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Pharmacological potential of an underutilized legume *Pithecellobium dulce* (Roxb.) Benth.

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ABSTRACT: Indian subcontinent is full of plant diversity and these plants have immense food and medicinal values. Legume plants are mainly appreciated for their high content of proteins stored in seeds. The legumes are not only main source of vegetarian proteins but also possess diverse types of phytochemicals in different plant parts. These phytochemicals are important for pharmacological activities. *Pithecellobium dulce* is a legume plant that can thrive in harsh environment. Its fruits are edible and nutritious in nature. Different types of phytochemicals present in various plant parts make this plant pharmacologically important. The scientific literatures were searched in different search engines using different keywords and studied for the preparation of the manuscript. All plant parts viz. leaves, fruits, seeds, bark and roots have shown pharmacological activities. The antidiabetic, antioxidant, hepatoprotective, anticancer, anti-inflammatory, antihyperlipidemic activities etc. have been evaluated by researchers and found positive results. More planned studies are required for harnessing its full potential and to use this plant as a source of nutraceuticals.

KEYWORDS: Underutilized, nutraceuticals, pharmacological potential, therapeutic, legumes

I. INTRODUCTION

Legume plants are important source of nutraceutical biomolecules. They thrive well in diverse climates all over the world. Indian subcontinent has enormous biodiversity of legume plants due to presence of different climatic zones. Some of these legume plants are cultivated for food purposes but many wild and underutilized legume plants are also important because of their phytomolecules. These secondary phytomolecules provide immense therapeutic potential to the legume plants (Kapoor, 2015; Cornara et al., 2016).

Pithecellobium dulce (Roxb.) Benth. is a moderate sized tree legume that can grow in harsh environmental conditions. It belongs to family Fabaceae (Goyal et al., 2014). It has spines in its branches and crowded leaves are present on the branches. The flowering and fruiting time is from April to June. The fruit has characteristic coiling and the edible portion of fruits is aril. It is commonly known as *Jungle Jalebi* due to its characteristic fruits. The photographs of plants are presented in Figure-01. The present review tries to focus on the recent developments in the pharmacological research on this plant.

II. METHODOLOGY-

The scientific literatures were searched in search engines Google Scholar, Pubmed, Science Direct and ResearchGate by using keywords *Pithecellobium dulce*, antimicrobial, anticancer, antiinflammatory, hepatoprotective, antioxidants, Antiulcerative etc. The relevant literatures were studied during the preparation of the manuscript. The pharmacological activities are documented in Table-01

Antimicrobial Activity-

The *P. dulce* root extract in ethanol was found to be effective against both Gram positive and Gram-negative bacteria with zone of inhibition 19.0 mm against *Klebsiella pneumonia* and 11.0 mm against *Staphylococcus aureus* (Bhat et al., 2018). The extracts prepared from the leaves in benzene, chloroform, acetone and methanol solvent also

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showed potent antibacterial and antifungal activity with *Enterococcus faecalis* was found to be more susceptible towards all the extracts. The benzene and chloroform extracts represented better antimicrobial properties than acetone and methanol extracts (Kumar et al., 2013).

Anticancer / Antitumor-

Aqueous extract from the leaves of *P. dulce* demonstrated anticancer activity against breast cancer MCF-7 cell lines selectively in a concentration and time dependent manner. It upregulated expression of proapoptotic Bax, p21, p53, TNF and fas genes. At the same time the gene expression of Bcl-2 and NF-κB was downregulated by the extract (Sharma, 2016).

Antioxidant Activity-

The application of methanolic seed extract (250 and 500 mg/kg dose) improved the levels of antioxidant enzymes and relieved oxidative stress in hepatic and renal tissues of diabetic wistar rats (Nagmoti et al., 2015). The CCl_4 intoxication to Swiss albino mice resulted in increase of reactive oxygen species and a decrease in antioxidant enzyme activity in hepatic tissue. Application of aqueous fruit extract alleviated these pathophysiological conditions and played a protective role in pre and post treatment experiments (Manna et al., 2011). CCl_4 intoxication significantly increased cellular ROS in renal tissues and application of aqueous fruit extract decreased their production and enhanced activities of CAT, SOD, GST and GR, the antioxidant enzyme system. The quantitative phytochemical estimation revealed high amount of phenol (45.12± 1.08 mg/g), flavonoid (55.47± 1.57 mg/g) and saponin (72.81± 2.35 mg/g) (Pal et al., 2012). Three polysaccharide fractions were isolated from *P. dulce* fruits and evaluated for their antioxidant potential. All three fractions showed remarkably high antioxidant potential with fraction PDP-3 (IC_{50} 5.1µg/ ml) was found to be most effective. These three polysaccharide fractions were water soluble and can act as an adjuvant in drug delivery and development (Preethi and Mary, 2016). The seed extracts of *P. dulce* in water and methanol showed remarkable antioxidant potential in a concentration dependent manner. The methanolic extract was found to be more effective than aqueous extract probably due to presence of high amount of phenolic content (1.74 ± 0.0035 mg/g GAE) than aqueous extract (Nagmoti et al., 2012). Similarly, the bark from woods and leaves were also evaluated for antioxidant activity by using different types of *in vitro* assays. In DPPH assay, the 70% acetone extract of bark and leaves was more effective (IC_{50} 16.83± 0.38 and 18.30± 0.43 µg/ml respectively) than methanolic extract (IC_{50} 150.23± 2.8 for bark and 250.32± 4.8 for leaves) (Kalekhaye and Kale, 2012). Seed polysaccharides demonstrated free radical scavenging activity with IC_{50} value 0.16 mg/ml in DPPH assay (Bagchi and Kumar, 2016). The acidified methanolic extract from fruit pericarp also have free radical scavenging properties. It has high content of anthocyanins (32±0.3 mg/g) and total flavonoid (6.2±0.01 mg/g) (Ponmozhi et al., 2011).

Antidiabetic-

In wistar rat models, the prior administration of methanolic extracts from *P. dulce* seeds significantly inhibited elevation of blood glucose level in a concentration dependent manner. It also reduced fasting blood glucose levels in diabetic models when measured on 7, 14 and 21 days of experiment. The 250 and 500 mg/kg dose of seed extract elevated the serum insulin level in diabetic rats (Nagmoti et al., 2015). A saponin enriched extract obtained from seeds of the plant demonstrated inhibition of α-amylase and α-glucosidase, key enzymes in sugar metabolism. The IC_{50} value for α-amylase was 17.28±0.23 µg/ml and for α-glucosidase it was 5.12±0.15 µg/ml. The toxicological studies revealed safety of 2000 mg/kg dose in experimental mice (Kumar et al., 2017). The application of ethanolic fruit extract at a dose of 300 mg/kg/day to streptozotocin exposed diabetic rats for 30 days decreased blood glucose levels and also demonstrated a decrease in the level of glycosylated hemoglobin. The fruit extract significantly increased hemoglobin and plasma insulin in experimental diabetic models and reduced tissue damage marker enzymes Aspartate transaminase, Alanine transaminase and Alkaline phosphatase (Pradeepa et al., 2013). The 200 mg and 400 mg/kg dose of aqueous and ethanolic extracts from leaves also exhibited antidiabetic activity. Both types of extracts reduced blood glucose and marker enzymes of tissue damage and improved glycogen levels in liver and skeletal muscles of wistar diabetic rats (Mule et al., 2016). The methanolic extracts from seeds exhibited α-glucosidase and α-amylase inhibition

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with IC_{50} value for maltase, sucrase and α-amylase was 10.32±1.52, 2.84±0.96 and 16.75±1.81 mg/ml respectively. The α-glucosidase inhibition was found to be reversible and non-competitive type. Phytochemical analysis revealed

presence of oleanolic acid triterpenoid (0.244 mg/100 gm) as the active component (Nagmoti and Juvekar, 2013). The anthocyanins present in the fruit aril also showed α-glucosidase inhibitory activity (0.06±0.01 mg/ml) which was better than the synthetic drug Acarbose (2.54±0.19 mg/ml). The anthocyanins concentrated fraction demonstrated presence of pelargonidin 3-O-glucoside and cyanidin 3-O- glucoside as the main component (López-Angulo et al., 2018).

Renal Protective activity-

The aqueous fruit extract was also found to be effective in carbon tetra chloride provoked renal injury models. The CCl_4 toxicity enhanced oxidative stress and caused necrosis to renal cells. The fruit extracts alleviated these conditions and showed protective effects in pre or post application experiments. The aqueous fruit extract activity was found to be dose and time dependent (Pal et al., 2012).

Hepatoprotective-

The pre and post treatment of aqueous fruit extract to CCl_4 intoxicated mice demonstrated reduction in the level of hepatic injury marker enzymes Alanine transaminase and Alkaline phosphatase. The administration of aqueous fruit extract also reduced lipid peroxidation and protein carbonylation. The CCl_4 induced liver damage caused low level cytochrome P450 activity and CYP2E1 expression while pre or post application of aqueous fruit extract ameliorated these pathophysiological conditions (Manna et al., 2011). Similarly, the ripe fruit ethanolic and aqueous extract showed hepatoprotective effect in alcohol and paracetamol induced liver injury models. Both types of extracts reduced the level of liver injury marker enzymes and total bilirubin content. The toxicological studies revealed 200 and 400 mg/kg/day dose safe and effective in albino mice. The hepatoprotective effect was mainly attributed to the presence of phytochemicals as revealed in phytochemical investigation (Raju and Jagdeeshwar, 2014).

Antihyperlipidemic-

The seeds methanolic extract has profound effect on lipid profile of diabetic rat models and decreased elevated levels of total cholesterol, very low-density lipoproteins (VLDL-C), low density lipoprotein (LDL-C) and triglycerides. It increased HDL-cholesterol levels in a concentration dependent manner with effective dose of 250 mg/kg and 500 mg/kg (Nagmoti et al., 2015). Similarly, the aqueous and ethanolic extracts from leaves at 200 and 400 mg/ml significantly reduced levels of triglycerides and total cholesterol and increased the levels of HDL in diabetic rats (Mule et al., 2016).

Toxicological Studies-

P. dulce fruit hydroalcoholic extract was found to be non-toxic in toxicological studies on albino rats. The *in vivo* experiments revealed safety of 100 to 300 mg/kg bw dose as indicated by behavioural and histopathological observations. The LD_{50} value for fruit extract was reported to be 3916.66 mg/kg bw (Megala and Geetha, 2012 a).

Antiulcerogenic Activity-

The hydroalcoholic extract from *P. dulce* fruits has gastroprotective properties. It significantly reduced the ulcer score in rat ulcer models when pre-administered at a dose of 200 mg/kg bw consecutively for 30 days. The hydroalcoholic extract decreased the activity of neutrophil associated enzyme myeloperoxidase in gastric mucosa in pretreated rats and hence reduced the inflammatory activity augmented by ulcer causing agents. The activity of proton pump H^+, K^+-ATPase necessary for acidic secretions was also reduced in extract pretreated ulcer models (Megala and Geetha, 2012

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b). The *in vitro* study also supported the H^+, K^+- ATPase inhibitory action of hydroalcoholic extracts from *P. dulce* fruits with IC_{50} 13.04µg/ml which was better than standard drug Omeprazole (IC_{50} 15.2 µg/ml) (Megala and Geetha, 2010). In duodenal ulcer models induced by a single dose of cysteamine, the hydroalcoholic extract from fruits showed cytoprotective activity and reduced ulcer score when applied for 30 days at 200 mg/kg bw dose. The extract also improved the level of antioxidants in the duodenum of pretreated rats (Megala and Geetha, 2015).

Figure-01 *Pithecellobium dulce* (a) tree, (b) leaves, (c) inflorescence, (d) fruits and seeds

(a) (b) (c)

(d)

III. CONCLUSION

The leaves, fruits, seeds, roots and bark of *P. dulce* have many pharmacological activities. These activities are mainly due to presence of several types of phytochemicals present in different plant parts. The plant has immense potential to be used in pharmaceutical industry. However, there is a lack of systematic investigation of various pharmacological activities and more scientific investigations are required in a planned way to exploit its full potential for the welfare of society.

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Table- 01

Pharmacological activities of *Pithecellobium dulce*-

S. No.	Plant part	Extract	Activity	Model	Reference
01.	Root	Ethanol	Antibacterial	*Acetobacter aceti*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Enterobacter aerogens*	Bhat et al., 2018
02.	Leaves	Benzene, chloroform, acetone, methanol	Antibacterial and antifungal	*Enterococcus faecalis*, *Staphylococcus epidermidis*, *Aspergillus niger*, *Aspergillus flavus*, *Alternaria solani*	Kumar et al., 2013
03.	Seeds	Methanol	Antidiabetic	Streptozotocin challenged Wistar diabetic rats	Nagmoti et al., 2015
04.	Seeds	Saponin enriched fraction	Antihyperglycemic	*In vitro* inhibition of α-amylase and α-glucosidase, Swiss Albino mice	Kumar et al., 2017
05.	Fruits	95% ethanol	Antidiabetic	STZ challenged Wistar rats	Pradeepa et al., 2013
06.	Leaves	Water and Ethanol	Antidiabetic	Alloxan challenged Wistar albino diabetic rats	Mule et al., 2016
07.	Fruits	Aqueous	Hepatoprotective	Swiss albino mice	Manna et al., 2011
08.	Fruits	Aqueous and ethanol	Hepatoprotective	Wistar albino rats	Raju and Jagadeeshwar, 2014
09.	Fruits	Aqueous	Renal protective	CCl_4 induced Swiss Albino mice	Pal et al., 2012
10.	Fruit	Hydroalcoholic	Gastroprotective	Alcohol, Acetyl Salicylic Acid, Hypothermic-restraint stress challenged male Wistar rat ulcer models	Megala and Geetha, 2012 b

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