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A Review on Phytochemical and Phytochemical Perspective of Custard Apple Leaves

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ABSTRACT

The tropical plant Annona squamosa, often known as the custard apple, has many medicinal uses in traditional medicine because of its many benefits, including its ability to lower blood sugar. Insulinotropic action has been shown in studies on warm water and a methanol extract of leaves by promoting insulin production in pancreatic β-cells, enhancing glucose absorption, and blocking enzymes such DPP-IV, starch digestion, and glucose diffusion. Important bioactive substances that contribute to these positive benefits include flavonoids and rutin. The plant is very beneficial for diabetic wound care since it also possesses hepatoprotective, antibacterial, anti-inflammatory, anticancer, antioxidant, and wound-healing qualities. The leaves are high in proteins, fats, carbs, calcium, and Fiber, according to nutritional assessments. Applications of ethnopharmacology include the management of lice infestations, ulcers, dysentery, and other illnesses. Comparative research shows that the antibacterial action is stronger than the antifungal effects. Different genotypes have different levels of antidiabetic activity; smaller fruits are more effective. Using leaf extracts in the creation of value-added food items is an economical and wholesome strategy. All things considered, A. squamosa is a viable natural possibility for creating innovative antidiabetic treatments derived from plants.

Keywords: - Annona squamosa, antibacterial, antidiabetic activity, antioxidant, methanol extract.

Introduction

Annona squamosa Linn, commonly known as custard apple and widely found in India, has demonstrated significant therapeutic potential, particularly in the treatment of type 2 diabetes mellitus (T2DM), which accounts for 90–95% of diabetes cases globally. T2DM is characterized by insulin resistance and impaired pancreatic function, resulting in elevated blood glucose levels. Although oral hypoglycemic agents (OHAs) are initially effective, they often have adverse side effects and limited availability, prompting interest in herbal alternatives like Annona squamosa.

Traditionally used in Indian medicine, various parts of the plant—fruits, seeds, bark, leaves, and roots—have been employed to treat fevers, parasitic infections, diarrhea, dysentery, and neurological disorders. The plant is rich in bioactive compounds including flavonoids, phenolics, tannins, alkaloids, glycosides, and acetogenins, which contribute to its therapeutic properties. Studies have shown that extracts from different parts of the plant possess astringent, anti-tumor, sedative, anti-parasitic, antifungal, antibacterial, and wound-healing properties.

Phytochemical analysis highlights compounds like 16-hentriacontanone and squamocin derivatives with antifungal activity, while antioxidant properties of the leaves may benefit colitis. Its hypoglycemic effects occur through mechanisms like alpha-glucosidase inhibition, insulin stimulation, and improved insulin signaling—comparable to standard antidiabetic drugs. Additionally, specific polysaccharides like GASP3-3-I enhance insulin sensitivity and glucose uptake.

Moreover, alkaloid-rich extracts show potent antimalarial activity against chloroquine-resistant and sensitive *Plasmodium falciparum* strains. Overall, Annona squamosa Linn offers multiple pharmacological benefits, making it a promising natural therapy for diabetes and its complications.

Taxonomy

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Magnoliales

Family: *Annonaceae*

Genus: *Annona* L.

Species: *Annona squamosa*[1]

In English, it's called custard apple, sugar apple, sweet après; in Hindi and Telugu, it's called sharifa; in French, it's called corossolier & cailleux, pommier cannelle.[2]

The genus Annona and the family Annonaceae include the small, well-branched tree or shrub Annona squamosa, which produces tasty sugar-apples. Unlike its relatives Annona reticulata and Annona cherimola, this species is more tolerant of growing at lower elevations. With regular watering and adequate light, the custard apple tree can thrive with little maintenance. In contrast to other plants in its family, it can adapt to any type of soil and thrive in hot, dry areas. If the seeds have been planted, the plant will produce fruit in two to three years. The typically round or conical fruits will take three to four months to ripen.[3]

Morphological Characters

The small, semi-deciduous Annona squamosa tree grows 3–7 meters tall. It has a broad, open crown or branches that spread out irregularly. The bark is light brown with visible leaf scars and smooth to slightly fissured into plates. The inner bark is light yellow and slightly bitter, and the twigs turn brown with light brown dots.[4] Changes in temperature, light, or precipitation can induce dormancy in A. squamosa plants, which have green leaves that are 3–5 cm wide and up to 15 cm long. A. squamosa is another plant species that has bisexual flowers that may grow up to 2.5 cm long and are grouped in groups of two to four.[5]

Table 1: Morphological characterization of *Annona squamosa Linn*.

Characters	Seeds	Leaves	Stem	Roots	Fruits
Colour	Black	Green	Green to brown	Light brown/Dark brown	Greenish outside, whitish pulpy inside
Odour	Odourless	Characteristic Odour	Characteristic Odour	Odourless	Sweetish
Taste	Tasteless	Bitter	Slight bitter	Bitter	Sweetish

Geographical Distribution

Although the actual origin of Annona squamosa is uncertain, it is native to the tropical Americas and West Indies. Because of its fruit, it is currently the most frequently farmed species of Annona throughout the tropics and warmer subtropics, including Taiwan, Thailand, and Indonesia. It arrived in southern Asia prior to 1590. A. squamosa is known for being a resilient crop that can withstand drought, especially in India. It's only partially true. The tree can withstand a harsh dry season thanks to its rest time and leaf fall, but it needs enough hydration during the growing season and responds well to additional treatment. Despite the extended flowering season, fruit set in India and Southeast Asia is mostly restricted to the start of the rainy season, highlighting the significance of moisture.

Like the majority of Annona species, it needs a tropical or subtropical environment with mean winter temperatures above 15 °C (59 °F) and summer temperatures between 25 °C (77 °F) and 41 °C (106 °F). It is susceptible to cold and frost; temperatures a few degrees below freezing kill it, and temperatures below 10 °C (50 °F) defoliate it. It needs at least 700 mm of rainfall per year and is only moderately drought tolerant; it will not bear fruit well in drought conditions. It can grow up to 2,000 meters (6,600 feet) above sea level and thrives in hot, dry settings. It is not as tolerant of lowland tropical temperatures as many of the other Annona fruit bearers. The custard apple tree doesn't need much maintenance and will thrive if it receives regular watering and adequate light. Other plants in its family find it a bit challenging to adapt to any type of soil. Although loose, sandy loams are preferred, it thrives in deep rocky, well-drained, rich soils. In as little as two to three years, it bears fruit, making it a very prolific bearer. In India, fruiting

occurs in July or August, and the leaves are regenerated in April or May when the flowers emerge. The leaves fall in January or February. Up to fifty sugar apples can be produced by a tree that is five years old.[6]

Phytochemical Constituents

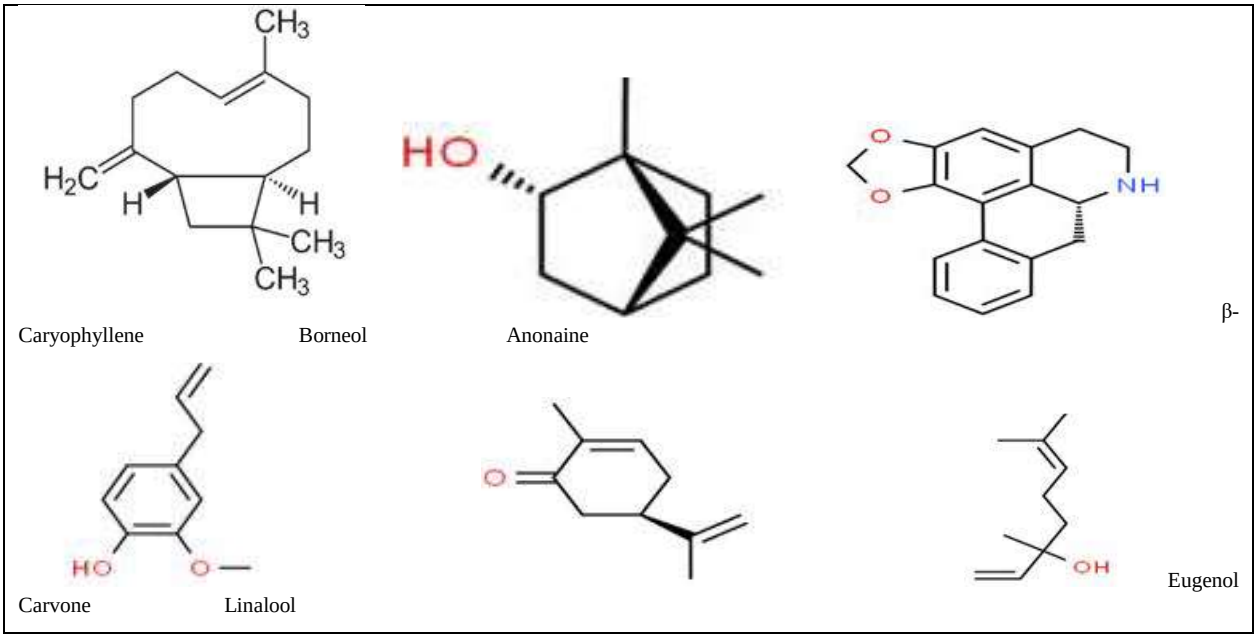
4-(2-nitro-ethyl 1) is present in leaves. -1-6-((6-o-β-Dxylopyranosy1- β-D-glucopyranosyl)-oxy)benzene, Anonaine, Benzyl tetrahydro isoquinoline, Borneol, Camphene, Camphor, car-3-ene, Carvone, β- Caryphyllene, Eugenol, Farnesol, Geraniol, 16- Hetriacontanone, Hexacontanol, Higemamine, Isocorydine, Limonine, Linalool acetate, Menthone, Methyl anthranilate, Methylsalicylate, Methylheptenone, p-(hydroxybenzyl)-6,7-(2- hydroxy,4-hydro)isoquinoline, a- Pinene, b-Pinene, Rutin, Stigmasterol, β-Sitosterol, Thymol, and n-Triacontanol. The leaf extract contains no proteins, amino acids, or alkaloids. [7]

Phytochemicals found in plant leaf extract include alkaloids, amino acids, flavonoids, glycosides, phenolic compounds, proteins, steroids, triterpenoids, tannins, starch, saponins, anthraquinones, aleurone grains, and inulin.

The following substances were separated from Annona reticulata L. leaf extracts. 14α-hydro-19-al-ent-kauran-17-oic acid, 6β-hydroxystigmast-4-en-3-one, 17-acetoxy, β-sitosterol, taraxerol, kaurenoic acid, and anonaretin A (2S)-di-O-methyl quiritigenin, 16β-ent-kauran-19-oic acid, 16α-hydro-ent-kauran-17,19-dioic acid, and GC- The following chemicals were found via MS analysis: Benzene, 1-methyl butyl, palmitic acid, mitoflaxone, oleic acid, piperidine, 2-propyl-, piracetam, and (1,1′bicylopropyl) -2 octanoic acid, methyl ester of 2-hexyl 3-methoxy-phenyl-3,4-dihydroxy-1,6-bis 1,6-dione -hexa-2,4-diene, 2-(3,4 dimethoxyphenyl), 4H-1-Benzopyran-4-one, and Cholesta-7,14-diene 3,6,7-trimethoxy-5-hydroxy, N-(4-Hydroxyphenyl)acetamide, 2,6,10,14-Hexadecatrienoic acid, 4-(4-nitrophenylazo)-benzoic acid, and methoxy carbonyl methyl ester. [8]

N-trans-feruloyltyramine, N-p-cpoumaroyltyramine, N-trans-caffeoyltramine, lignans, and β-sterol are the chemicals that make up stem (Barbalho 2012). [3] The stem's GC-MS examination revealed the following chemicals. The following are listed: Megastigmatrienone (1.901%), Ar-turmerone (3.952%), Oleicacid (10.028%), Gentisic acid (8.496%), 13-Docosenamide (23.190%), Deconoin acid ethyl ester (14.730%), 2,3-Dimethoxysuccinicaciddimethyl ester (4.021%), 3-Hexadecyne (13.035%), Allo-Aromadendrene (1.970%), Allo-Aromadendrene (6.739%), and Megastigmatrienone (1.901%).[9]

Table 2: Phytochemical structures of A. squamosa leaves.



Caryophyllene Borneol Anonaine β-

Carvone Linalool Eugenol

Uses

The plant's leaves, shoots, bark, and roots have all been reported to have medicinal qualities; the unripe fruit is astringent, the root is a drastic purgative, the seeds are thought to have antifertility activity, the leaves are used as a vermicide, for treating cancerous tumors, and for treating abscesses, insect bites, and other skin complaints; scrapings of root bark are used for toothaches; and powdered seeds are used to kill fleas and head lice, but it's important to keep the powder out of the eyes because it hurts a lot. [10]

According to the results of numerous studies on the health benefits of A. squamosa leaves, these leaves' phytochemical composition contributes to a variety of health advantages. The phenol-based chemicals found in A. squamosa leaves include proanthocyanidins and eighteen additional phenolic

compounds. Leaf extract from A. squamosa has biological properties such as antioxidant, lipid-lowering, hepatoprotective, anticancer, and antidiabetic effects.

A. squamosa leaves are also said to contain a variety of chemical substances that are good for the body, such as hydroxyl isomers of alkaloids and ketones. Insect bites, cancer, abscesses, and skin conditions can all be treated with A. squamosa leaves, which can also be used as a vermicide. Wounds and skin ulcers have been treated with A. squamosa leaves that have been broken down into smaller components. Dried and powdered A. squamosa leaves are used to make laxatives and an alternative remedy for cases of sticky diarrhoea.[11]

Pharmacological activity

Antidiabetic activity

These compounds may be the cause of A. squamosa leaf extract's antidiabetic and antioxidant qualities. Blood glucose levels rise when streptozotocin is induced because it specifically damages islet cells. Gliclazide is frequently employed as the standard medication in STZ-induced models of mild diabetes to assess the antidiabetic qualities of different substances, despite its well-known ability to cause hypoglycemia. Blood glucose levels in STZ-induced diabetic rats significantly decreased after receiving A. squamosa leaf extract.[12]

Anti-bacterial Activity

The antibacterial properties of Annona squamosa's leaves, seeds, and barks have been studied in relation to common infections that are frequently seen in clinical practice. Additionally, Annona squamosa leaf extract exhibits antimicrobial activity against Proteus species, Vibrio alginolyticus, Staphylococcus epidermidis, Enterococcus faecalis, Streptococcus pneumoniae, and Klebsiella pneumoniae. Gram-positive bacteria are more susceptible to the powerful antibacterial effects of Annona squamosa leaf extracts than Gram-negative ones.

Annona squamosa seed extract exhibits antimicrobial activity against Escherichia coli and Pseudomonus aeruginosa. Annotemoyin-1, Annotemoyin-2, squamocin, and cholesteryl glutamyranoside are antibacterial components found in Annona squamosa seeds.[13]

Wound healing

The leaf extract of A. squamosa L. proved successful in healing open back excision wounds in diabetic rats produced by streptozotocin–nicotinamide. Skin tensile strength, speed of epithelialization, total protein, DNA, collagen, and uranic acid were measured during follow-up on days 4, 8, 12, and 16, which were significantly improved with rapid healing. The findings were validated by the histological investigation. The extract also improved human dermal fibroblast culture and cellular proliferation when applied topically, as seen by increased collagen and glycosaminoglycan levels.[14]

Antinociceptive activity

The methanolic extract of Annona reticulata leaves was tested for its antinociceptive properties in male Swiss albino mice. The mice were given doses of 50, 100, 200, and 400 mg of the extract per kilogram of body weight; the writhing was decreased by 47.0, 55.1, 67.3, and 69.4%, respectively. The plant extract of Annona reticulata is predicted to have high analgesic effect, and leaf extract demonstrated antinociceptive efficacy in a dose-dependent manner.[15]

Analgesic

Swiss albino mice's analgesic efficacy was investigated using the hot-plate method. The mice were given injections of petroleum ether extract, ethyl acetate extract, and methanol extract of Annona reticulata L. bark at a dose of 100 mg/kg, whereas the usual medication was pentazocin (20 mg/kg). Analgesic action was demonstrated by all of the extract. The petroleum ether extract's maximum activity was seen between 60 and 120 minutes.[16]

CNS depressant

The locomotor activity and pentobarbitone sleeping duration were examined in order to investigate the CNS depressing action of Annona reticulata L. bark. By injecting 100 mg/kg of bark extract, locomotor activity was investigated. Diazepam (2 mg/kg) was the standard medication utilized. Locomotor activity was successfully reduced by all extracts; this reduction began at 30 minutes and lasted for 180 minutes. When compared to the usual medication pentobarbitone sodium (40 mg/kg), all of the extracts considerably extended the amount of time that the animals slept after being administered with an extract at a dosage of 100 mg/kg. A reduction in locomotor activity and an increase in sleeping duration demonstrate the effectiveness of bark extracts as a central nervous system depressant.[17]

Anti-inflammatory activity

According to reports, extracts from A. squamosa reduce the activity of inflammatory mediators, which are crucial in a variety of inflammatory disorders. It was discovered that by lowering IL-6 secretion, methanolic leaf and bark extracts had a strong anti-inflammatory impact.[17] The aqueous extracts of A. squamosa demonstrated analgesic effects against thermal and chemical stimuli, as demonstrated by the marked decrease in acetic acid-induced writhing and increase in reaction time by the thermal stimuli, as well as anti-inflammatory effects against oedema caused by carrageenan and histamine.[17]

Anticancer activity

All components of A. squamosa are traditionally used by ethnic populations to cure a variety of illnesses, including skin conditions, cancerous tumors, bug stings, and other ailments. Two benzyl isoquinoline alkaloids were found in an investigation of the alkaloids section of A. squamosa. In relation to the action of benzyl isoquinoline alkaloids in cancer cells, isolated alkaloids I exhibit outstanding activity against human breast cancer cells (MCF-7) as well as colon cancer cells (HTC116).[18]

Conclusion

Custard apple, or Annona squamosa, is a medicinal plant known for its strong antidiabetic properties, which are mostly brought about by phytochemicals such phenolic acids, flavonoids, and rutin. Its hot water leaf extract inhibits starch digestion, delays the absorption of glucose, reduces the activity of the DPP-IV enzyme, and increases the release and action of insulin. The leaves' nutritional analysis reveals that they are low in carbs and high in protein, fiber, and moisture. Significant α-amylase inhibition has been shown in studies, suggesting that it may reduce blood glucose levels. Foods including yogurt, falafel, and oat cheela produced acceptable tastes and reasonably priced value-added goods when dried leaf powder was applied. Furthermore, because of its antibacterial, anti-inflammatory, and antioxidant qualities, A. squamosa has the potential to improve diabetic wound healing; its therapeutic benefits may be enhanced by nanocarrier administration. Its extensive availability and therapeutic advantages, notwithstanding its underutilization, underscore the need for more research. Its use as a herbal remedy to treat type 2 diabetes and associated oxidative stress disorders is supported by both traditional and modern scientific research.

REFERENCES:

1. Safira A, Widayani P, An-Najaaty D, Rani CAM, Septiani M, Putra YAS, Solikhah TI, Khairullah AR, Raharjo HM. A Review of an Important Plants: Annona squamosa Leaf. Pharmacogn J. 2022 Mar-Apr;14(2):456-63. doi: 10.5530/pj.2022.14.58.
2. Pandey N, Barve D. Phytochemical and pharmacological review on Annona squamosa Linn. Int J Res Pharm Biomed Sci. 2011 Oct-Dec;2(4):1404-1412.
3. Palai S, Patra R, Jena S, Nikunj M, Sardar KK, Parija SC. A comprehensive review on potential benefits of *Annona squamosa* L. leaves for the treatment of diabetic wounds. *Ann Phytomed.* 2023;12(2):149–160. doi:10.54085/ap.2023.12.2.17
4. Bhattacharya A, Chakraverty R. The pharmacological properties of *Annona squamosa* Linn: A review. *Int J Pharm Eng*. 2016;4(2):692–699.
5. Ahirwar S, Jain S, Nisha P. Annona squamosa L.: A brief review on biological activities and their phytochemicals. *Asian J Pharm Pharmacol.* 2023;9(1):13–19. doi:10.31024/ajpp.2023.9.1.3
6. Saha, Rajsekhar. "Pharmacognosy and pharmacology of Annona squamosa: A review." *International Journal of Pharmacy & Life Sciences (IJPLS)*, vol. 2, no. 10, Oct. 2011, pp. 1183-1189. ISSN: 0976-7126.
7. Win Min Oo, Myat Mon Khine. Pharmacological Activities of Annona squamosa: Vol. 3, No. 6, 2017, pp. 86-93. doi: 10.11648/j.ijpc.20170306.14
8. Moussa AY, Siddiqui SA, Elhawary EA, Guo K, Anwar S, Xu B. Phytochemical constituents, bioactivities, and applications of custard apple (Annona squamosa L.): A narrative review. Food Chemistry. 2024;459:140363. doi:10.1016/j.foodchem.2024.140363
9. Kumari A, Sharan L, Patnaik A. Annona reticulata L. phytoconstituents and pharmacology: A review. International Journal of Ecology and Environmental Sciences. 2021;3(3):159-65. Available from: www.ecologyjournal.in
10. assin S, Elsohafy SM, Darwish FA, Amer ME. Annona squamosa L.: A promising herbal remedy - insights into its biological activities and phytochemical composition. Journal of Advanced Pharmaceutical Sciences. 2024;1(1):82-97. doi:10.21608/JAPS.2024.254019.1008
11. Mondal P, Biswas S, Pal K, Ray DP. Annona squamosa as a potential botanical insecticide for agricultural domains: A review. *Int J Bioresour Sci*. 2018;5(1):81–89. doi:10.30954/2347-9655.01.2018.11
12. Mahobia Y, Saxena G. Analysis of physicochemical parameters of *Annona squamosa* Linn leaves and development of value-added products for diabetic patients. *Int J Nutr Lifestyle*. 2022;2(4):257–263

13. Ansari P, Flatt PR, Harriott P, Abdel-Wahab YHA. Evaluation of the antidiabetic and insulin releasing effects of *Annona squamosa*, including isolation and characterization of active phytochemicals. *Plants.* 2020;9(10):1348. doi:10.3390/plants9101348

14. Dwivedi S, Khan K, Jain S. Evaluation of In-vitro Antioxidant and Antimutagenic Effect of Annona squamosa Leaves Extract. J Drug Deliv Ther. 2024;14(8):10-14. doi:10.22270/jddt.v14i8.6698

15. Simon K N, Santhoshkumar R, Kumar NS. Phytochemical analysis and antimicrobial activities of Annona squamosa (L) leaf extracts. J Pharmacogn Phytochem. 2016;5(4):128-131.

16. Subramanian S, Basha SKH. Biochemical evaluation of antidiabetic and antioxidant potentials of Annona squamosa leaves extracts studied in STZ induced diabetic rats. Int J Pharm Sci Res. 2011;2(3):643-655.

17. Kumar Y, Chandra AK, Shruti, Gajera HP**.** Evaluation of antidiabetic and antioxidant potential of custard apple (Annona squamosa) leaf extracts: A compositional study. *Int J Chem Stud.* 2019;7(2):889–95.