Characterizing ADME/T and Physicochemical Properties of Bioactive Compounds from Manila Tamarind for Therapeutic Insights

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Abstract
Medicinal plants have been utilised in traditional medicine for centuries, providing healthcare to 80% of the global population. Manila tamarind (Pithecellobium dulce) is an underutilised plant with limited study into its therapeutic uses. This work is to investigate the physicochemical features and therapeutic potential of bioactive compounds from Pithecellobium dulce using computational drug analysis databases. A total of 38 active phytocompounds were found through a comprehensive analysis of plant bioactive chemicals based on a literature survey. Additionally, the physicochemical characteristics and toxicity of these compounds with therapeutic advantages were examined using computational databases such as PubChem and Swiss ADME/T, Boiled egg, Bio-radar.

Manila tamarind (P. dulce) components contain phenols, flavonoids, saponins, and other compounds. Furthermore, these chemicals have been shown to be effective in the management of health benefits. The study highlights P. dulce as a valuable medicinal plant due to its wide variety of biologically active compounds with nutraceutical properties. However, further clinical research is necessary to confirm its therapeutic applications and potential for commercial use.

Keywords: Phytochemicals, Traditional medicine, PubChem, Boiled egg, ADME/T.

Introduction

Natural products and plants have long been important sources of pharmaceutical substances, which have been utilised to treat a wide range of human illnesses[1]. Many natural substances with a broad range of pharmacological activity can be found in medicinal plants. As dietary supplements, nutraceuticals have been getting a lot of attention recently because of their beneficial physiological activity on the human body[5]. In addition to being a suggested source of nutrients, plants are also recommended for their medicinal properties. The mixture of molecules that comprises of phytochemicals derived from plants has special biological action[8,14]. *Pithecellobium dulce* (Roxb) Benth, belonging to the Fabaceae family, is a small to medium-sized, spiny, evergreen tree that grows widely across the plains of India and the Andaman Islands. The fruit is edible and has rich source of protein (2.3–3 g), fat (0.4–0.5 g), carbohydrates (18.2–19.6 g) and energy (79 cal)[3]. *Manila tamarind* contains considerable amounts of vitamins and minerals such as vitamin C (133 mg), thiamine, vitamin A, riboflavin, niacin, calcium, phosphorus, iron, sodium, and potassium. With this nutrient-rich profile, it provides many health benefits.

Additionally, the fruit is a good source of bioactive phytochemicals[6]. The present study aims to investigate the physicochemical and therapeutic properties with chemical structure of bioactive compounds and toxicity level of compounds in *Pithecellobium dulce* by using the computational data base.

Plant morphology: The tree *Pithecellobium dulce* has bipinnate compound leaves and can reach a height of 10 to 15 meters. Two ovate-oblong, apiculate leaflets, each measuring roughly 2–4 cm in length, are present on each pinna. At its base, each leaflet usually includes a pair of slender spines that range in size from 2 to 15 mm. The tree has a spiky trunk as well. They are white or greenish, with a faint scent, and are between 0 and 1.5 cm in size. Fused together at the base, each flower bears 50 thin stamens and a hairy corolla. The pods are reddish-pink to greenish-brown[4,14].

Botanical description[15]
Domain: Eukaryota
Kingdom: Plantae
Phylum: Spermatophyta
Subphylum: Angiospermae
Class: Dicotyledonae
Order: Fabales
Family: Fabaceae
Genus: *Pithecellobium*
Species: *Pithecellobium dulce*

Table 1
Chemical constituents

Component	Percentage /Amount
Tannins (Bark)	25.36%
Fixed Oil (Olein)	18.22%
Protein Content (Seeds)	50.3-67.1%
Polyphenols (Total)	294mg/100g

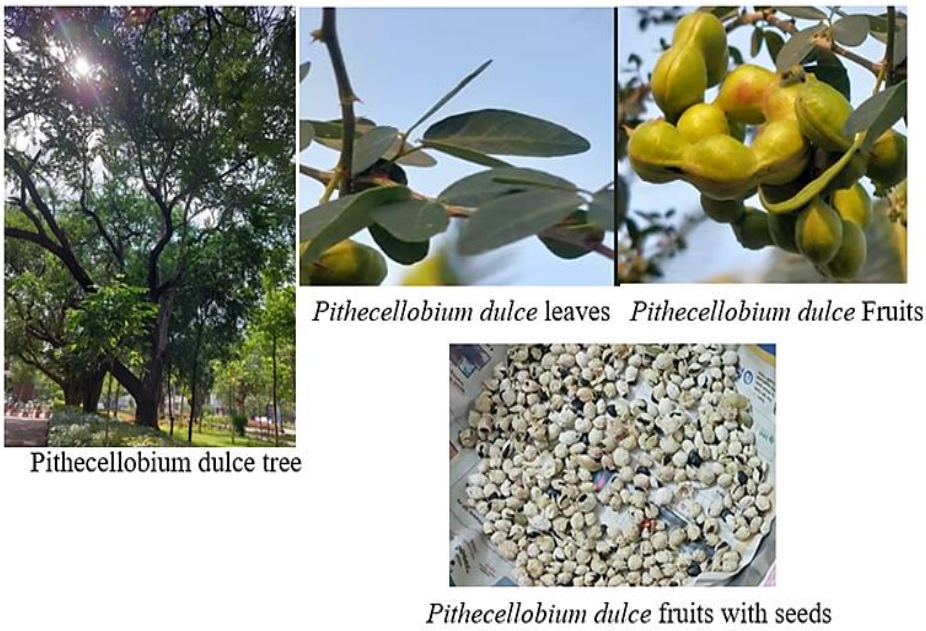


Figure 1: Fruits, leaves and seeds of *Pithecellobium dulce*

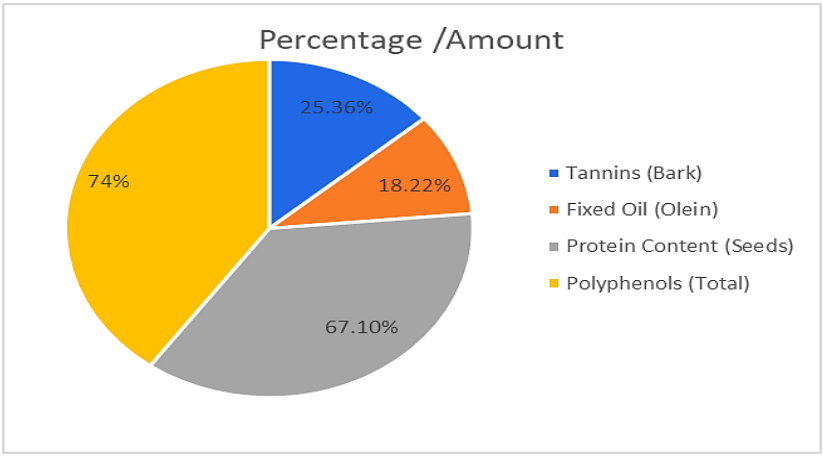


Figure 2: Pie chart showing chemical constituents in percentages.

Chemical constituents

- There are 18.22% fixed oil, mostly olein, and 25.36% tannins in the composition. The plant contains a glycoside that has been identified as quercetin.
- Steroids, saponins, lipids, phospholipids, glycosides, glycolipids, and polysaccharides are among the many substances described in the seeds.
- 37% of the bark contains catechol-type tannins. The leaves contain afzelin, dulcitol, kaempferol, and quercetin.
- Seed extract's fatty acid composition revealed nine saturated and seventeen unsaturated fatty acids. From 50.3% to 67.1%, seeds have the highest total protein concentration. Stems, roots, leaves, flowers, and fruits come next.
- Protein content of 39.22%, calcium of 48 mg, and phosphorus of 542 mg per 100 g were found in the seed protein flour.
- Leucine, arginine, aspartic acid, glutamic acid, lysine, valine, and threonine were the main amino acids. An amino acid's essential to non-essential ratio was 0.61. The total amount of polyphenols was 294 mg/100g[10,11].

Material and Methods

Screening of Bioactive compounds from *Pithecellobium dulce* by database and literature: All the bioactive compounds of *Pithecellobium dulce* were obtained from literature survey, and their physicochemical and toxicity properties data were obtained using PubChem software. We retrieved the chemical structures of the bioactive compounds in 2D formats, along with their molecular formulas and molecular weights, all sourced from https:// pubchem.ncbi.nlm.nih.gov/[9].

Physicochemical properties retrieved by Swiss ADMET data bases: Swiss ADMET software was used to predict the physicochemical properties of the selected active compounds, which included hydrogen bond donors (HBD), hydrogen bond acceptors (HBA), the total number of rotatable bonds (TNRB), partition coefficient (log P),

aqueous solubility (log S), polarizability, total polar surface area (TPSA), and atomic molar refractivity (AMR). Furthermore, data on gastrointestinal absorption (GI), blood-brain barrier (BBB) permeability, lipophilicity, bioavailability, and Lipinski's rule including any breaches, were acquired using the Swiss ADME software http://www.swissadme.ch[2,12,13].

Results and Discussion

Physicochemical properties retrieved by Swiss ADMET data bases: The physicochemical properties of all bioactive substances obtained from the Swiss ADME database, as well as data from boiled egg assays, proved their potential to penetrate the blood-brain barrier (BBB) and indicated gastrointestinal absorption. According to the bio-radar principle, the pink lines indicate that these chemicals are deemed safe medications.

Canonical smiles of bioactive compounds: Canonical SMILES is a type of system that uniquely encodes the structure of chemical compounds, making them simple to read and analyse. Each bioactive chemical has a unique SMILES sequence that encodes its molecular properties which is used in computational biology and drug discovery. While it does not immediately reflect biological activity, it connects to databases that allow for the study of chemical compounds and their biological impacts.

Boiled egg: Through the boiled egg database obtained through the Swiss ADME software, we found that out of 21 bioactive compounds processed, 3 molecules have shown outside specified ranges, while 8 molecules were able to cross the blood-brain barrier (BBB), and 10 molecules were detected in the gastrointestinal region. This data indicates that these active compounds possess potential nutraceutical properties.

Bioavailability Bio radar: Bio-radar is graphical presenting data which was retrieved from the Swiss ADME to show a compound's drug-likeness. The bio-radar graphic shows various pharmacokinetic and physicochemical properties including lipophilicity, size, polarity, solubility, flexibility, and saturation. Compounds in the "pink area" of the radar appear to have favourable drug-like characteristics indicating possible safety and efficacy.

Physicochemical Properties: The table 4 indicates that the ADME property with molecular weight should be <500 g/mol, total polar surface area (TPSA Å²) <140, Log Po/w (iLOGP) lipophilicity <5. Physicochemical properties are crucial in the pharmaceutical field because they directly affect the development, efficacy, safety, and performance of drugs.

Health benefits[7]

- Prevents infection by boosting immune system
- Brightens the skin
- Prevents hair loss
- Treats greasy scalp
- weight management
- improves the fertility
- beneficial for the bile-related disorders
- Helps in reducing fever
- Remedies malaria
- Combats jaundice
- Improves blood flow
- Helps regulate blood glucose
- Reduces inflammation
- Soothes mouth sores
- Helps prevent cancer
- Reduces skin pigmentation
- Heals acne and blemishes
- Fades dark spots
- Acts as a natural skin hydrator
- Used to treat sexually transmitted diseases
- improves the digestion
- Bark – Helps relieve constipation
- Manila tamarind is also recommended for managing diabetes
- Rich in vitamin C, which enhances antioxidant properties

Table 2
List of Bioactive compounds form *Pithecellobium dulce* various parts of tree[11]

Sources	List of bioactive compounds
Leaf extract of Manila tamarind	• Cyclitol, Dulcitol, Octacosanol, α-Spinasterol, Quercetin, Afzelin
Fruit extract of Manila tamarind	• Naringenin, Quercetin, Rutin, Gallic Acid, Stigmasterol, Clonazepam, Quinoline, Nootkatone, Juipene, Calarene, Eremophiline, Valencene, Baicalin, 2,5,6-Trimethyl 1,3-oxathiane, Trans 3-methyl-2N-propylthiophane, D-Pinitol, Hexadecanoic Acid, Hepatacosanoic Acid, Tetraneurin-F, Ethyl 2-bromo-4-methyl-6-dimethylsilylbenzothiophene-5-carboxylate,2-Propyl Tetrahydropyran-3-ol
Seed extract of Manila tamarind	• Pithedulosides A, B, C, D, F, I, K, Pithecelloside, Dulcin
Bark extract of Manila tamarind	• β-sitosterol, Stigmasterol, α-spinasterol C, Ampesterol.

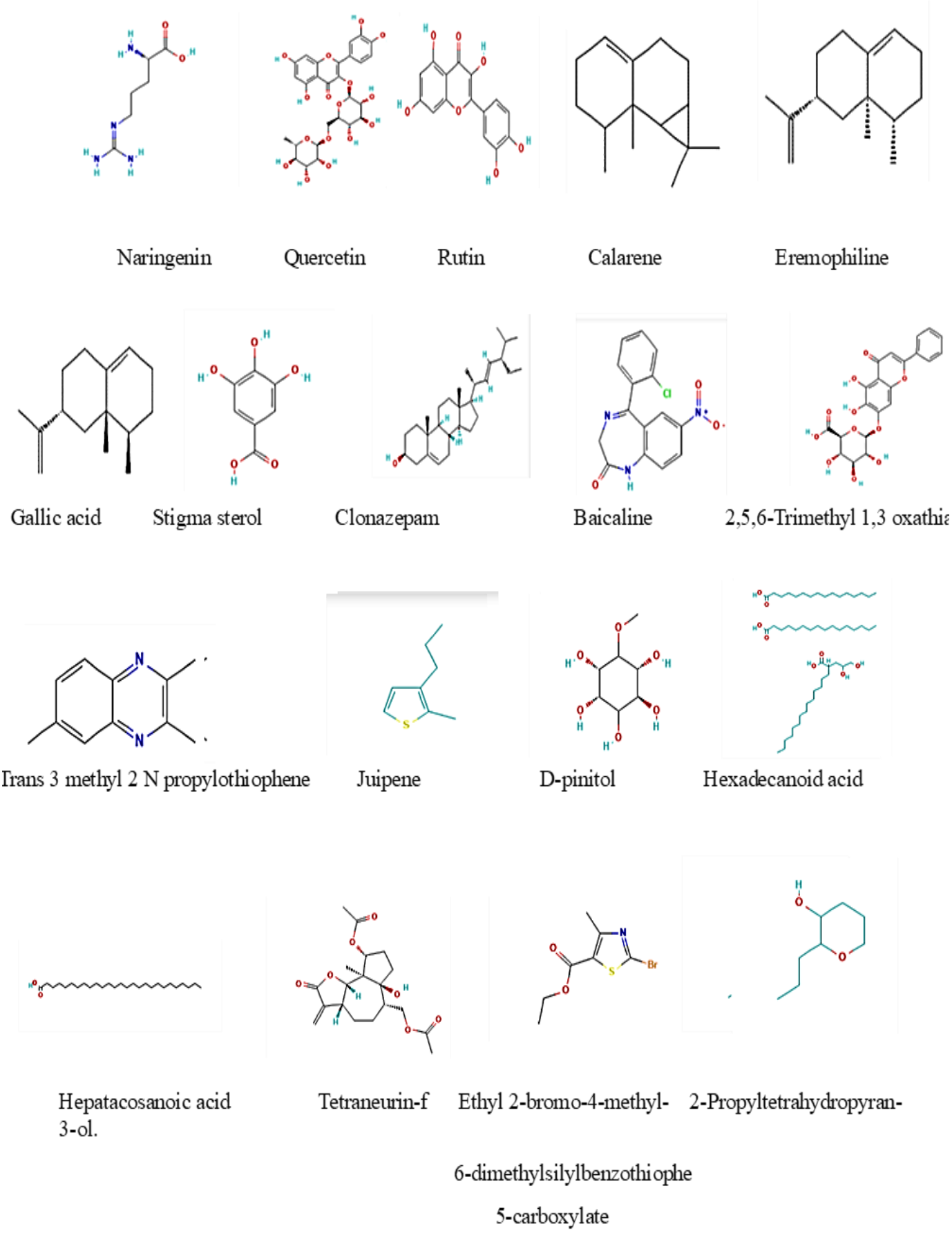


Figure 3: Chemical structure of Bioactive compounds from *Pithecellobium dulce* fruits

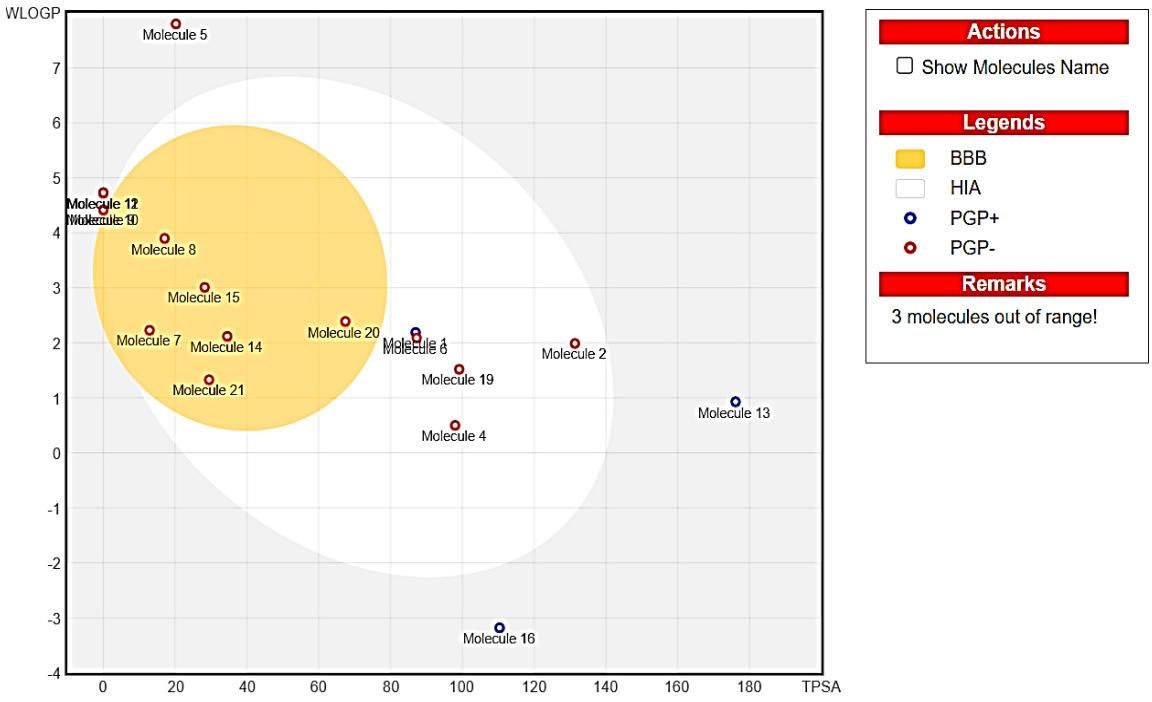
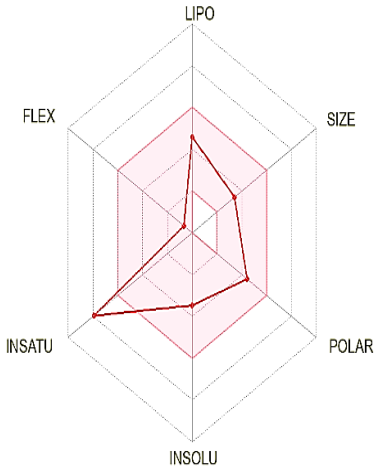


Figure 4: Boiled egg indicating yellow region -BBB (Blood brain barrier) and white region- GI (Gastro intestinal absorption)

Table 3
List of Canonical Smiles

S.N.	Compound Name	Canonical Smiles
1	Naringenin	C1C(OC2=CC(=CC(=C2C1=O) O) O) C3=CC=C(C=C3) O
2	Quercetin	C1=CC(=C(C=C1C2=C(C(=O) C3=C(C=C(C=C3O2) O) O) O) O) O
3	Rutin	CC1C(C(C(C(O1) OCC2C(C(C(C(O2) OC3=C(OC4=CC(=CC(=C4C3=O) O)O)C5=CC(=C(C=C5)O)O)O)O)O)O)O)O
4	Gallic acid	C1=C(C=C(C(=C1O)O)O)C(=O)O
5	Stigma sterol	CCC(C=CC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)O)C)C)C(C)C
6	Clonazepam	C1C(=O)NC2=C(C=C(C=C2)[N+](=O)[O-])C(=N1)C3=CC=CC=C3Cl
7	Quinoline	C1=CC=C2C(=C1)C=CC=N2
8	Nootkatone	CC1CC(=O)C=C2C1(CC(CC2)C(=C)C)C
9	Juipene	CC1(CCCC2(C3C1C(C2=C)CC3)C)C
10	Calarene	CC1CCC=C2C1(C3C(C3(C)C)CC2)C
11	Eremophiline	CC1CCC=C2C1(CC(CC2)C(=C)C)C
12	Valencene	CC1CCC=C2C1(CC(CC2)C(=C)C)C
13	Baicaline	C1=CC=C(C=C1)C2=CC(=O)C3=C(C(=C(C=C3O2)OC4C(C(C(C(O4)C(=O)O)O)O)O)O)O
14	2,5,6-Trimethyl 1,3 oxathiane,	CC1CSC(OC1C)C
15	Trans 3 methyl, 2N-propylthiophane	CCCC1=C(SC=C1)C
16	D-pinitol	COC1C(C(C(C(C1O)O)O)O)O
17	Hexadecanoid acid	CCCCCCCCCCCCCCCC(=O)O.CCCCCCCCCCCCCCCC(=O)O.CCCCCCCCCCCCCCC(CC(CO)O)C(=O)O
18	Hepatacosanoic acid	CCCCCCCCCCCCCCCCCCCCCCCCCC(=O)O
19	Tetraneurin-f	CC(=O)OCC1CCC2C(C3(C1(CCC3OC(=O)C)O)C)OC(=O)C2=C
20	Ethyl 2-bromo-4-methyl-6-dimethylsilylbenzothiophe 5-carboxylate	CCOC(=O)C1=C(N=C(S1)Br)C
21	2-Propyltetrahydropyran-3-ol	CCCC1C(CCCO1)O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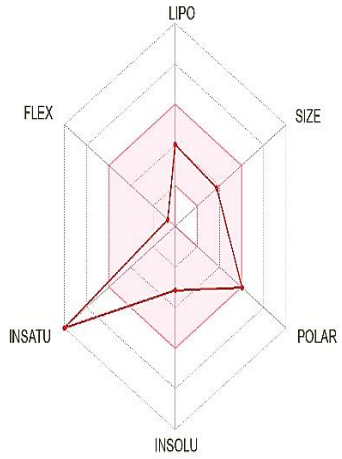
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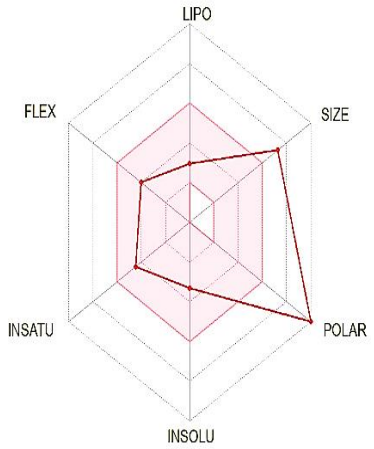
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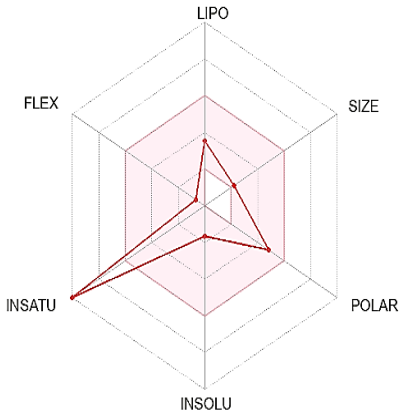
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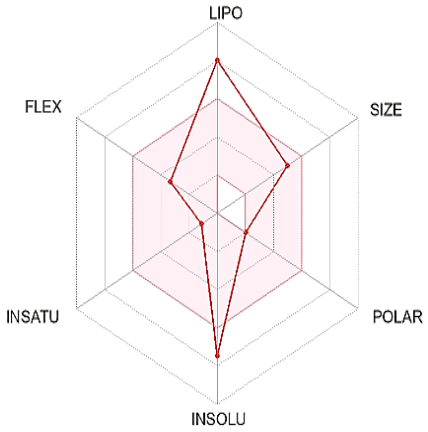
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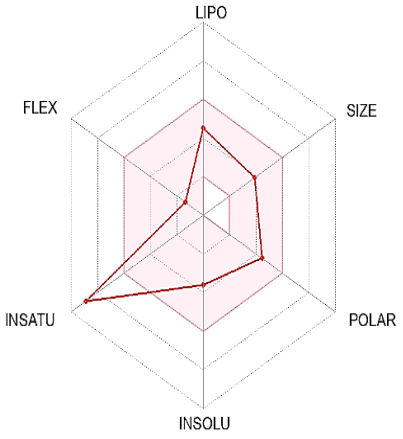
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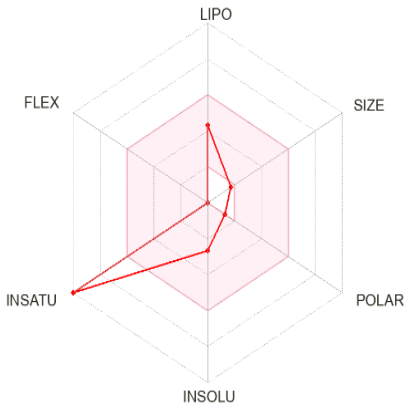
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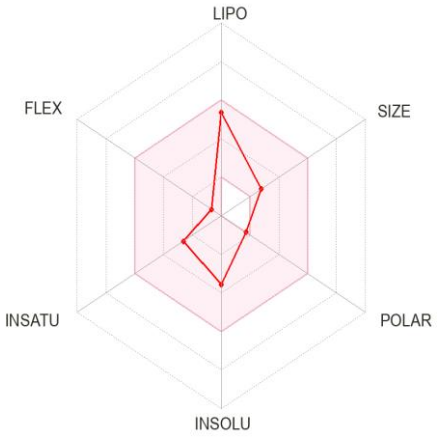
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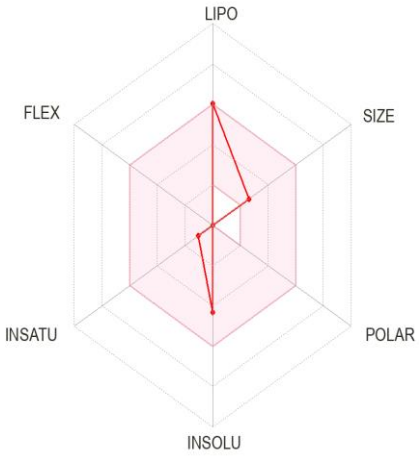
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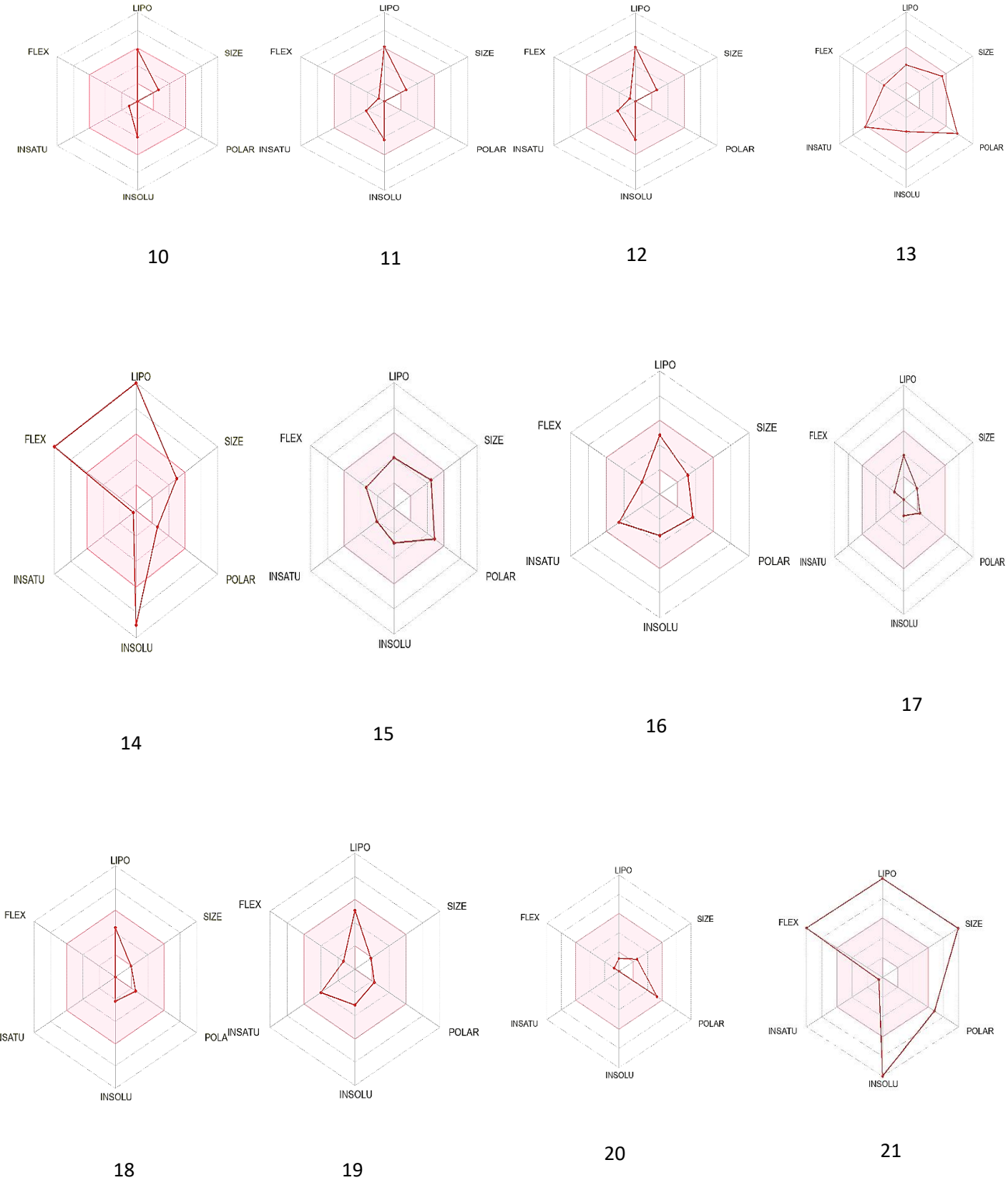

Figure 5: *Pithecellobium dulce* fruits Bioavailability Radar (Bio radar) a. red area: This indicates the optimal range for each parameter. B. Blue polygon: Represents the properties of the molecule. 1. Naringenin, 2. Quercetin, 3. Rutin, 4. Gallic acid, 5. Stigma sterol, 6. Clonazepam, 7. Quinoline, 8. Nootkatone, 9. Juipene, 10. Calarene, 11. Eremophiline, 12. Valencene, 13. Baicaline, 14. 2,5,6-Trimethyl 1,3 oxathiane, 15. Trans 3 methyl, 2N-propylthiophane, 16. D-pinitol, 17. Hexadecanoid acid, 18. Hepatacosanoic acid, 19. Tetraneurin-f, 20. Ethyl 2-bromo-4-methyl-6-dimethylsilylbenzothiophe-5-carboxylate, 21. 2 Propyltetrahydropyran-3-ol.

Table 4
Physicochemical properties with detail data.

S. N.	Name of the bioactive compounds	Molecular weight <500 g/mol	Formula	TPSA Å² <140	Log Po/w (iLOGP) <5	Water Solubility	GI absorption	BBB permeant	Bioavailability Score
1	Naringenin	272.25	$C_{15}H_{12}O_5$	86.99	1.75	Soluble	High	No	0.55
2	Quercetin	302.24	$C_{15}H_{10}O_7$	131.36	1.63	Soluble	High	No	0.55
3	Rutin	610.52	$C_{27}H_{30}O_{16}$	269.43	1.58	Moderately soluble	Low	No	0.17
4	Gallic acid	170.12	$C_7H_6O_5$	97.99	0.21	Soluble	High	No	0.56
5	Stigma sterol	412.69	$C_{29}H_{48}O$	20.23	5.01	Poorly soluble	Low	No	0.55
6	Clonazepam	315.71	$C_{15}H_{10}ClN_3O_3$	87.28	1.63	Soluble	High	No	0.55
7	Quinoline	129.16	C_9H_7N	12.89	1.73	Very soluble	High	No	-5.65
8	Nootkatone	218.33	$C_{15}H_{22}O$	17.07	2.86	Soluble	High	No	-4.89
9	Juipene	204.35	$C_{15}H_{24}$	0.00	3.14	Moderately soluble	Low	No	0.55
10	Calarene	204.35	$C_{15}H_{24}$	0.00	3.20	Moderately soluble	Low	No	0.55
11	Eremophiline	204.35	$C_{15}H_{24}$	0.00	3.32	Moderately soluble	Low	No	0.55
12	Valencene	204.35	$C_{15}H_{24}$	0.00	3.32	Moderately soluble	Low	No	0.55
13	Baicaline	446.36	$C_{21}H_{18}O_{11}$	176.12	1.94	Moderately soluble	Low	No	0.11
14	2,5,6-Trimethyl1,3 oxathiane,	146.25	$C_7H_{14}OS$	34.53	2.29	Soluble	High	Yes	0.55
15	Trans3methyl,2N-propylthiophane	140.25	$C_8H_{12}S$	28.24	2.47	Soluble	High	Yes	0.55
16	D-pinitol	194.18	$C_7H_{14}O_6$	110.38	0.36	Highly soluble	Low	No	0.55
17	Hexadecanoid acid	843.35	$C_{51}H_{102}O_8$	152.36	11.34	Insoluble	Low	No	0.11
18	Hepatacosanoic acid	410.72	$C_{27}H_{54}O_2$	37.30	6.52	Insoluble	Low	No	0.85
19	Tetraneurin-f	366.41	$C_{19}H_{26}O_7$	99.13	99.13	Soluble	High	No	0.55
20	Ethyl 2-bromo-4-methyl-6dimethylsilyl benzothiophe 5-carboxylate	250.11	$C_7H_8BrNO_2S$	67.43	2.58	Moderately soluble	High	Yes	0.55
21	2-Propyltetrahydro pyran-3-ol	144.21	$C_8H_{16}O_2$	2.15	2.15	Very soluble	High	Yes	0.55

Conclusion

Our findings highlight that the bioactive compounds from M *Pithecellobium dulce* provide significant nutraceutical potential. The fruits exhibit pharmaceutical properties. Through PubChem, we identified the physicochemical properties and chemical structures of these compounds while ADME software provided insights into their toxicity, including their ability to cross the blood-brain barrier (BBB) and undergo gastrointestinal absorption. All bioactive compounds show a range of health benefits, highlighting that often-overlooked fruits can be valuable resources. With its content of micronutrients and nutraceuticals, this fruit has the potential to contribute to a balanced diet.

Further research, including *in vivo* and *in vitro* studies, is needed to explore the full efficacy of these compounds for therapeutic applications.

Acknowledgement

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