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Review Article

Traditional, Phytochemical, Nutritional and Biological Importance of *Pithecellobium dulce* (Roxib.) Benth

Alaa A. ELHEWEHY*[1], Engy MOHSEN[2], Ahlam M. EL-FISHAWY[3], Marwa A. A. FAYED[4]

[1,4]Department of Pharmacognosy, Faculty of Pharmacy, University of Sadat City, Sadat City 32897, Egypt
[2,3]Pharmacognosy Department, Faculty of Pharmacy, Cairo University, Kasr El-Ainy Street, Cairo 11562, Egypt

[1]https://orcid.org/0000-0001-9622-2932, [2]https://orcid.org/0009-0007-5723-9476, [3]https://orcid.org/0000-0003-4925-7395
[4]https://orcid.org/0000-0001-5609-7436

*Corresponding author e-mail: alaa.ashraf@fop.usc.edu.eg

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Traditional uses

Abstract: *Pithecellobium dulce* (*P. dulce*) is described in this review in terms of its botanical features, traditional uses, phytoconstituents, biological activities, and nutritional value. The aril of the fruit is consumed raw as food in many countries like India for its sweet taste. The plant phytoconstituents possess anti-ulcerogenic, anti-microbial, anti-inflammatory, and anti-diabetic properties. The plant's different extracts contain a variety of bioactive phytochemicals, including flavonoids, saponins, and tannins. People have been paying attention to medicinal plants over the past few years due to their incredible significance in the medication discovery process, their effectiveness, safety, and lack of negative side effects. *P. dulce* is a highly regarded plant in traditional medicine because of its diverse biological and nutraceutical properties. This review covers information regarding traditional uses, nutritional values, phytochemicals, and pharmacological activities of the different extracts as well as the pure compounds isolated from *P. dulce's* different parts and extracts.

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1. Introduction

Medicinal plants are a great source of several natural components with various pharmacological properties. Nutraceuticals are nutritional supplements that have recently drawn much interest because of their profound physiological effects on the human body. Traditional natural medicine practices are gaining popularity, in rural to urbanized areas. Notably, substances derived from plants have enormously valuable benefits for maintaining good health and treating a wide range of diseases including diabetes, cancer, inflammation, etc. (Jamshidi et al., 2018).

Leguminosae family is one of the largest families of flowering plants, which contains 12000 species grouped into over 600 genera. Papilionoideae, Caesalpinioideae, and Mimosoideae are the three subfamilies subdivided into the family *Pithecellobium* is one of the genera belonging to the Mimosoideae subfamily.

P. dulce (Roxb.) Benth. is a widespread evergreen tree. It is one of the 100-200 *Pithecellobium* species and it is the only one that has spread beyond its origin. The Latin species name "*dulce*" refers to the sweet edible pulp of the pod, while the genius's name is derived from the "Pithekos" (ape) and

“Lobos" (pod) (Sneha et al., 2020). The aril is eaten raw, roasted, or combined with atole (a cornstarch-based hot beverage) or agua fresca (a cold tea). The seed may be used raw, cooked, or roasted as a coffee substitute or as a condiment (Kirthy et al., 2022).

P. dulce is locally known by various names in different regions. In Arabic, it is known as Showkat madras. In English, it is known as Quamachil, Madras thorn, Manila tamarind, Black bead tree, and Monkeypod. In French, it is known as Campeche (New Caledonia) and Cassie de Manille. In Spanish, it is known as Guamuchil, Guama americano, Quamachil, Huamuche, and Chiminango. In Hindi, it is known as Vilayati imli, Vilayati babul, and Jangle jalebi. In Chinese, it is known as Niu ti dou. In Bengali, it is known as Dekhani babul. In German, it is known as Camambilarinde. In Greek, it is known as Pithekos ellobion. In Gujarati, it is known as Bakhai Ambli, Goras ambli. In Japanese, it is known as Huamuche, Guamuche, and Asambelanda. In Javanese, it is known as Asem londo and Asam belanda. In Kannada, it is known as Seeme hunase. In Malayalam, it is known as Korukkapuli. In Marathi, it is known as Ingraji chinch. In Odia, it is known as Seema Kaiyan. In the Philippines, it is known as Camachile. In Sanskrit, it is known as Kodukkaapuli. In Tamil, it is known as Kodukkaapuli. In Telugu, it is known as Seema Chintakaya. In Thai, it is known as Makham-khong and Makham-tha. In Vietnamese, it is known as Gang Tay, Me nuoc, Keo Tay, and Me Keo (Orwa et al., 2009; Kulkarni and Jamakhandi, 2018; Srinivas et al., 2018; Sneha et al., 2020).

P. dulce has been utilized traditionally in treating many disorders in different countries by using the extracts of different parts of the plant (Kulkarni and Jamakhandi, 2018; Rao et al., 2018; Srinivas et al., 2018; Dhanisha et al., 2022b). The plant contains many biologically active phytoconstituents which may contribute to the various scientifically proven biological activities such as the anti-inflammatory, anti-diabetic, anti-diarrheal, anti-microbial, anti-convulsant, anti-ulcer, anti-oxidant, anti-cancer, hepatoprotective, cardioprotective and nephroprotective activities (Sneha et al., 2020; Dhanisha et al., 2022b). Also, *P. dulce* provides important vitamins, amino acids, critical minerals, and many fatty acids that contribute to its nutritive value (Murugesan et al., 2019; Dhanisha et al., 2022b).

2. Search Strategy

Due to the wide use of *P. dulce* in traditional medicine and the presence of a variety of phytochemicals that have been proven by different *in vitro* and *in vivo* studies to have many biological activities. This systematic review highlights these traditional uses and the biologically active phytoconstituents that may contribute to the various biological activities of *P. dulce* during the period (1994-2023). Several available scientific databases were searched like PubMed, Science Direct, Scopus, Web of Science, and Google Scholar using different keywords related to the topic discussed in this review.

3. Botanical Description

P. dulce is a medium-sized evergreen tree that grows to a height of 10 to 15 meters. Leaves (Figure 1A) are bipinnate compound leaves, with 2 pairs of 2 ovate-oblong apiculate (kidney-shaped) leaflets which are approximately 2-4 cm long. Usually, at the base of the leaflet thin, paired spines ranging from 2 to 15mm in length are present. Flowers are small (1 cm in diameter) white heads colored flowers, which possess a hairy corolla and about 50 thin stamens surrounded in the calyx in the form of a tube at the base. Pods (Figure 1B) are tightly coiled and irregularly shaped greenish brown to reddish pods, which measure approximately 10-15 cm long and 1.5 cm wide and dehiscent on both sides. Each pod has about 5-10 seeds. Seeds (Figure 1C) are shiny black (1 cm in diameter) and attached to the pods by a red funicle. The bark (Figure 1D) is gray and when gets matured it becomes rougher and starts peeling (Murugesan et al., 2019; Sneha et al., 2020).

Figure 1. Photo of *Pithecellobium dulce* (Roxib.) Benth. different organs. (A) Trunk, (B) Fruit, (C) Seeds, and (D) Leaf.

3.1. Taxonomy

Domain	Eukaryote
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order:	Fabales
Family	Leguminosae
Genus	*Pithecellobium*
Species	*dulce*
Binomial Name	*Pithecellobium dulce* (Roxb.) Benth

3.2. Distribution

P. dulce has spread widely outside its origin. It can be found in northern South America, along the Pacific coast, close to Mexico, Brazil, Argentina, Bolivia, Colombia, Central America, Huawei, and in India and Southeast Asia. Now it is common in tropical Africa, especially along coasts (Dhanisha et al., 2022b).

4. Traditional Uses

The various parts of the plant were utilized traditionally in treating many disorders summarized in Table 1. *P. dulce* fruit has numerous health and nutritional advantages. Owing to its delicious flavor and medicinal properties, these fruits are eaten raw, as a decoction, roasted, or combined with atole (a cornstarch-based hot beverage) or agua fresca (a cold tea) in many regions of India for gastrointestinal disorders, and to control diabetes. The seed may be used raw, cooked, or roasted as a remedy against peptic ulcers and diabetes mellitus. The leaf decoction is used to treat intestinal and gall bladder disorders also it is used for toothache, and earache. It has both emollient and astringent properties. The bark and the root decoctions are used to treat diarrhea and dysentery (Dhanisha et al., 2022b; Kirthy et al., 2022; Roselin and Parameshwari, 2022).

Table 1. Traditional uses of *P. dulce* different parts

Plant organ	Traditional uses	Reference
Bark	Prevent hemorrhage. Treatment of gum disorders and toothache. Treatment of dysentery, diarrhea, and constipation. Treatment of dermatitis and eye inflammation.	(Kulkarni and Jamakhandi, 2018; Rao et al., 2018;)
Fruits	As an astringent and for hemoptysis. (Fruit pulp). Treatment of gastrointestinal disorders such as peptic ulcer. To control diabetes (chewing raw fruit peel or as a decoction). Swellings treatment (fruit peel decoction).	(Srinivas et al., 2018; Dhanisha et al., 2022b)
Leaves	Abortifacient. Astringent. Emollient. In toothache and earache. Larvicidal. Treatment of intestinal disorders (as a decoction) and gall bladder disorder. To prevent miscarriages. Treatment of leprosy. Used for Venereal sores (as plasters).	(Shweta, 2013; Rao et al., 2018; Srinivas et al., 2018; Sneha et al., 2020)
Roots	Antipyretic. Treatment of dysentery and diarrhea.	(Srinivas et al., 2018; Dhanisha et al., 2022b)
Seeds	Anti-edematous (Seed Oil). Remedy against peptic ulcers. Spermicidal. Treatment of diabetes mellitus. To cleanse ulcers (grounded seed).	(Kulkarni and Jamakhandi, 2018; Rao et al., 2018; Dhanisha et al., 2022b)

5. Chemical Constituents

The different organs of *P. dulce* contain numerous bioactive substances summarized in Table 2 such as flavonoids, anthocyanin, tannins, coumarin, triterpenoids, saponins, alkaloids, sterols, and fatty acids.

Table 2. Different classes of chemical constituents of *P. dulce*

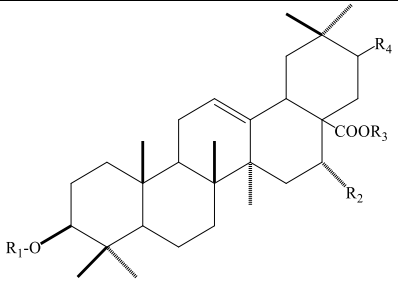
No.	Compound	Structure	Plant Organ	References
1.	**Terpenoids**			
	1.1. Triterpenoids			
				
1	Pitheduloside A	R_1= Glu.– Ara., R_2=OH, R_3=R_4=H.	Seed	(Nigam et al., 1997)
2	Pitheduloside B	R_1= Glu.– Ara.– Ara., R_2=H, R_3=R_4=H.		
3	Pitheduloside C	R_1= Glu.– Ara.– Xyl., R_2=H, R_3=R_4=H.		

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

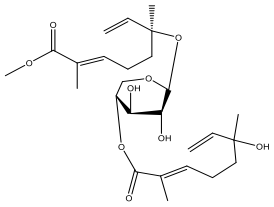
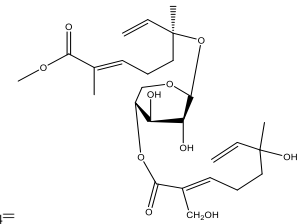
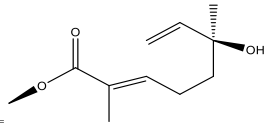
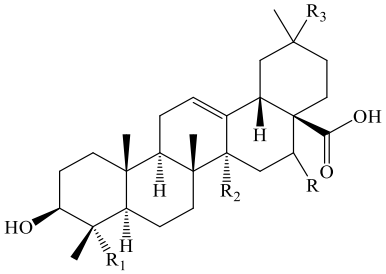
No.	Compound	Structure	Plant Organ	References
1.	**Terpenoids**			
	1.1. **Triterpenoids**			
4	Pitheduloside D	R_1= Glu. – Ara. – Ara., R_2=OH, R_3=R_4=H.		
5	Pitheduloside E	R_1= Glu. – Ara. – Xyl., R_2=OH, R_3=R_4=H.		
6	Pitheduloside F	R_1= Glu. – Ara. – Ara., R_2=H, R_3=R_4=H. | Glu		
7	Pitheduloside G	R_1= Glu. – Ara. – Xyl., R_2=H, R_3=R_4=H. | Glu		
8	Pitheduloside H	R_1= Glu. – Ara. – Ara., R_2=OH, | Glu R_3= Glu. – Ara. – Ara. | Glu  R_4=		
9	Pitheduloside I	R_1= Glu. – Ara. – Ara., R_2=OH, | Glu R_3= Glu. – Ara. – Ara. | Glu  R_4=	Seed	(Yoshikawa et al., 1997)
10	Pitheduloside J	R_1= Glu. – Ara. – Ara., | Glu R_2=OH R_3= Glu. – Rha.. – Ara. | Glu.  R_4=		
11	Pitheduloside K	R_1= Glu. – Ara. – Ara., R_2=OH, R_3= R_4=H | Glu 		
12	Oleanolic acid	R=H, R_1= R_2= R_3=CH_3	Seed	(Murugesan et al., 2019)
13	Hederagenin	R= H, R_1=CH_2OH, R_2=, R_3=CH_3		

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

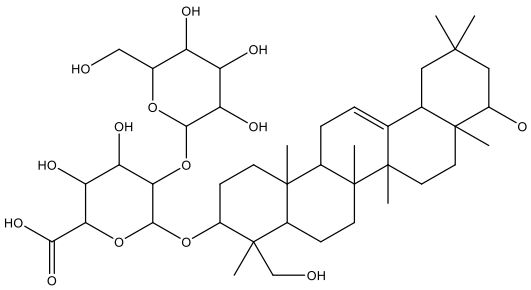
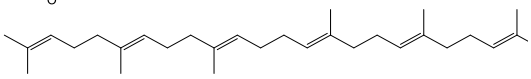
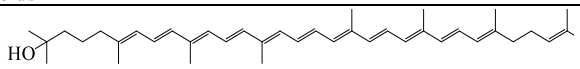
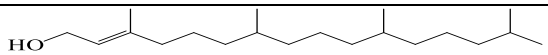
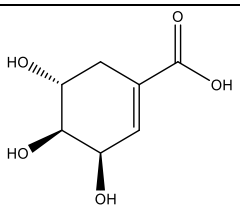
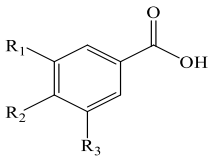
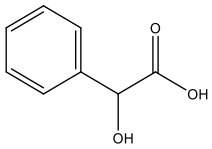
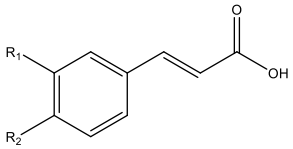
No.	Compound	Structure	Plant Organ	References
1. **Terpenoids**				
	1.1. **Triterpenoids**			
14	Echinocystic acid	R= OH, R_1= R_2= R_3=CH_3	Seed Stem Bark	(Katekhaye and Laddha, 2015)
15	Soyasaponin III		Seed	(Alhamed et al., 2023)
16	Squalene		Leaves	(Bobade, 2017)
	1.2. Tetraterpenoids			
17	Rhodopin		Leaf	(Bobade, 2019)
	1.3. Diterpenoids			
18	Phytol		Leaf	(Srinivas et al., 2018)
2. Phenolic compounds				
	2.1. Phenolic Acids			
19	Shikimic acid		Fruit	(Vargas et al., 2020)
				
20	Gallic acid	R_1=R_2=R_3=OH		
21	Vanillic acid	R_1=OCH_3, R_2=OH, R_3=H		
22	Mandelic acid		Fruit	(Murugesan et al., 2019)
				
23	Cinnamic acid	R_1=R_2=H		(Vargas et al., 2020)
24	Coumaric acid	R_1=H, R_2=OH	Fruit	(Murugesan et al., 2019)
25	Caffeic acid	R_1=R_2=OH		(Vargas et al., 2020)

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

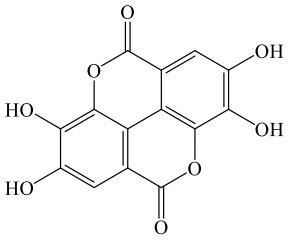
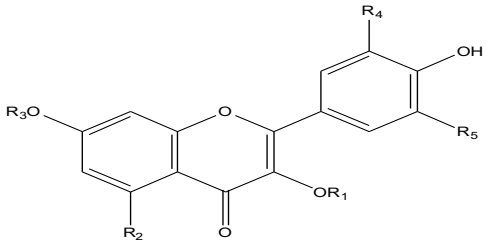
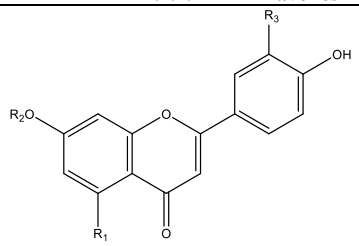
No.	Compound	Structure	Plant Organ	References
2. **Phenolic compounds**				
	2.1. **Phenolic Acids**			
27	Ellagic acid		Fruit	(Vargas et al., 2020)
	2.2. Flavonoids			
	2.2.1. Flavonols			
				
28	Kaempferol	R_1=H, R_2=OH, R_3=R_4=R_5=H	Leaf	(Srinivas et al., 2018)
29	kaempferol-3-rhamnoside (Afzelin)	R_1=Rha., R_2= OH, R_3= R_4= R_5 =H	Seed	(Alhamed et al., 2023)
30	Kaempferol 7-O-*β*-D-glucopyranoside	R_1=H, R_2=OH, R_3=Glu., R_4= R_5 =H	Leaf Fruit Fruit Peel	(Srinivas et al., 2018; Kulkarni and Jamakhandi, 2018)
31	Quercetin	R_1=H, R_2= R_3=H, R_4=OH, R_5=H	Fruit	(Murugesan et al., 2019)
32	Rutin	R_1=Glu–Rha., R_2= OH R_3= H, R_4=R_5= OH	Fruit	(Vargas et al., 2020)
33	Myricetin	R_1=Rha., R_2= OH, R_3= R_4= R5=H.		
	2.2.2. Flavones			
				
34	Apigenin	R_1=OH, R_2=R_3=H	Fruit	(Vargas et al., 2020)
35	Luteolin	R_1=OH, R_2=H, R_3=OH		(Vargas et al., 2020)
36	Prenylapigenine	R_1=OH, R_2=H, R_3= CH_2-CH-CH-$(CH_3)_2$	Stem	(Kulkarni and Jamakhandi, 2018)
37	3'-prenylapigenin-7-O-glucoside	R_1=OH, R_2=Glu., R_3= CH_2-CH-CH-$(CH_3)_2$	Stem Bark	(Katekhaye and Laddha, 2015; (Saxena and Singhal, 1999)
38	3'-prenylapigenin-7-O-rutinoside	R_1=OH, R_2=Glu. -Rha., R_3= CH_2-CH-CH-$(CH_3)_2$		

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

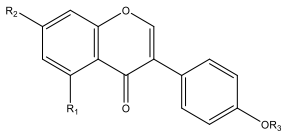
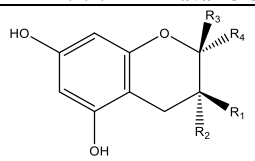
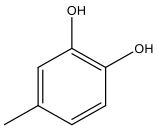
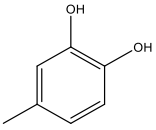
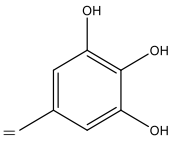
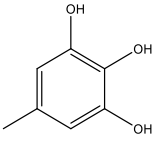
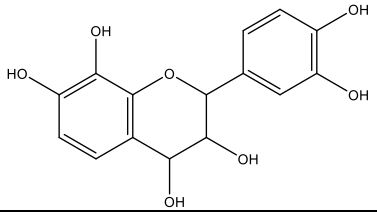
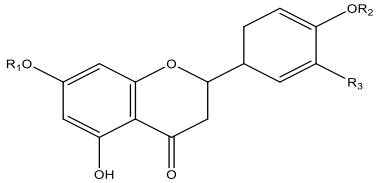
No.	Compound	Structure	Plant Organ	References
2. **Phenolic compounds**				
2.2. Flavonoids				
2.2.3. Isoflavonoids				
				
39	Genistein	R_1=OH, R_2= OH, R_3= H.	Fruit	(Vargas et al., 2020)
40	Genistein 4'-O-*α*-L-rhamnopyranoside	R_1=OH, R_2= OH, R_3= Rha.	Root	(Saxena and Singal, 1998)
41	Daidzein	R_1=H, R_2= OH, R_3= H.	Fruit	(Murugesan et al., 2019)
2.2.4. Flavan-3-ol				
				
42	Catechin	R_1=OH, R_2= H, R_3=H, R_4= 		
43	Epicatechin	R_1=H, R_2= OH, R_3=  R_4 =H.	Fruit	(Vargas et al., 2020)
44	Epigallocatechin	R_1=H, R_2= OH, R_3=H, R_4 = 		
45	3',4',5',7-tetrahydroxy flavan-3-ol (Robinetinidol)	R_1=OH, R_2= H, R_3=  , R_4 =H	Stem Bark	(Katekhaye and Laddha, 2015)
46	Melacacidin		Wood	(Murugesan et al., 2019)
2.2.5. Flavanones				
				
47	Naringin	R_1= Glu. -Rha., R_2= CH_3, R_3= OH	Fruit	(Murugesan et al., 2019)
48	Hesperetin	R1= Glu. -Rha., R2= H, R3= H		(Vargas et al., 2020)

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

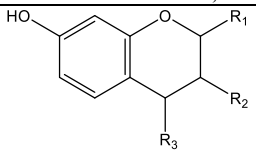
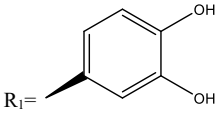
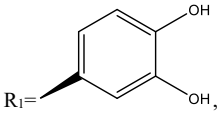
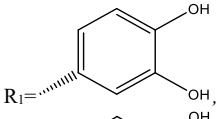
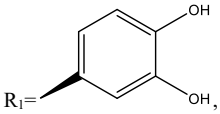
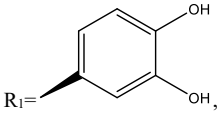
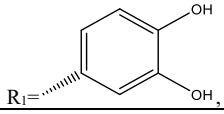
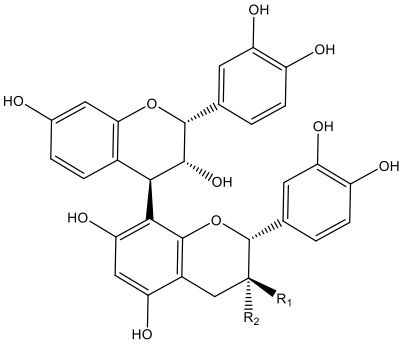
No.	Compound	Structure	Plant Organ	References
2. Phenolic compounds				
2.2. Flavonoids				
2.2.6. Flavan-3,4-diol				
49	3',4',7-trihydroxy flavan-3,4-diols	 R_1= , R_2=R_3=OH		
50	Epifisetinidol-4α-ol	 R_1= , R_2=R_3=α-OH		
51	Epifisetinidol-4β-ol	 R_1= , R_2=R_3=β-OH	Stem Bark	(Katekhaye and Laddha, 2015)
52	Fisetinidol-4α-ol	 R_1= , R_2= β-OH, R_3=α-OH		
53	Fisetinidol-4β-ol	 R_1= , R_2=R_3=β-OH		
54	Leucofisetinidin	 R_1= , R_2= α-OH, R_3=β-OH	Wood	(Murugesan et al., 2019)
2.3. Procyanidins and Proanthocyanidins				
				
55	Epifisetinidol-(4β,8)-catechin	R_1=OH, R_2=H	Stem Bark	(Katekhaye and Laddha, 2015)`
56	Epifisetinidol-(4β,8)-epicatechin	R_1=H, R_2= OH		

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

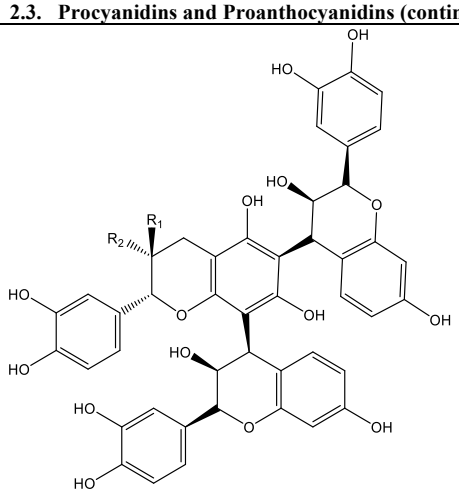
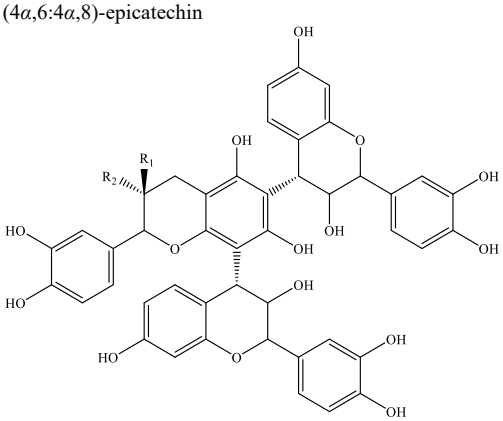
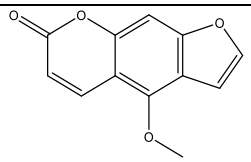
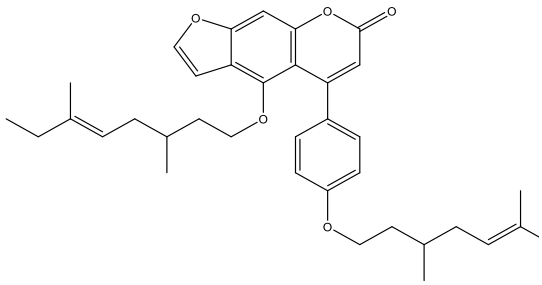
No.	Compound	Structure	Plant Organ	References
	2. Flavonoids			
	2.3. Procyanidins and Proanthocyanidins (continue)			
				
57	Bisepifisetinidol-(4*α*,6:4*α*,8)-catechin	R_1=OH, R_2=H	Stem Bark	(Katekhaye and Laddha, 2015)
58	Bisepifisetinidol-(4*α*,6:4*α*,8)-epicatechin	R_1=H, R_2=OH		
				
59	Fisetinidol-(4*α*,8)-catechin-(6,4*α*)-epifisetinidol	R_1=OH, R_2=H	Stem Bark	(Katekhaye and Laddha, 2015)
60	Fisetinidol-(4*α*,8)-epicatechin-(6,4*α*)-epifisetinidol	R_1=H, R_2=OH		
	2.4. Coumarins			
61	Bergapten.			
62	4(2,3-dihydro geranyl oxy)-5(4(2,3-dihydro geranyl oxy) phenyl bergapten		Stem Bark	(Katekhaye and Laddha, 2015)

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

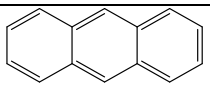
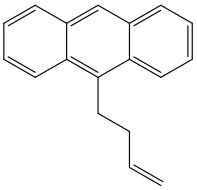
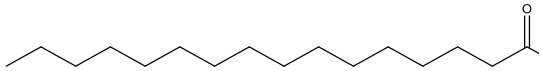
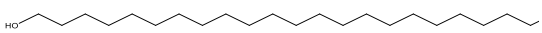
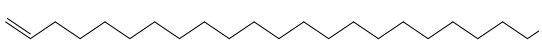
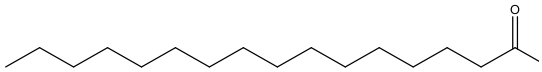
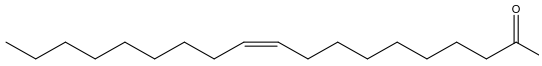
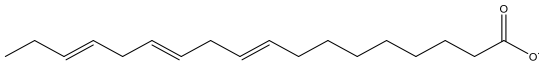
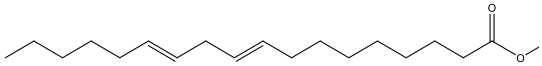
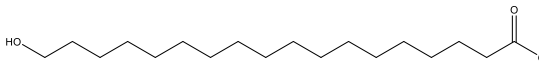
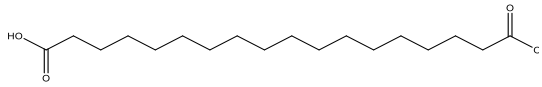
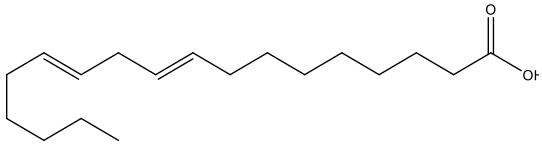
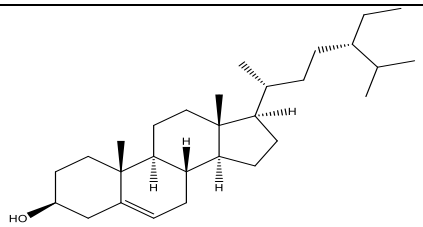
No.	Compound	Structure	Plant Organ	References
	3. Anthracenes			
63	Anthracene			(Srinivas et al, 2018)
64	9(3butenyl) anthracene		Leaf	(Vanitha and Manikandan, 2016)
	4. Fatty Acids			
65	Heptacosanoic acid			
66	Hexadecenoic acid (palmitic acid)		Fruit	(Kulkarni and Jamakhandi, 2018)
67	Tetracosanol			
68	22-tricosenoic acid			
69	Hexadecenoic acid methyl ester			(Bobade, 2019)
70	9 Octadecenoic acid (Z),			(Bobade, 2017)
71	9,17-octadecadienal		Leaf	
72	Ethyl 9,12,15-octadecatrienoate			(Vanitha and Manikandan, 2016)
73	9,12-octadecadienoic acid ethyl ester			
74	Hydroxystearic acid			
75	Octadecanedioic acid			
76	Linoelaidic acid		Seed	(Alhamed et al., 2023)
	5. Sterols			
77	β-sitosterol		Stem Bark	(Katekhaye and Laddha, 2015)

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

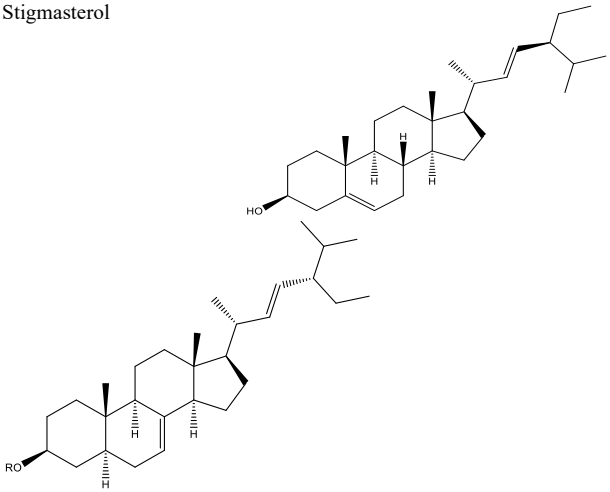
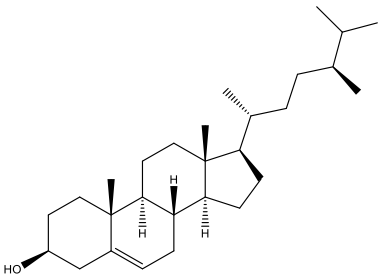
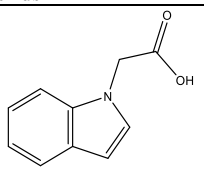
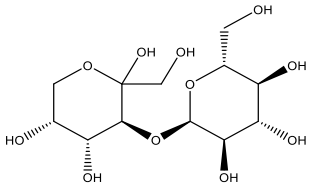
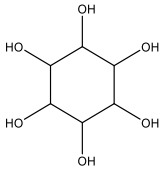
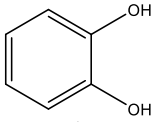
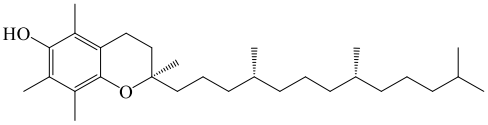
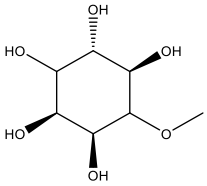
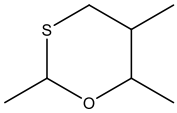
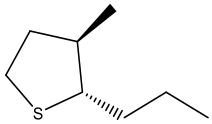
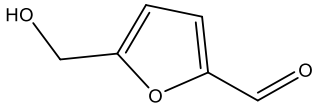
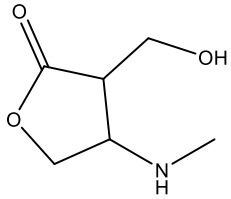
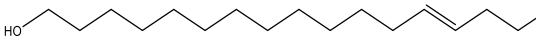
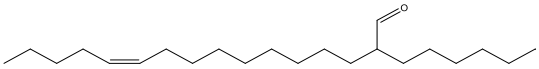
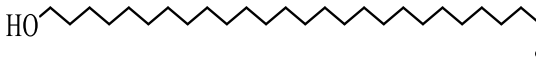
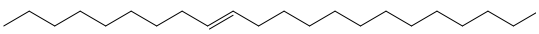
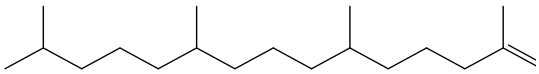
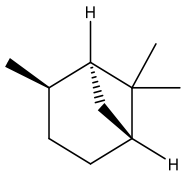
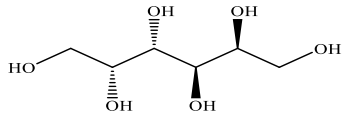
No.	Compound	Structure	Plant Organ	References
	5. Sterols			
78	Stigmasterol		Stem Bark Seeds Fruit Peel	(Kulkarni and Jamakhandi, 2018)
79	ά-spinasterol	R=H.	Stem Bark Leaf	
80	β-Glucoside–*α* spinasterol	R=Glu.	Leaf	
81	Campesterol		Wood Stem Bark	(Katekhaye and Laddha, 2015)
82	Pithogenin	C28H44O4	Seed	(Murugesan et al., 2019)
	6. Miscellaneous Compounds			
83	Indole-1-acetic acid			
84	D-Turanose		Seed	(Aldarhami et al., 2023)
85	Inositol			
86	Catechol		Bark	(Murugesan et al., 2019)
87	Tocopherol		Fruit	(Vargas et al., 2020)

Table 2. Different classes of chemical constituents of *P. dulce* (continued)

No.	Compound	Structure	Plant Organ	References
	6. Miscellaneous Compounds			
88	D-Pinitol		Fruit Peel	
89	2, 5, 6-trimethyl 1, 3-oxathiane			(Vargas et al., 2020)
90	Trans-3-methyl-2-N-propylthiophane		Fruit	
91	2-furan carboxaldehyde-5 (hydroxymethyl)			
92	3-(hydroxymethyl)-4-(methylamino)-dihydrofuran-2(3H)-one		leaf	(Wichaidit and Thongyoo, 2021)
93	13 octadecenol			(Vanitha and Manikandan, 2016)
94	2-octyl-cis-11-hexdecenal		Leaf	
95	Octacosanol			(Murugesan et al., 2019)
96	13-docosenamide			
97	2-hexadecene,3,7,11,15-tetramethyl-,[R-[R*,R*-(E)]		Leaf	(Vanitha and Manikandan, 2016)
98	Bicyclo[3.1.1]heptane,2,6,6-trimethyl-, (1alpha,2beta,5alpha			
99	Dulcitol		Leaf	(Srinivas et al., 2018)

6. Nutritional Value

P. dulce fruits provide important vitamins like thiamine, ascorbic acid, riboflavin (Figure 2A), and several necessary amino acids like phenylalanine, valine, tryptophan, and lysine (Figure 2B). They also contain a small number of critical minerals including K, P, Na, Ca, and F (Figure 2C) (Dhanisha et al., 2022b). *P. dulce* fruit has the potential to stop oxidative damage and to scavenge free radicals due to the phenols, flavonoids, and saponins content (Katekhaye and Kale, 2012). According to reports, 100 g of seeds contain the following: ash (2.8%), carbohydrate (41.4%), fiber (7.8%), protein (17.7%), and water (13.5%) (Figure 2D). The fat is composed of many fatty acids as described in (Figure 2E) (Murugesan et al., 2019).

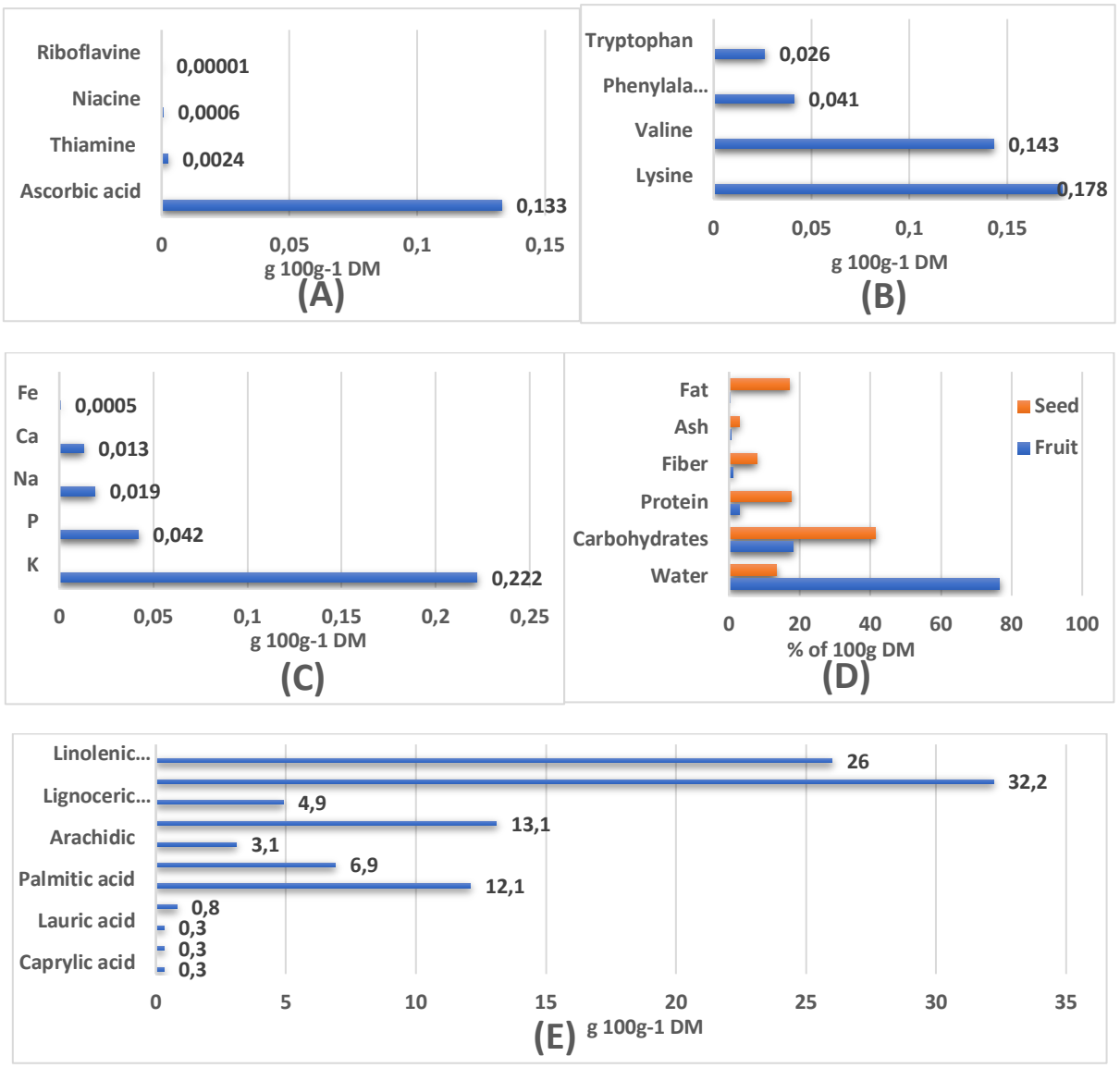


Figure 2. Nutritional value of different parts of *Pithecellobium dulce* (Roxib.) Benth. A. Fruit vital vitamin content. B. Fruit amino acids content. C. Essential minerals in fruit arils. D. Composition of dried fruit and seed. E. Seed Fat content).

7. Biological Activities

The different parts of *P.dulce* were used traditionally for many biological activities in which many of these activities have been proved scientifically by different studies. The presence of many biologically active phytoconstituents in the different parts of *P. dulce* may contribute to the anti-inflammatory, anti-diabetic, anti-diarrheal, anti-microbial, anti-convulsant, anti-ulcer, antioxidant, anti-cancer, hepatoprotective, cardioprotective and nephroprotective activities summarized in (Figure 3).

7.1. Analgesic /anti-inflammatory activity

The anti-inflammatory bisdesmodic triterpenoidal saponin (Dulcin) was identified from the seeds of *P. dulce* (Sahu and Mahato, 1994).

Leaves methanolic, ethanolic, and aqueous extract showed significant results when evaluated using the hot plate assay and acetic acid-induced writhing assay in mice for the analgesic activity and rat paw edema test for the anti-inflammatory activity (Sugumaran et al., 2009; Selvan and Muthukumaran, 2011). Another study in which the leaf's ethanolic extract was tested using the membrane stabilization of the HRBC (human red blood cell) assay and the albumin denaturation

inhibition assay compared to aspirin. The percentage of HRBC membrane stabilization was found to be 59.25% and the inhibition of albumin denaturation was 62.80% (Kalavani et al., 2016).

The anti-inflammatory properties of the aqueous extract of the bark, leaf, and fruit were investigated utilizing the inhibition of albumin denaturation method against diclofenac sodium as a standard medication. The three extracts inhibited albumin denaturation effectively. The maximum inhibition percentage for the bark extract was 52.73% (Nagendra et al., 2019).

The radiographic and histopathological examination of the joints revealed the antiarthritic activity of *P. dulce* leaf ethanolic extract at a dose of 250 mg kg^{-1}. Indomethacin was utilized as a reference drug and formaldehyde was used for the induction of arthritis (Mishra et al., 2021).

7.2. Anti-diabetic activity

The bark hydro-alcoholic extract was screened for antidiabetic activity using oral doses of 200 mg kg^{-1} and 400 mg kg^{-1} in alloxan-induced diabetic rats. The 400 mg kg^{-1} concentration showed significant antidiabetic activity and reduced cholesterol and triglyceride levels. glibenclamide was used as a reference drug (Praveen et al., 2010).

In vitro, α-amylase and α-glucosidase activity were evaluated using methanolic and 70% acetone leaves and bark extracts against acarbose. The extracts inhibited the sucrase enzyme more effectively than the maltase enzyme. (Katekhaye and Nagmoti, 2013).

The fruit ethanolic extract was tested for antidiabetic activity against gliclazide utilizing a daily 300 mg kg^{-1} oral dose administered to streptozotocin (STZ) induced diabetic rats. The extract showed significant inhibition in the blood glucose, glycosylated hemoglobin (HBA1C), urea, and creatinine levels. Aminotransferases, alkaline phosphatase (ALP), plasma protein, plasma insulin, and hemoglobin levels were all normalized. (Pradeepa et al., 2013).

The seed methanolic extract was studied for the inhibitory activity of α-glucosidase and α-amylase enzymes. The results demonstrated considerable efficacy against pancreatic-amylase and superior activity against maltase over sucrase enzyme (Nagmoti and Juvekar, 2013). Also, the oral administration of different doses of the methanolic extract resulted in a significant drop in HbA1C and fasting blood glucose while increasing serum insulin, total protein, liver glycogen levels, and body weight. Metformin was used as a reference drug (Nagmoti et al., 2015).

Two isolated compounds from the fruit peel methanolic extract which tested positive for the Molisch test were tested using non-enzymatic glycosylation of hemoglobin assay and enzymatic α-amylase assay. Compound 1 was more potent than compound 2 at concentrations of 0.2 mg dl^{-1} to 1.0 mg dl^{-1} (Praylin et al., 2015).

The anti-diabetic effect of the fruit peel aqueous extract was examined in STZ-induced diabetic rats by administering 200 mg kg^{-1} of the extract orally. Glibenclamide is used as a standard drug. The levels of urine sugar, blood glucose, HBA1C, ALP, glucose-6-phosphatase, fructose-1,6-bisphosphatase, aspartate transaminase (AST), total cholesterol, alanine transaminase (ALT) and triglycerides were reduced while the levels of liver glycogen, insulin, hexokinase, protein, superoxide dismutase, glutathione peroxidase, and catalase were decreased (Sukantha et al., 2016).

In dexamethasone-induced diabetic rats, aqueous and ethanolic leaf extracts were evaluated against pioglitazone via oral administration of 200 mg kg^{-1} and 400 mg kg^{-1}. They demonstrated considerable anti-diabetic and anti-hyperlipidemic efficacy. (Mule et al., 2016).

The saponin-enriched fraction from the seed extract was investigated for possible antihyperglycemic activity using the *in vitro* α-glucosidase and α-amylase inhibitory assay and *in vivo* sucrose tolerance test against standard drug acarbose. The extract inhibited both glucosidase and amylase enzymes more effectively than the conventional medication employed. It may be linked to limiting sucrose hydrolysis (Kumar et al., 2017).

7.3. Anti-diarrheal activity

Castor oil-induced diarrhea in rats was used to test the aqueous and ethanolic extracts of the leaves. The aqueous extract was more powerful. Diphenoxylate HCl was utilized as a control medication(Sugumaran et al., 2008a). Another study only employed the ethanolic extract of the leaf and loperamide as a control medication. The results demonstrated considerable antidiarrheal activity by prolonging the latent period and decreasing defecation frequency (Venu et al., 2016).

7.4. Anti-hyperlipidemic activity

In triton-induced hyperlipidemic rats, an oral dosage of 200 g kg^{-1} of *P. dulce* leaves aqueous extract was employed. The extract significantly reduced serum total cholesterol, phospholipids, triglyceride, LDL, and very low-density lipoproteins (VLDL) levels while increasing serum HDL levels. Fenofibrate was used as a standard treatment (Rajan and Kumar, 2010).

The crude methanolic extract of the seeds resulted in significant inhibition of the LDL, VLDL, triglycerides, and total cholesterol (Nagmoti et al., 2015).

7.5. Anti-microbial activity

Agar well diffusion assay was utilized for evaluating the anti-microbial effect of *P. dulce* leaf extract in aqueous and different organic solvents against *Enterococcus faecalis, Bacillus subtilis*, *Staphylococcus aureus, Micrococcus luteus*, and *Staphylococcus epidermidis* Gram-positive bacteria and *Alcaligenes faecalis, Aeromonas hydrophila*, *Escherichia coli, Enterobacter aerogenes, Klebsiella pneumoniae*, *Salmonella typhimurium* and *Pseudomonas aeruginosa* gram-negative bacteria and eight fungi *Aspergillus niger, Aspergillus flavus, Aspergillus oryzae*, *Alternaria alternata*, *Alternaria solani, Alternaria vitis*, and *Alternaria alternata.* The aqueous leaf extracts demonstrated no antimicrobial effect against all the examined microbes. While the different organic solvent extracts demonstrated outstanding activity against most of the examined bacteria (Kumar et al., 2013).

The antimicrobial activity of leaf methanolic extract against, *S. aureus*, and *S typhimurium*, as well as two fungal strains, *A. niger,* and *Candida albicans,* was studied using chloramphenicol as a standard drug. The extract demonstrated antibacterial activity against *S. aureus* greater than against *S. typhimurium*. Conversely, it had greater antifungal activity against *A. niger* than against *C. albicans* (Idris et al., 2020).

Different organic solvents and alkaloidal extracts of *P. dulce* leaves were evaluated for anti-microbial activity against *Mycobacterium tuberculosis, C. albicans, and A. niger* using rifamycin, fluconazole, and nystatin as standard drugs. All the extracts were inactive against *A. niger*. while the alcoholic and total alkaloidal extracts were active against *M. tuberculosis* and *C. albicans* (Shanmugakumar et al., 2006).

Bark methanolic extract was tested for anti-microbial activity against *A. fumigatus, C. albicans, S. aureus, E. coli, B. subtilis,* and *Proteus vulgari.* Gentamycin and ketoconazole were used as standard drugs. The extract was only active against *E. coli* and *P. vulgari* (Kotb et al., 2022).

7.5.1. Anti-bacterial activity

Using streptomycin as the reference medication, the ethyl acetate floral *P. dulce* fraction containing the flavonoid glycoside quercetin was shown to have antibacterial activity against *S. typhi* and *E. coli* gram-negative and *S. aureus* gram-positive (Chandran and Balaji, 2008).

The antibacterial activity of *P. dulce* fruit peel aqueous and several organic solvent extracts against various organisms was investigated. According to (Sukantha et al., 2011), the ethyl acetate fraction was effective against *S. aureus, E. coli, S. epidermis, K. pneumonia, E. faecalis, P. putida,* and *P. aeruginosa*. Whereas the methanolic extract was effective against *P. putida, S. aureus,* and *K. pneumonia*, the aqueous extract was active against *S. aureus* and *K. pneumonia* only, while the petroleum ether extract was effective only against *P. putida***.** On the other hand (Sukantha et al., 2014) reported that all the extracts displayed antibacterial properties, although the methanol extract had superior antimicrobial properties compared to the aqueous and ethyl acetate extracts. *S. aureus* and *K. pneumonia* were the organisms that were most sensitive to all the extracts, whilst *P. mirabilis* and *P. vulgaris* were the most resistant organisms. Polymyxin and rifampicin are used as standard drugs.

P. dulce biologically generated silver nanoparticles exhibited satisfactory antibacterial activity against *S. aureus*, *E. coli, P. aeruginosa,* and *C. albicans*. The higher the concentration of crude extract, the higher the diameter of the inhibition zone (Lakshmi et al., 2014).

The disc diffusion assay was utilized to test the leaves methanolic extract, n-hexane, ethyl acetate, chloroform, and aqueous fractions against two gram-positive bacteria (*B. cereus* and *S. aureus*) and four gram-negative bacteria (*Proteus, Shigella boydii, Pseudomonas specious* and *E. coli*). Kanamycin was used as a conventional medication. The growth of the gram-negative bacteria was

inhibited effectively by the ethyl acetate fraction, while the methanolic fraction was most active against gram-positive bacteria (Akter et al., 2020).

Ethyl acetate aril parts extract was evaluated against some gram-negative strains using the disc diffusion and the agar well diffusion assays and chloramphenicol as a standard drug. The treated sample showed activity against *Shigella flexneri, Salmonella enteric*, and *K. pneumoniae* (Hepzibah et al., 2017).

The leaf ethanolic extract was screened using three assays against seven gram-negative and gram-positive bacteria including *S. boydii, S. typhi, Pseudomonas, Shigella dyst-1, S. sonnie, S. fleas, Plesiomonas*, *Staphylococcus saprophyticus, S. aureus, and S. epidermidis*. Only *S. dyst-1* was susceptible to the antimicrobial effects of the leaf extract (Kulkarni and Jamakhandi, 2018).

P. dulce root extracts in hexane, benzene, ethyl acetate, and ethanol were evaluated using the disc diffusion assay against three gram-negative *(Acetobacter aceti, Acetobacter aceti,* and *K. pneumoniae)* and one gram-positive bacteria *(S. aureus).* The results demonstrated that polar extracts have more antibacterial activity than non-polar extracts (Bhat et al., 2018).

The methanolic extract of the seed demonstrated significant activity against clinically relevant multidrug-resistant bacteria in which *Acinetobacter baumannii* had a MIC of 233 mg ml^{-1}, while *E. coli* and *S. aureus* had MIC of 300 mg ml^{-1}. A molecular docking study was conducted to identify the best compounds with high affinity for two *S. aureus* receptors and low binding energy. Turanose had energy values of (-6.6 and -7.4) kcal mol^{-1}, whereas inositol had (-5.4 and -7.2) kcal mol^{-1} for 2XCT and 1JIJ receptors, respectively (Aldarhami et al., 2023).

7.5.2. Anti-fungal activity

Fungistatic and fungicidal activities of *P. dulce* seeds on plant pathogens such as *Penicillium digitatum, Botrytis cinerea, Rhizopus stolonifer,* and *Fusarium oxysporum.* The anti-fungal activity of the aqueous extract against *P. digitatum, B. cinerea,* and *R. stolonifera* is mostly due to the presence of kaempferol and a few other compounds (Bautista-Baños et al., 2003). In addition, the triterpenoidal saponins Pithedulosides A, B, E, F, and I inhibited the growth of *Colletotrichum gloeosporioides* mycelium and *R. stolonifer in vitro* (Shweta, 2013).

7.6. Anti-obesity activity

P. dulce fruit peel different organic solvent extracts at two different doses (100 and 200 mg kg^{-1}) were used for the assessment of anti-obesity compared to orlistat. The findings indicated that the petroleum ether, ethyl acetate, and methanolic extracts had potential anti-obesity activity (Jagadeeshwar et al., 2021).

7.7. Antioxidant activity

Six different methods were utilized to evaluate the antioxidant activity of the fruit pericarp methanolic and acidified methanol extracts and the anthocyanin extracted from them. According to the findings, acidified methanol extract has a higher vitamin C concentration and antioxidant scavenging activity than methanolic extract (Ponmozhi et al., 2011).

Leaves and wood bark methanolic and 70% acetone extracts were studied using DPPH, hydroxyl radical, superoxide radical, hydrogen peroxide (H_2O_2), nitric oxide (NO), hypochlorous acid, and singlet oxygen scavenging activity assays. The results revealed that the leaves and wood bark have significant antioxidant activity with good content of total phenolic and flavonoid and have good iron chelating activity (Katekhaye and Kale, 2012). *In-vitro* antioxidant activity assessment of different fractions of the crude methanolic leaf extract using DPPH, reducing power, hydroxyl radical, and H_2O_2 scavenging assays, revealed a significant antioxidant property with higher activity of ethyl acetate fraction (Akter et al., 2020).

Water-soluble polysaccharides isolated from the seeds were tested using scavenging of DPPH radicals, H_2O_2, and reducing power assays. The polysaccharides fraction showed a strong dose-dependent free radical scavenging activity compared to the standard ascorbic acid (Bagchi and Kumar, 2016).

In-vitro ferric-reducing antioxidant power (FRAP), DPPH, and NO assays were performed on aqueous, methanolic, and acetone *P. dulce* leaf extracts. The FRAP assay demonstrated that the water

extract had the most scavenging activity, while the DPPH assay revealed that the acetone extract had the highest activity and the NO assay revealed that the methanolic extract had the highest activity (Kumari, 2017).

A flavanol glycoside kaempferol- 3-O-α-rhamnoside isolated from the leaf ethyl acetate fraction demonstrated strong activity in the DPPH assay (IC_{50} 14.6 µg ml^{-1}). It effectively inhibited the oxidative damage of erythrocytes induced by AAPH and protected the plasmid DNA from oxidative degradation (Akter et al., 2022).

7.8. Antiparasitic activity

P. dulce fruit methanolic extract, the ethyl acetate fraction, and the identified compound N-malonyl-(þ)-tryptophan which was isolated from the methanolic extract were found to possess *in vitro* activity against *Hymenolepis nana* the most common intestinal tapeworm in humans globally (López-Angulo et al., 2019).

7.9. Anti-ulcerogenic activity

The hydroalcoholic fruit extract was tested for the anti- gastric (Megala and Geetha, 2010 and 2012b) and anti-duodenal ulcer (Megala and Geetha, 2015) activity, and the extract was administered pre- and post-ulcer induction. The gastric ulcer was induced by chemicals and stress and omeprazole was used as a reference drug. On the other hand, the duodenal ulcer was induced by cysteamine, and ranitidine was used as a reference drug. Both studies demonstrated significant anti-ulcerogenic activity.

When compared to ranitidine, the *P. dulce* alcoholic and aqueous extract of seeds were effective in preventing ulcers in pyloric-ligated rats and significantly lowered stomach volume, total acidity, free acidity, and ulcer index (Palanivel et al., 2014).

7.10. Anti-venom activity

P. dulce water bark extract was able to reduce the venom's capacity to necrotize tissue and hindered its lethality. Due to the extract's high tannin concentration, it successfully inhibited 90% of acetylcholine esterase activity. Using Autodock 3, the binding energies of tannic acid (14.7 kcal mol^{-1}), di-gallic acid (10.38 kcal mol^{-1}), and four other tannin compounds were examined. The extract non-selectively precipitates the venom protein while blocking the nicotinic acetylcholine receptor (Pithayanukul et al., 2005).

7.11. Cardio-protective activity

The cardioprotective activity of the aqueous and ethanolic fruit peel extract was assessed using the marker enzymes lactate dehydrogenase (LDH), serum glutamate oxaloacetate transaminase (SGPT), serum glutamate pyruvate transaminase (SGOT), and creatine phosphokinase (CPK) all of which were considerably increased by isoproterenol. The cardiac damage was greatly reversed by extract coadministration. Verapamil was used as a reference medication (Thangarajan et al., 2015).

Isoproterenol-induced heart injury is reversed by *P. dulce* fruit and floral extracts. The effects of plant extracts against myocardial infarction were substantially identical to those of the common cardioprotective drug verapamil (Srinivas et al., 2018).

7.12. Cytotoxicity activity

P. dulce leaf extract demonstrated a significant effect on breast cancer cells. The methanolic extract was used by (Poongodi and Hemalatha, 2015) and The IC_{50} value was found to be 112 µg $ml^{-1,}$ and 100% cell inhibition was achieved at 300 µg ml^{-1}. On the other hand, (Sharma, 2016) used the crude aqueous extract and the cytotoxicity was time and dose-dependent because 300 mg ml^{-1} of the extract reduced cell viability to 50% (IC_{50}) in 48 hours.

The bark and leaf extracts were studied against cervical cancer cells (HeLa) (López et al., 2013), human colorectal adenocarcinoma cell line (Caco-2) (Knauth et al., 2018), and hepatocellular (HepG-2) and colon (HCT-116) cell lines (Kotb et al., 2020). The first demonstrated that the aqueous bark extract was more cytotoxic than the leaf aqueous and ethanolic extracts. The second showed that the

methanolic leaf extract was more cytotoxic than the bark extract. While the third reported that the lipophilic fractions had no significant cytotoxic effect against HCT-116 and HepG-2.

P. dulce aqueous and ethanolic bark extracts' cytotoxic effects were assessed against three cell lines MCF-7, HCT-116, and HepG2 using the conventional MTT colorimetric technique at various doses. With a 1.71% cell viability, the plant's aqueous extract showed the highest level of toxicity against HepG2. On the other hand, with a viability of 6.05%, the ethanolic extracts had the highest toxicity against HCT-116. The plant's bark can be used to make anticancer medications using the right standardized techniques (Jalique et al., 2017).

The identified component Kaempferol-3-O-α-L-rhamnoside from the ethyl acetate fraction of the leaves methanolic extract demonstrated an anti-tumor effect on Ehrlich ascites carcinoma cells (EAC). The standard anticancer medicine vincristine demonstrated growth inhibition of 77.84±6.69% while the extract demonstrated 70.89 ± 6.62% EAC cell growth inhibition (Akter et al., 2022).

A significant activity of hydroalcoholic fruit extract against murine melanoma (B16F10) and lung adenocarcinoma in humans (A549) by MTT assay was reported with IC_{50} =119 and 114 g ml^{-1} respectively (Dhanisha et al., 2022a).

P. dulce seeds crude methanolic extract at different concentrations was utilized to evaluate the cell viability of colorectal (LoVo), human umbilical vein endothelial cells (HUVECs), MCF-7, and A-549 cell lines using MTT assay and doxorubicin as positive control. The LoVo cell line viability % was inhibited in a concentration-dependent manner by increasing the cell apoptosis rate, the number of cells at the sub-G1 phase of the cell cycle, and decreasing the rate of migration of LoVo cells in the scratch assay. When compared to LoVo cells IC_{50} 3.03 ± 0.1, the extract had a reduced cytotoxic effect on HUVEC with an IC_{50} of 6.24 ± 0.25 µg/ml. Octadecanedioic acid, hydroxystearic acid, linoelaidic acid, soya-saponin III, and kaempferol 7-O-beta-D-glucopyranoside were isolated in the same study and correlated to the anticancer activity (Alhamed et al., 2023).

7.13. Hepato-protective activity

Two studies were made to prove the hepatoprotective effect of *P. dulce* fruit (Manna et al., 2011) used the aqueous extract against carbon tetrachloride (CCl_4)-induced hepatic injury, while (Raju and Jagadeeshwar, 2014) used the ethanolic and aqueous extracts against alcohol and paracetamol-induced hepatic injury and silymarin as a standard drug. The first study showed that both pre and post-treatment with the extract protected against hepatic damage induced by CCl_4.The second study showed a significant hepatoprotective effect of the extracts compared to the toxic control.

Under *in vivo* conditions, *P. dulce* bark extract exhibited hepatoprotective activity at concentrations of 100 and 200 mg kg^{-1}. The extract resulted in a significant reduction in hepatic enzymes when compared with acetaminophen (Singh and Shukla, 2013).

In paracetamol-induced hepatotoxicity, an ethanolic extract of *P. dulce* leaves significantly reduced SGOT, SGPT, alkaline phosphatase (ALP), triglyceride, and bilirubin levels (Sul et al., 2021).

7.14. Mosquito repellent activity

Mosquito repellents obtained from natural sources can be used instead of chemically based repellents, which are usually poisonous to other creatures and may cause respiratory defects in humans. The aqueous leaf extract used for the synthesis of silver nanoparticles showed significant larvicidal activity against *C. quinquefasciatus* (Raman et al., 2012).

Various *P. dulce* leaf and seed extracts were tested for larvicidal and ovicidal effectiveness against mosquito vectors *Anopheles stephens*i and *Aedes aegypti*. The methanolic leaf extract demonstrated the most activity(Govindarajan et al., 2013).

Govindarajan and Rajeswaryn (2014) tested the adulticidal activity of *P. dulce* leaf and seed various solvent extracts against the filariasis vector mosquito *Culex quinquefasciatus*. Methanol extract had the strongest larvicidal and ovicidal action, followed by ethyl acetate, chloroform, benzene, and hexane extracts. The highest death rate (100%) was recorded at 500 mg L^{-1} and 750 mg L^{-1} of the leaf and seed extracts, respectively. Furthermore, crude extracts of the plant's leaf and seed protected against mosquito bites in a concentration-dependent way while causing no adverse reactions (Govindarajan and Rajeswary, 2015).

P. dulce leaf hydroalcoholic extract and its fractions were reported to possess an ovicidal activity against *Haemonchus contortus.* The isolated compounds coumaric acid, ferulic acid, quercetin, luteolin 7-O-rhamnoside and may be responsible for the activity (Olmedo-Juárez et al., 2022).

7.15. Nephroprotective activity

P. dulce fruit aqueous extract was given orally before and after the CCl4-producing toxin. Because of *P. dulce's* antioxidant activity, the crude extract reduced lipid peroxidation and protein carboxylation following CCl4 toxication. When compared to untreated rats given CCl4, the reactive oxygen species (ROS) were lower in the extract-treated animals, while antioxidant enzymes were higher. The aqueous extracts also inhibited and protected against renal DNA damage and cell death, hence preserving the kidneys from CCl4-induced oxidative damage (Pal et al., 2012).

A study was made to investigate the antioxidant benefits of *P. dulce* fruit methanolic extract against methotrexate (MTX)-induced hepatic and renal toxicities. Following oral administration of the extract at 40 mg kg^{-1} body weight for 10 days straight, the serum markers of the hepatic and renal toxicity and the levels of the pro-inflammatory cytokines, such as tumor necrosis factor-alpha (*TNF-α),* interleukin 6 (*IL-6)* and interleukin 1-beta *(IL-1β)* were reduced. When compared to the MTX alone group, the extract reduced the levels of tissue oxidative stress markers and improved the antioxidant status in the liver, kidneys, and lungs of mice (Dhanisha et al., 2021).

7.16. Neuropharmacological activity

Leaf aqueous and alcoholic extracts showed a clear reduction in locomotor activity, motor coordination, and hypnosis production but were unable to reduce the convulsions or mortality in mice. The alcoholic extract significantly reduced CNS activity better than the aqueous extract (Sugumaran et al., 2008b; Mule et al. 2011).

The aqueous, ethanolic extracts and the crude flavonoid fraction of the leaf were assessed for anticonvulsant activity using the maximal electroshock-induced seizure test and pentylenetetrazol (PTZ) assay. Phenytoin sodium was used as a standard drug. The results showed significant anticonvulsant activity (Sugumaran et al., 2008; Dhivya and Niranjan, 2013).

7.17. Spermicidal activity

Given the significance of saponins as potential spermicidal agents, tests for spermicidal properties were conducted on the saponins of *P. dulce*. Sapogenin demonstrated activity against human semen in a dilution of 0.03% (Shweta, 2013).

7.18. Acute and sub-acute toxicity

The hydroalcoholic fruit extract did not cause any hematological or biochemical abnormal changes. The LD_{50} was reported to be 3916 mg kg^{-1} and the potential minimum and maximum effective doses were found to be 100 and 300 mg kg^{-1} respectively (Megala and Geetha, 2012).

The up-down regulation approach was used to investigate the acute oral toxicity of the leaf ethanolic extract and the crude flavonoid fraction. They were safe at doses of up to 2000 mg kg^{-1} (Dhivya and Niranjan, 2013), whereas the saponin-enriched fraction of the seed extract was safe in mice at doses of up to 2000 mg kg^{-1} (Kumar et al., 2017).

The oral administration of 5 g kg^{-1} body weight as a single dose of the bark hydroalcoholic extract to Wistar rats resulted in no deaths or hazardous signs for 4 hours post-dose administration and 14 consecutive days. The LD_{50} of stem bark extract is higher than 5 g/kg (Toudji et al., 2017).

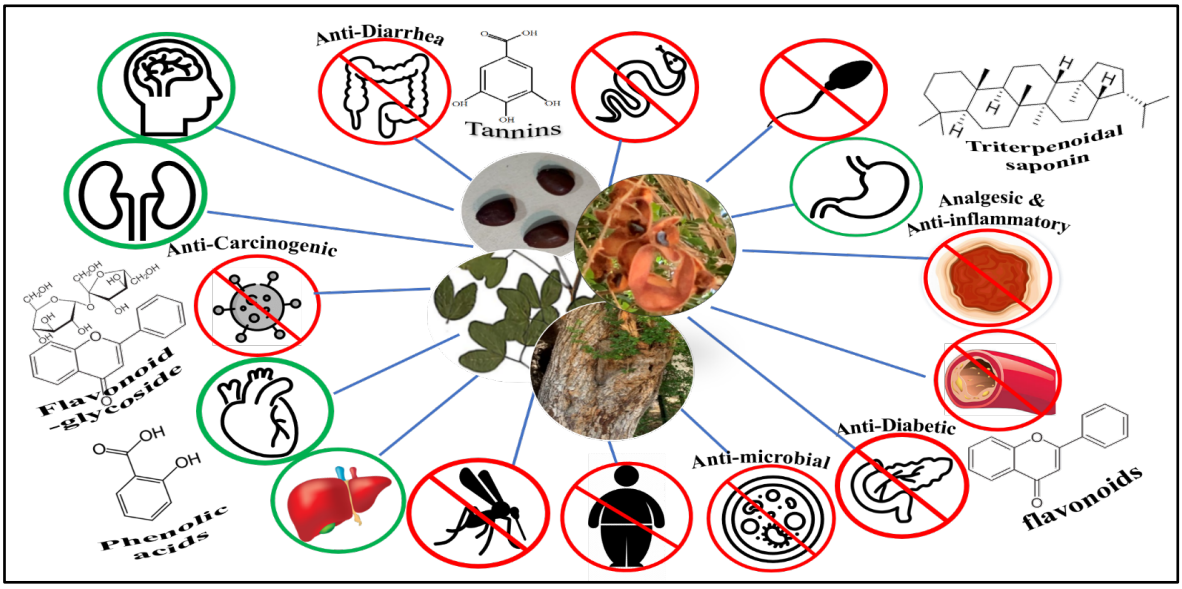


Figure 3. Different pharmacological activities of *Pithecellobium dulce* (Roxib.) Benth.

8. Conclusion

This review covers information regarding traditional uses, nutritional values, phytochemicals, and pharmacological activities of the different extracts as well as the pure compounds and the analysis of active compounds related to *P. dulce.* The various parts of the plant were utilized traditionally in treating many disorders in many countries. *P. dulce* provides important vitamins, amino acids, critical minerals, and many fatty acids which contribute to its nutritive value. The plant contains many chemical constituents such as triterpenoids, flavonoids, saponins, steroids, and glycosides which are responsible for many pharmacological activities. There is evidence from different *in-vivo* and *in-vitro* studies that the extracts and pure compounds found within *P. dulce* have antimicrobial, hepatoprotective, nephroprotective, cardioprotective, anticancer, antidiabetic, and antiulcerogenic activities via multiple pathways. Even though the chemical structure and pharmacological potential of a few of the constituents are known, the mechanisms of action must be studied further before they can be developed into therapeutics.

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Conflict of Interest

The authors have confirmed that there are no conflicting interests.

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