and always correlated with abnormal and excessive electroencephalogram discharge. Anticonvulsant activity of the crude flavonoid fraction of the leaf of *P. dulce* (CFFPD) using the subcutaneous Pentylenetetrazole (PTZ) and Maximal electroshock test (MES) models in rats, the crude flavonoid fraction exhibited significant reduction in the duration of hindleg extension and onset of convulsion dose in both Maximal Electroshock Test and Pentylenetetrazole model (Divya and Babu, 2013) [27]. Ethanolic and aqueous leaf extract of *Pithecellobium dulce* were studied for its anticonvulsant activity using maximal electroshock-induced seizure (MES) in rats. Both extracts showed significant anticonvulsant activity by lowering the duration of extension phase at the tested dose level. The aqueous extract showed better result comparable to phenytoin sodium, a standard antiepileptic drug (Sugumaran *et al*., 2008) **[28-30]**.

Cardio protective activities

The cardio protective effect of ethanol and aqueous extract *Pithecellobium dulce* fruit in isoproterenol (ISO) induced biochemical and hista pathological changes using rats revealed that the ISO-induced rats showed a significant increase in the activities of marker enzymes such as serum glutamate pyruvate transaminase (SGOT), serum glutamate oxaloacetate transaminase (SGPT), cardiac marker enzymes such as creatine phosphokinase (CPK) and lactate dehydrogenase (LDH). Pretreated with aqueous and ethanolic extract of *P. dulce* fruit peel, positively altered the activities of marker enzymes and the biochemical parameters in ISO-induced rats (Thangrajan *et al.,* 2014) [31]. (Bhavani *et al.,* 2014) [32] reported that the aqueous extracts of *P. dulce* fruit and flower reverses the cardiac damage induced by (ISO) isoproterenol. When compared with the standard cardioprotective agent Verapamil, the plant extracts were nearly having same effects against myocardial infarction.

Antidiarrhoeal activites

(Sugumaran *et al.,* 2008) [30] studied the ethanolic and aqueous extract of leaves of *Pithecellobium dulce* for its antidiarrhoeal

activity using castor oil induced diarrhea model in wistar albino rats and reported that the extracts reduced the frequency and wetnesss of faeces when compared to control group. The aqueous extract showed more significant activity than the ethanol extract at the tested dose level. (Venu *et al*., 2016) [33] Evaluated the antidiarrhoeal effect of ethanol extract of *P. dulce* using castor oil induced diarrhea in rats and reported that the Loperamide, the standard antidiarrhoeal drug, was same in reducing the number of faeces by 70.94%, while *P. dulce* extract was found to be most effective, reducing diarrhoeal droppings by 70.90%. The extract significantly ($p<0.01$) reduced the wet faeces and total number of faeces, when compared to control group and concluded that the *P. dulce* had antidiarrhoeal activity in dose dependent manner.

Larvicidal and ovicidal activities

Larvicidal and ovicidal potential of the crude hexane, benzene, chloroform, ethyl acetate and methanol solvent extracts from the medicinal plant *Pithecellobium dulce* against filariasis vector mosquito, Culex quinquefasciatus studied and reported that the methanol extract of the leaves and seed of *P. dulce* was the most effective against the larvae with LC_{50} and LC_{90} values 164.12 mg/L, 214.29 mg/L, 289.34 mg/L and 410.18 mg/L being observed after 24 h of exposure. The efficacy of methanol was followed by that of the ethyl acetate, chloroform, benzene and hexane extracts. About 100% mortality was observed at 500 mg/L for leaf and 750 mg/L for seed methanol extracts of *P. dulce* (Marimuthu and Mohan, 2014) [34]. Similar results were observed against larvae of *An. stephensi* and *Ae. aegypti* and thus concluded that seed extracts of *P. dulce* have the potential to be used as an ideal eco-friendly approach for the control of mosquitoes (Govindrajan *et al*., 2013) [35].

Antiulcerogenic

Peptic ulcer disease (PUD) is a major chronic gastrointestinal disorder caused due to hypersecretion of gastric acid and pepsin. *Pithecellobium dulce* exerts exerted a proton pump inhibitor like activity. It was observed that the expression of MUC6 and MUC2 genes in the gastric and duodenal mucosa of the *P.dulce* pre-treated rats were significantly higher ($p<0.05$) in comparison with the disease models. It was also observed that the expression of these gastroprotective proteins is up regulated in the *P. dulce* pretreated animals and the effect is similar to that of the control animals. The western blot and densiometric analysis of the expression of H+, K+-ATPase β subunit in the gastric mucosa of the control, gastric ulcer model, drug control groups and drug pretreated animal groups of gastric ulcer model shows down regulated (Megala and Devaraju, 2015) [7].

Antifungal Activity

MIC against tested fungus, and extract was further fractionated by solvent-solvent fractionation and MIC was tested. MIC for *A. fumigatus* was 0.62 mg/ml and for *A. niger* was 1.25 mg/ml, and the results were comparable with effective synthetic drug Amphotericin B (Kumari, 2017) [15]. (Sawasdipuksa *et al*., 2011) [36] Isolated, purified and identified a lysozyme from *Pithecellobium dulce* seeds by using chromatography techniques and tandem mass spectrometry with Mascot database searching resulted that *P. dulce* lysozyme had molecular mass of 14.4 kDa, which is close to the molecular mass of chicken egg white lysozyme (14.3 kDa), with which it also shares a high degree of partial amino acid sequence similarity. Moreover, plant lysozyme showed the antifungal ability against *Macrophomina phaseolina* with a rather high thermal stability at up to 80 °C for 15 min (at pH=8.0).

Conclusion

Pithecellobium dulce has a strong potent in health promoting, disease preventing and life prolonging properties which has been described, investigated and verified by modern researchers. However, the intrinsically active compounds and the chemical responsible have been determined yet, and some mechanisms of the action of *P. Dulce* are still unknown. Thus, bioassay-guided isolation and identification of the bioactive components must be developed to reveal the structure-activity relationship of these active components. However more studies are required to explore the application of the plant for commercialization of active ingredients of biological and herbal medicine applications.

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