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A comprehensive review on the medicinal properties of Manilkara zapota (L.) P. Royen

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ABSTRACT

Manilkara zapota (M.zapota), often known as Sapodilla or chikoo, is a tropical evergreen tree native to Central America but grown in diverse regions worldwide. Beyond its delectable fruit, M. zapota has been subject of growing interest due to its rich pharmacological properties. This review aims to compile and analyse the existing literature on the medicinal aspects of M. zapota, shedding light on its diverse range of bioactive compounds and potential health benefits. The major secondary metabolites obtained from M. zapota are polyphenols. Multiple researchers have documented a plethora of phytoconstituents derived from the plant, contributing to a spectrum of biological impacts, such as anti-inflammatory, rthritis, antibacterial, antifungal, antioxidant, antitumour, and antidiabetic effects, as well as central nervous system (CNS) depressant activities. Moreover, this review encompassed the extensive utilization of different plant parts, including leaves, fruit, and seeds. M. zapota leaves contains various bioactive compounds, including antioxidants and phytochemicals. Investigating its chemical composition can help identify compounds that may have neuroprotective or anti-inflammatory properties relevant to Parkinson's disease. Antioxidants from M. zapota leaves compound may help reduce oxidative damage to neurons and slow disease progression.

KEYWORDS: Manilkara zapota, Sapotaceous, polyphenols, antioxidant, CNS depressant activity.

I. INTRODUCTIONTO MANILKARA ZAPOTA

Sapodilla, scientifically known as M. zapota, is a perennial tree originating from Central America, southern Mexico, and the region of the West Indies. Its cultivation spans across regions, with substantial yields found not just in Mexico but also in a range of tropical Asian nations, including India, Pakistan, Thailand, Malaysia, Cambodia, Indonesia, Vietnam, and Bangladesh[1].

It thrives in rocky, highly calcareous, well drained soils prevalent in southern Florida, while also demonstrating adaptability to slightly alkaline soils and medium-textured loams[2].Sapota cultivation in India covers approximately 162 thousand hectares, contributing to an annual production of around 1358 thousand tonnes[3].

Additionally, it contains chemical compounds such as sugar, protein, ascorbic acid, phenolics, carotenoids, glycoside sapotinine, and minerals like iron, copper, zinc, calcium, and potassium. This makes it an outstanding nutrition with applications in managing various conditions such as inflammation, pain, and diarrhoea. In conventional practices, it is employed as a diuretic medication, expectorator, and in ophthalmology. The primary constituents found in sapodilla leaves include lupeol acetate, oleanolic acid, apigenin-7-O-α-L-rhamnoside, myricetin-3-O-α-L-rhamnoside, and caffeic acid[4].

Multiple researchers revealed that M. zapota leaves exhibit inherent cytotoxic, antioxidant, antimicrobial, and mild central nervous system (CNS) depressant activities. These properties suggest potential therapeutic applications in addressing cancer, tumours, infectious diseases, and oxidative stress[5].

II. BOTANICAL DESCRIPTION

Branches: M. zapota is an evergreen tree that grows slowly, ranging from 5-20 m in cultivation but reaching heights of up to 40 m in forested conditions. The trunk typically has a mean diameter of 1.5 m.The crown exhibits a pyramidal to rounded shape, and the branches can be either horizontal or drooping[6].

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Figure 1: Tree of M. zapota

Leaves: Characterized by their ornamental quality, the leaves of the M. zapota are evergreen and glossy. They are arranged alternately in a spiral cluster at the tips of forked twigs. These elliptic leaves feature pointed ends, possess a firm texture, and measure between 7.5-11.25 cm in extend in lengthwise and 2.5-4 cm in breadth[7].


Figure 2: Leaves of M. zapota

Flower: The flowers are diminutive and bell-shaped, adorned with three outer sepals exhibiting a brown-hairy texture, and three inner sepals that envelop the pale-green corolla accompanied by six stamens. These blooms are supported by slender stalks located at the bases of the leaves.


Figure 3: Flowers of *M. zapota*

Fruit: The sapodilla fruit, categorized as a berry, is abundant in sugars, ranging from 13 to 18 percent. When fully ripe, this fruit is not only delicious but is also commonly. Maturation typically takes about 240 to 270 days after flowering, and at full ripeness, the fruit adopts a dull orange or potato colour. In addition to its culinary uses, sapodilla fruits are incorporated into some Ayurvedic preparations. Sapodilla trees produces fruit twice annually, with flowering persisting year-round[7].


Figure 4: Fruits of *M. zapota*

Seeds: While certain sapodilla fruits are seedless, typically, there are 3 to 12 seeds that are easily detachable. These seeds are loosely arranged in a spiral pattern within slots at the centre of the fruit. They exhibit a brown or black colour with a white margin, characterized by a hard and glossy texture. These seeds are long-oval and flat, often presenting a distinct curved hook on one margin, measuring approximately 2 cm in length[8].


Figure 5: Seeds of *M. zapota*

Reproductive cycle: Sapodilla, characterized by outbreeding and self-incompatibility, features bisexual flowers with a stigma extending beyond the corolla, promoting cross-pollination. In the case of self-incompatible varieties, other sapodilla varieties facilitate cross-pollination for fruit production. The flowering and fruiting cycles persist throughout the year, with fruit maturation taking approximately 4 months. Seedlings generally start bearing fruit after 5-8 years, whereas grafted varieties tend to flower earlier, typically within 2-3 years of being planted[9].Essential to sapodilla is insect pollination, with key pollinators including Hermitia spp., Oecophylla smaragdina, Thripshawaiiensis, and Haplothrips tenuipennis. Honeybees also contribute to pollination by visiting sapodilla flowers for nectar collection, contributing to the pollination process[10].

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III.TAXONOMICAL CLASSIFICATION[11]

Kingdom: Plantae
Phylum: Magnoliophyta
Class: Magnoliopsida
Subclass: Dilleniidae
Order: Ebenales
Family: Sapotaceae
Genus: Manilkara
Species: zapota.

IV. VERNACULAR NAMES[12]

Hindi: Chikoo
Kannada: Chikku, Sapota
Marathi: Chiku
Tamil: Chimaiyiluppai, Chapotta
Telugu: Simaippacettu
Bengali: Sapeta
Konkani: Chikku
Mizo: Thei-chini.

V. HABITAT

Sapota thrives in environments with moderate to full shade and requires minimal watering. It prefers temperatures ranging from 12 to 36^0C and does not tolerate extremely high or low temperatures. Sapota flourishes in alluvial sandy loam soil or black soil with a pH level of 6-8. To optimize yield, it is recommended to sow sapota seeds between February and March, as well as August and October. Commonly used fertilizers for sapota cultivation include Farmyard Manure (FYM), phosphorous, potassium, and nitrogen[8].

VI. GEOGRAPHICAL DISTRIBUTION OF M. ZAPOTA

Sapodilla, native to tropical America, has its roots in regions such as Yucatan, southern Mexico, northern Belize, and northeastern Guatemala. It was cultivated in these areas long before the Spanish arrived and eventually introduced it to the Philippines. From there, it spread to Southeast Asia, including India, and now thrives in warm regions across the globe.

The M. zapota referred to Sapodilla as "chicle," and the Mayan Indians traditionally chewed the raw chicle latex. Interestingly, M. zapota prostitutes used chewing gum made from Sapodilla to advertise their trade during the pre-Columbian era.

Today, Sapodilla is cultivated commercially in various countries due to its delicious fruits. Indiastands out as one of the largest producers. Sapodilla, introduced to India in 1898, initially took root in the village of Gholwad in Maharashtra. With the support of Maharashtra farmers, it thrived and has since become a significant fruit industry in India, as noted by Singh (2004). It has been cultivated in Central America since ancient times and was introduced to tropical regions across the Americas, the West Indies, and even parts of the United States like Florida.

In Asia, it was first introduced to the Philippines by the Spanish and later spread to other countries in the region. Sri Lanka welcomed Sapodilla in 1802, primarily growing it in home gardens and parks.

Despite its long history and widespread cultivation, Sapodilla's commercial potential remains largely untapped, and it is not yet regarded as a mainstream fruit in many places. Limited literature is available on Sapodilla, and in Sri Lanka, it is mainly found in home gardens, parks, and fruit farms, primarily as a minor crop.

Overall, Sapodilla's journey from ancient civilizations to modern cultivation showcases its significance as a fruit crop with vast potential yet to be fully explored and exploited commercially [13].

VII. PHYTOCONSTITUENT OF M. ZAPOTA

The plant encompasses a diverse array of phytochemical elements, alkaloids, carbohydrates, glycosides, tannins, triterpenes, and flavonoids. Additionally, it harbours amino acids, proteins, ascorbic acid, phenols, carotenoids, and essential minerals like iron, copper, zinc, calcium, and potassium. Noteworthy is the substantial presence of vitamins, enhancing Chickoo's significance in the cosmetic application. The distribution of these constituents varies across distinct plant parts, including leaves, fruits, latex, seeds, and bark. Particularly, polyphenols emerge as the predominant compounds isolated from M. zapota fruits[14].

VIII. TRADITIONAL USES

- The diuretic properties of M. zapota fruits and chagrined seeds are employed to prevent swelling. Additionally, they play a role in averting the accumulation of renal and gall bladder stones.
- Sapota fruit is effective in reducing inflammation and pain associated with enterogastritis, acid reflux esophagitis, and bowel disorders. The paste derived from sapota seeds is utilized to reduce discomfort and inflaming caused by prick and bites. Furthermore, M. zapota contributes to intestinal

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strength, enhances immunity, and provides protection against bacterial infections, due to its Vitamin C content.

- Due to its rich nutritional content, Sapota is beneficial during pregnancy, helping to alleviate weakness, nausea, and dizziness while also preventing anaemia.
- A concoction prepared from the bark and fruit is employed to address body temperature and loose motions. Bark tea is effective in treating dysentery, and it is also beneficial for alleviating constipation and haemorrhoid.
- The inclusion of fibre and vitamin A in sapota fruit acts as a preventative measure against colorectal cancer (CRC), bronchogenic carcinoma, and oropharyngeal cancers.
- The infusion of M. zapota flowers and fruits not only alleviates respiratory disorders but also serves as a preventive measure against them.
- Sapota fruit also possesses effective anti-spasmodic agent.
- Because of its nutrient-rich composition, sapodilla can be utilized as a natural remedy for skin infections, particularly for enhancing beauty.
- The inclusion of antioxidants like ascorbic acid, polyphenols, and flavonoids assists in reducing wrinkles.
- The milky sap of the sapota plant effectively clears warts and fungal growth on the skin. Additionally, the seed oil serves to moisturize the scalp and soften the hair.
- Sapota seed oil has shown effectiveness in treating hair loss associated with seborrheic dermatitis.
- Chicle, the latex extracted from the sapodilla tree, serves as a key component in chewing gum and is also employed as an adhesive for repairing items in India.
- The crimson heartwood extracted from the sapota tree finds versatile applications in crafting a range of items including archer's bows, furniture, banisters, and other decorative pieces[14].

IX. REPORTED PHARMACOLOGICAL ACTIVITIES OF M. ZAPOTA

S. No	Plant part	Activity	Extract	Model / method	Outcome	References
1.	Bark	Wound healing activity	Ethanolic extract	Scratch assay, Linear incision wound model Excision wound model.	Study results revealed that an ointment infused with the ethanolic bark extract demonstrate wound healing properties and notably reduces wound size.	Alsareii et.al., 2023[15]
2.	Bark	Antifungal activity	Ethanolic extract	Agar-well diffusion method	The study's finding demonstrated that the ethanolic bark extract antifungal activity against Staphylococcus auries and Escherichia coli.	Alsareii et.al., 2023[15]
3.	Leaves	Antioxidant activity	Methanolic extract	DPPH assay	The antioxidant activity assessed	Angelica ramos et.al.,

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					by the DPPH assay revealed that the raw methanolic extract of M. zapota displayed the highest total antioxidant activity, measuring 3.523±0.382 mmol Trolox equivalents/g.	2022[16]
4.	Leaves	Anticancer property	Hexane and ethyl acetate extract	A549 adenocarcinoma cell lines/ MTT assay	The MTT assay, employed to assess the anticancer activity against human lung adenocarcinoma cells, demonstrated that the hexane extract achieved the highest percentage of growth inhibition at 70±1%.	Angelica ramos et.al., 2022[16]
5.	Leaves, pericarp and seeds	Antibiotic-Modulating Effects	Methanolic extract	Minimum inhibitory concentration	The study observed significant antibiotic-modulating effects with extracts at MIC/2 and MIC/4.	Franclin et.al., 2020[17]
6.	Leaves	Hepatocellular carcinoma activity	Aqueous extract	HepG2 cell line	The overall studies indicated that the water extract of M. zapota leaves enhance. The proportion of early apoptotic cells increases, leading to the generation of reactive oxygen species (ROS). Additionally, there is an elevation in the	Tan et. al., 2018[18]

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					expression levels of c-Jun N-terminal Kinase 1 (JNK1) and inducible nitric oxide synthase (iNOS), while the transcriptional activities of Akt1 and vascular endothelial growth factor A (VEGFA) decrease.	
7.	Leaves	CNS depressant activity	Methanolic and petroleum ether extract	-	The results of the study suggest that both extracts obtained from leaves extract exhibits CNS depressant activity.	Manirujjaman et.al., 2016[19]
8.	Leaves	Analgesic activity	Methanolic and petroleum extract	Acetic acid-induced writhing test	Analgesic activity of Methanolic and petroleum extract of M. zapota leaves varies depending on the dosage.	Sultana et.al., 2014[20]
9.	Leaves	Antidiarrheal activity	Methanolic, petroleum ether extract	Magnesium Sulfate induced model and Castor oil induced model	In the Castor oil-induced method, only the PEMZ extract exhibited statistically significant results. In the Magnesium Sulfate-induced method, both the MEMZ and PEMZ extracts reduced diarrhoea in mice, along with a decrease in stool weight.	Manirujjaman et.al., 2013[21]
10.	Leaves	Anti pyretic activity	Ethanol, ethyl acetate, petroleum ether	Yeast-induced pyrexia method	In the anti-pyretic study utilizing yeast-induced pyrexia in albino Wistar	Ganguly et.al., 2013[22]

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					rats, the ethanol extract reduced the temperature from 37.90°C to 37.41°C. and further to 37.07°C.	
11.	Leaves	Anti-inflammatory effect	Ethanolic extract	Carrageenan induced paw oedema method	In the evaluation of anti-inflammatory activity, the crude ethanolic extract and ethyl acetate extract demonstrated significant inhibition of paw oedema, with percentages of 91.98% and 92.41%, respectively.	Ganguly et.al., 2013[22]
12.	Leaves	Antimicrobial activity	Acetone extract	Agar well diffusion method	The leaves of M. zapota exhibit potent antioxidant and antimicrobial properties, making them a promising and cost-effective source of antioxidants and antimicrobials for the therapeutic or nutraceutical industries, as well as for food and pharmaceutical manufacturers.	Mital kineria et.al., 2012[23]
13.	Seeds	Antibacterial activity	Acetone extract	MIC method	The findings reveal that the acetone extract of M. zapota was effective against both gram-positive and gram-negative bacteria. The minimum inhibitory	Kothari et. al., 2012[24]

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					concentration (MIC) values of the potent extracts against susceptible organisms ranged between 53-380 µg/mL.	
14.	Leaves	Anti-hyperglycaemic effect	Alcoholic extract	Alloxan induced model	Sterols and triterpenes were identified as having potential antihyperglycemic properties.	Fayek et.al., 2012[25]
15.	Leaves	Hypocholesterolemic effects	Alcoholic extract	Cholesterol induced model	Oleic acid, linoleidic acid, and linoleic acid, recognized as the main fatty acids in the lipid content of the leaves, might also play a role in the Hypocholesterolemic effect of the alcoholic extract.	Fayek et.al., 2012[25]
16.	Leaves	Anti-arthritic effect	Ethanolic extract	Inhibition of protein denaturation	The potential anti-arthritic effects of the ethanolic extract derived from M. zapota was extensively investigated through in-vitro testing, focusing on its ability to inhibit protein denaturation.	Madan et.al., 2011[26]

X. CONCLUSION AND FUTURE PERSPECTIVE

From the above research, M. zapota significance as a noteworthy minor fruit crop, establishing its status as a healthful and nutritious fruit with a rich array of beneficial components. M. zapota fruit serves as a rich source of vitamins, minerals, and fibre, boasting elevated levels of both vitamin C and A. Furthermore, scientists have discovered a multitude of phytochemicals over the years, contributing to its broad range of biological effects, which encompass anti-inflammatory, antiarthritis, antibacterial, antifungal, antioxidant, antitumor, antidiabetic, and CNS depressant activities. This review may help finding cure in the neurological disease treatment with either part of the Manilkara zapota.

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