EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 12
Issue: 12
Year: 2025

ANNONA SQUAMOSA: A PROMISING MEDICINAL PLANT WITH DIVERSE PHARMACOLOGICAL ACTIVITIES – A REVIEW

[1]Poonam Ankush Jadhav (Asst. Proff.), [2]Priyanka Sandip Sabale, [3]Sanika Ajit Salvi, [4]Dipali Suresh Chormale (Lecturer)

Pune District Education Association's Shankarrao Ursal College of Pharmaceutical Sciences and Research Centre Kharadi. Pune- 411014.

***Corresponding Author: Poonam Ankush Jadhav (Asst. Prof.)**

Pune District Education Association's Shankarrao Ursal College of Pharmaceutical Sciences And Research Centre Kharadi. Pune- 411014. **DOI:** https://doi.org/10.5281/zenodo.17745761

How to cite this Article: 1Poonam Ankush Jadhav (Asst. Proff.), 2Priyanka Sandip Sabale, 3Sanika Ajit Salvi, 4Dipali Suresh Chormale (Lecturer) (2025). Annona Squamosa: A Promising Medicinal Plant With Diverse Pharmacological Activities – A Review. European Journal of Biomedical and Pharmaceutical Sciences, 12(12), 30–42.

Article Received on 28/10/2025 **Article Revised on 17/11/2025** **Article Accepted on 01/12/2025**

ABSTRACT

Annona squamosa, commonly known as custard apple or sugar apple, is a tropical fruit-bearing plant belonging to the family Annonaceae. cultivated in the West Indies, South and Central America, Ecuador, Peru, Brazil, India, Mexico, the Bahamas, Bermuda, and Egypt. The leaves of *Annona squamosa* have been extensively studied for their health-promoting properties, which are attributed to a diverse array of phytochemicals. The fruit of this plant is commonly known as the custard apple, which is edible. Various parts of the tree have been used in traditional folkloric medicine. The pharmacological activities of *Annona squamosa* leaves are antimicrobial, antifungal, anti-inflammatory, anticancer, antiulcer, antidiabetic, antidiarrheal, antiplatelet, antioxidant, and hepatoprotective, neuroprotective, and cytoprotective. Powdered seeds are used to kill the head-lice and fleas, but care should be taken that the alkaloids, carbohydrates, fixed oils, tannins & phenolic compounds. It is related to contain alkaloids, carbohydrates, fixed oils, tannins & phenolic compounds. Traditionally, nearly every part of the plant—from the leaves and seeds to the bark and roots—has been used in folk medicine to treat ailments such as infections, inflammation, digestive issues, and parasitic infestations. Recent scientific studies are increasingly exploring *Annona squamosa* for its potential in modern medicine, especially for its promising anticancer and antimicrobial effects.

KEYWORDS: *Annona squamosa*; biological activities; therapeutic applications; anti-ulcer.

INTRODUCTION

"Medicinal plants have been used for years, recognized as a rich resource, and play an important role in both traditional and modern medicine." Medicinal plants have been beneficial to human healthcare for thousands of years. Even today, they are widely used in Ayurveda, Unani, Homeopathy, and modern pharmaceutical medicine. Annona squamosa, a member of the Annonaceae family, has attracted considerable attention for its diverse pharmacological properties and ethnomedicinal significance. *Annona squamosa* is a small, semi-deciduous tree that produces edible fruits rich in nutrients and bioactive compounds. Nearly every part of the plant—including the leaves, bark, roots, seeds, and fruits—contains a wide range of nutrients and pharmacologically active constituents. It has been used in traditional medicine to treat various diseases, including diabetes, insecticidal, purgative, laxatives, astringent, anti-inflammatory, dysentery, ulcers, cardiac ailments, and parasitic infections. *Annona squamosa* twigs contain active constituents such as (+)-O-methylarmepavine, N-methylcorydaldine, and isocorydine, which possess antisecretory properties that help protect against peptic ulcers. These compounds reduce gastric acidity, pepsin, and gastrin levels, and inhibit the H+K+ATPase pump.

Taxonomy

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Magnoliidae
Order	Magnoliales

Family	Annonaceae
Subfamily	Maloideae
Tribe	Abrae
Genus	Annona.L
Species	*Annona squamosa. L*

Botanical Description & Distribution

Annona squamosa, commonly known as custard apple, is a well-branched shrub or small tree characterized by thin grey bark and a spherical or slightly flattened crown. The leaves are simple, alternate, and green, measuring approximately 10–15 cm in length and 3–5 cm in width. They are either sharp or blunt at the tip, with bases that are round or broadly wedge-shaped. The plant exhibits a response to environmental cues, such as fluctuations in rainfall, temperature, and light, which induce dormancy. However, not all trees respond simultaneously to these changes. Custard apple is a monoecious plant bearing bisexual flowers, typically arranged in clusters of two to four. Each flower is about 2.5 cm long. The outer petals are oblong, green, and purplish at the base, while the inner petals are reduced to minute scales or may be completely absent. Pollination is primarily carried out by nitidulid beetles, with wind and self-pollination playing only minor roles. Following pollination, the plant produces compound, tuberculate berries with prominent scales.[6] The edible fruits are round or heart-shaped, with numerous rounded protuberances and sweetly aromatic white pulp. Each fruit contains multiple carpels, each enclosing a single, smooth, oblong seed. The seeds are shiny, blackish to dark brown, measuring 1.3 to 1.6 cm in length. A pale swelling is present at the hilum, and the albumen is marked with numerous transverse brown clefts.

Leaves

The leaves of *Annona squamosa* (custard apple) are simple, green, and alternately arranged on short petioles along the branches. They are oblong to lanceolate in shape, typically measuring 10 to 15 cm in length and 3 to 5 cm in width. The apex may be acute or obtuse, while the base is usually rounded or broadly wedge-shaped. The leaf surface is smooth with visible venation and a thin texture. Young leaves are slightly hairy, and solitary or clustered crystals are often present in the epidermal cells.[20]

Flowers

The flowers of *Annona squamosa* (custard apple) are bisexual and borne on a monoecious plant, meaning both male and female reproductive structures are present on the same individual. The trees are semi-deciduous, and flowering typically occurs from spring to early summer; however, in regions with permanent humidity, flowering may continue throughout the year. Inflorescences are supra-axillary, and the flowers are borne in clusters of two to four, emerging from the axils of leaves or old wood. Each flower is pedicellate, actinomorphic, spirocyclic, and protogynous, where the pistils mature before pollen is released from the anthers (Vithanage, 1983). Flowers measure approximately 2.0 to 4.0 cm in length and are bracteate, with three degenerated sepals and six petals arranged in two whorls of three. The outer petals are thick, fleshy, oblong, green in colour, and often purplish at the base. The inner petals are highly reduced to small scales or may be entirely absent. In the floral structure, multiple pistils are situated on a conical receptacle at the centre, surrounded by numerous stamens at the periphery. The flowers are mildly fragrant but not showy, and pollination is primarily carried out by nitidulid beetles, while wind and self-pollination contribute minimally.[6]

Stem

The stem of *Annona squamosa* (custard apple) is woody, erect, and well-branched, supporting growth as a small tree or large shrub, typically 3–8 meters tall. Branches are irregular, with young stems green and slightly hairy, maturing to smooth, grayish bark with visible lenticels. The bark is thin and soft, aiding gas exchange. Internodes are short, forming a dense canopy. The stem is cylindrical with a solid core and well-developed vascular bundles for efficient nutrient transport.[6] It contains parenchymatous tissue and is rich in phytochemicals, including flavonoids and alkaloids such as N-nitrosoxylopine, roemerolidine, and duguevalline—compounds known for their antimalarial activity. Traditionally, the stem and bark are used for their astringent, analgesic, and anti-inflammatory properties.

Fruits

Annona squamosa trees begin to bear fruit at around 3 to 4 years of age. In India, fruiting typically occurs between July and August. Known as sugar apple, the fruit lives up to its name with a sweetness comparable to sugar, especially in the flesh closest to the rind, which has a texture similar to sugar granules. The fruit is usually conical in shape but can occasionally be nearly round. Ripeness is easily identified as the thick, knobby rind softens and often cracks open, releasing a distinctive sweet aroma. Optimal ripening occurs at temperatures ranging from 15°C to 30°C.[19]

Roots

The root system of *Annona squamosa* (custard apple) is typically shallow and spreading, comprising a primary taproot with numerous lateral roots that extend extensively within the upper soil layers. This fibrous root network enables efficient absorption of water and nutrients, supporting the plant's adaptability to various soil types, including sandy and loamy soils. The roots are woody and robust, providing strong anchorage. Phytochemical analyses have identified bioactive compounds in the roots, such as alkaloids and acetogenins, which contribute significantly to the plant's medicinal properties.[16] Traditionally, root extracts have been employed in folk medicine for their analgesic, anti-inflammatory, and antimicrobial activities.

Seeds

The seeds of *Annona squamosa* (custard apple) are oblong, smooth, and shiny, typically measuring between 1.3 to 1.6 cm in length. They are dark brown to black in colour and enclosed within the fleshy pulp of the fruit. Each seed contains a pale swelling at the hilum and is rich in various bioactive compounds, including acetogenins, which have been studied for their potential medicinal properties. Although the seeds possess pharmacological activities such as antimicrobial and insecticidal effects, they are considered toxic if ingested in large quantities. Traditionally, seed extracts have been utilized in folk medicine for their pesticidal and therapeutic applications.[16]

Figure 1. (A) *Annona squamosa. L* Tree. (B) *Annona squamosa. L Fruit.*
(C) *Annona squamosa. L Flower (*D) Annona *squamosa. L Seeds.*
(E) *Annona squamosa. L*Bark.

Table 1: Morphological characterization of *Annona squamosa Linn.*[10]

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	Sight bitter	Bitter	Sweetish

Table 2: Chemical composition of different parts *of Annona squamosal.*[22]

Various Parts	Chemical Composition
Leaves	Alkaloids like Aporphine, roemerine, norisocoryline etc., rhamnoside, quercetin-3-o-glucoside
Fruits	Liriodenine, norcorydine, isocorydine, Norushinsunine etc.
Bark	Acetogenins like 4-deoxyannoreticuline, annoreticuline-9, annosquamosins A, B cyclopeptides, squamone, squamotacin, 2,4 cis and trans squamoxinone.
Seeds	Annonastatin, asimicin, squamocin, essential oils like β farnesene, βpirene, α pirene, limorene etc
Roots	Liriodenine, norcorydine, isocorydine, Norushinsunine etc.

Phytochemistry

Phytochemicals are naturally present in all fruits and vegetables and play a vital role in scavenging free radicals, thereby helping to prevent diseases such as heart disease and cancer. The leaves of *Annona squamosa* are rich in various phytochemical compounds, including flavonoids, tannins, coumarins, cardiac glycosides, saponins, and carbohydrates, which exhibit antioxidant and antibacterial properties beneficial in food preservation and health. Extensive phytochemical studies have identified 88 alkaloids, 33 diterpenes (DITs), 33 annonaceous acetogenins (ACGs), and 13 cyclopeptides (CPs) in different parts of *A. squamosa*. Notable alkaloids found in both the leaves and seeds include anonaine, asimilobine, nuciferine, liriodenine, corypalmine, and reticuline. Essential oils from the plant have shown strong antiparasitic and antimalarial activity, with approximately 0.13% oil yield obtained through hydrodistillation in the Himalayan lowlands.[20]

GC-MS and flame ionization detection revealed around 40 compounds in the oil, with a total yield of 88.6%. The composition includes 63.4% hydrocarbon sesquiterpenes, 21.8% oxygenated sesquiterpenes, 2.0% monoterpenes, and 1.4% oxygenated monoterpenes. Identified compounds include (E)-caryophyllene, germacrene D, spathulenol, α-pinene, β-pinene, limonene, and β-elemene. The leaf extract of *A. squamosa* demonstrated significant antioxidant activity by neutralizing 43–54% of hydrogen peroxide. Additionally, the plant exhibits various biological effects, including antitumor, insecticidal, antiovulatory, and abortifacient properties. The leaves of *Annona squamosa* yield an essential oil rich in terpenes and sesquiterpenes, primarily β-caryophyllene, which is occasionally used in perfumery for its woody, spicy aroma. The bark provides fiber that has been traditionally used for cordage.[10] The average sugar content in the fruit is approximately 14.58%, composed roughly equally of glucose and sucrose.

The plant contains various chemical constituents, including borneol, camphene, camphor, car-3-ene, carvone, β-caryophyllene, eugenol, farnesol, geraniol, 16-heptatriacontanone, hexacontanol, higenamine, isocorydine, and limonene, which have been isolated from different parts such as the stems and roots. Volatile constituents from the bark have been identified through the essential oil obtained via steam distillation and analyzed using GC-MS. A chloroform extract of *A. squamosa* contains an active compound named annotemoyin. Flavonoids isolated from the aqueous leaf extract have demonstrated antimicrobial activity. Bullatacin, another bioactive compound, exhibits both antitumor and pesticidal properties. Additionally, two major alkaloids—liriodenine and oxoanalobine—belonging to the oxoaporphine group, were isolated from root extracts and identified by spectral analysis. The fruit has been reported to contain a wide range of volatile oils and phenolic compounds.[20] The seeds contain alkaloids and annonaceous acetogenins, and the leaves contain alkaloids and phenolic compounds. *Annona squamosa* is rich in the minerals iron, calcium, magnesium, zinc, and vitamins including thiamine, riboflavin, niacin, α-carotene, β-carotene, cryptoxanthin, and ascorbic acid.[18]

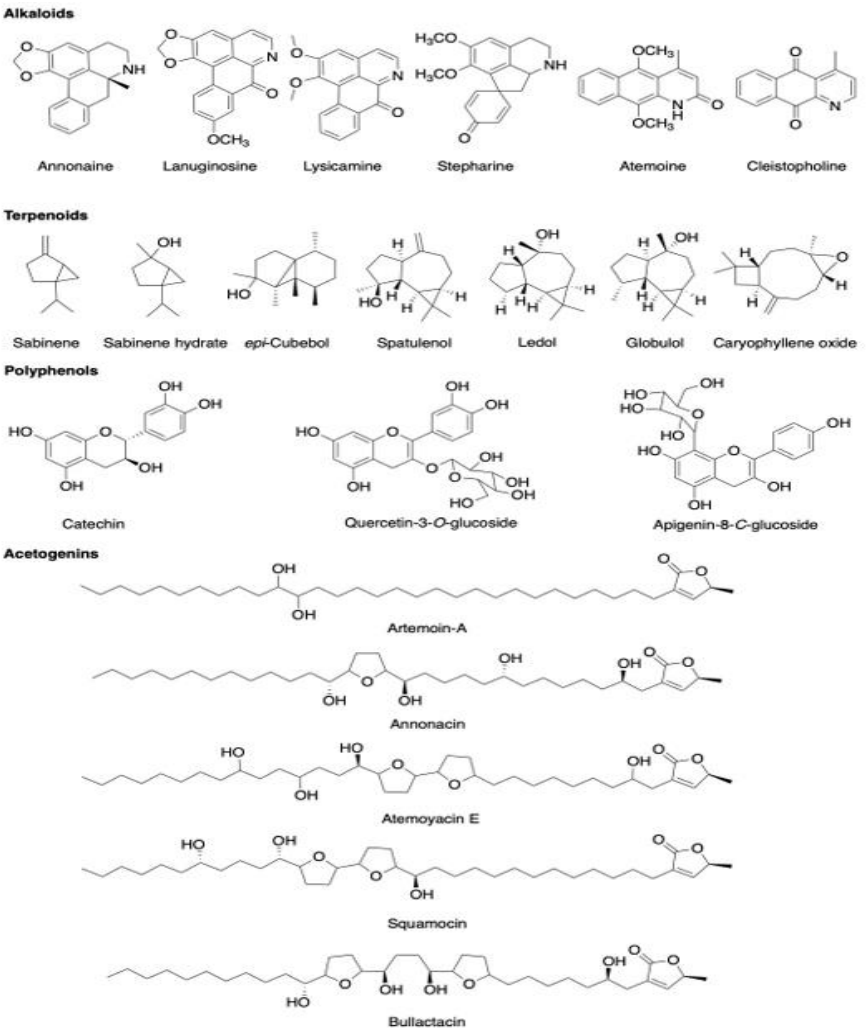

Figure 2: Structures of some representative phytochemical constituents of *Annona squamosal.*[18]

Phytochemical Investigation

Leaves

Phytochemical investigations of *Annona squamosa* (commonly known as custard apple or sugar apple) leaves have revealed a wide spectrum of bioactive constituents with notable medicinal potential. The plant, belonging to the family Annonaceae, has been traditionally used to treat various ailments, including diabetes, inflammation, and infections. Leaf essential oil has been found to contain 59 chemical compounds, with a high concentration of terpenes and sesquiterpenes—particularly β-caryophyllene (31.1%), δ-cadinene, α-murolene (5.5%), and α-cardinal (4.3%) (Kaur et al., 2015). Additionally, isoquinoline alkaloids such as dopamine, salsolinol, and coclaurine have been identified in both leaves and stems, along with other alkaloids like atropine, roemerine, and norisocoryline.[11] acetogenins—annoreticulin and isoannoreticulin—isolated from the leaves have demonstrated selective cytotoxicity against certain human tumor cells. Volatile and aromatic compounds, including borneol, camphor, carvone, eugenol, farnesol, geraniol, limonene, linalool, and menthone, have also been reported (Patel et al., 2008). Moreover, the presence of flavonoid glycosides such as rhamnoside and quercetin-3-glycoside contributes to the plant's antioxidant and therapeutic properties. Phytochemical screening of extracts prepared using solvents like methanol, ethanol, chloroform, and water has consistently confirmed the presence of major compound classes such as alkaloids, flavonoids, tannins, saponins, glycosides, phenols, terpenoids, and steroids. These constituents are associated with diverse biological activities, including antimicrobial, antioxidant, anti-inflammatory, and anticancer effects. Advanced analytical techniques such as UV-Vi's spectroscopy, HPLC, GC-MS, and FTIR are commonly employed to further characterize and quantify these compounds. Overall, the phytochemical richness of *Annona squamosa* leaves supports their traditional use in herbal medicine and indicates strong potential for pharmaceutical and therapeutic applications.[18]

Roots and Stem

Phytochemical investigations of the root and stem of *Annona squamosa* have revealed a diverse range of bioactive constituents with significant pharmacological potential. The root extracts are particularly rich in acetogenins—polyketide-derived natural products known

for their potent cytotoxic, antitumor, and pesticidal activities. Compounds such as annomontacin, squamocin, and bullatacin, isolated from the roots, have demonstrated selective cytotoxicity against various cancer cell lines. Additionally, the roots contain a variety of chemical constituents including borneol, camphene, camphor, carvone, β-caryophyllene, eugenol, geraniol, 16-hetricontanone, hexacontanol, higenamine, isocorydine, and limonene, contributing to their antimicrobial, antioxidant, and anti-inflammatory properties.[16] The stem has also been shown to contain isoquinoline alkaloids such as liriodenine and anonaine, along with terpenoids, phenolic compounds, and glycosides. Notably, six new ent-kaurane diterpenoids—annomosin A and annosquamosins C through G—have been isolated from the stem, highlighting the plant's chemical diversity.[18] These phytochemicals are associated with the traditional medicinal uses of the stem for treating infections, inflammation, and pain. Extraction using solvents like methanol, ethanol, and chloroform, followed by chromatographic and spectroscopic analyses (such as HPLC and GC-MS), has facilitated the identification and characterization of these compounds. Overall, the root and stem of *Annona squamosa* represent important sources of pharmacologically active natural products, supporting their traditional applications and potential for future drug development.[16]

Bark

Phytochemical investigations of the bark of *Annona squamosa* have revealed a rich composition of bioactive compounds that support its traditional medicinal use. The bark is known to contain various classes of secondary metabolites, including alkaloids, flavonoids, tannins, saponins, phenolic compounds, glycosides, and terpenoids. Notably, the presence of bullatacin, a potent acetogenin with cytotoxic properties, has been reported. Several other compounds, such as N-nitrosoxylopine, roemerolidine, and duguevalline, have also been identified, further contributing to the pharmacological significance of the bark.[17] In addition, unique compounds like mosinone-A, mosin-B, mosin-C, and squamone have been isolated, indicating the chemical diversity of this plant part. Alkaloids such as anonaine and liriodenine, previously found in the bark, have demonstrated antimicrobial and cytotoxic activity. The presence of flavonoids and phenolic compounds enhances the antioxidant potential, while tannins and saponins contribute to anti-inflammatory and astringent effects. The bark extract has also shown notable antimicrobial activity against various bacterial and fungal strains, supporting its traditional use in treating infections, wounds, and inflammatory conditions. Extraction is typically performed using solvents such as methanol, ethanol, or water, followed by compound identification and characterization through techniques like UV-Vis spectroscopy, FTIR, HPLC, and GC-MS. Overall, the stem bark of *Annona squamosa* represents a valuable source of pharmacologically active compounds and holds significant promise for future therapeutic applications.[16]

Fruits

Phytochemical investigations of the fruits of *Annona squamosa* and *Annona atemoya* have revealed a rich array of bioactive compounds that contribute to their nutritional and therapeutic potential. The fruit of *A. squamosa* contains a variety of secondary metabolites, including alkaloids, flavonoids, tannins, saponins, glycosides, phenolic compounds, and essential oils. Key phytochemicals such as quercetin, rutin, and catechin have been identified in the pulp, exhibiting strong antioxidant activity.[18] Additionally, the presence of natural sugars, dietary fiber, vitamin C, and essential minerals enhances the fruit's health benefits. Volatile constituents such as limonene, linalool, and β-caryophyllene contribute to both its aroma and medicinal properties. Acetogenins, particularly bullatacin, are primarily found in the seeds, although small amounts may occur in the pulp; these compounds have shown selective cytotoxicity against tumor cells. Analytical techniques such as solvent extraction, HPLC, GC-MS, and FTIR are commonly used for compound identification and quantification.[17]

Seeds

In the case of *A. atemoya*, the ripe fruit is known for its sweet, custard-like aroma, attributed to its high volatile content. GC-MS analysis of essential oils from mature fruits stored at 25 °C identified 40 phytochemical components, with esters comprising 94% of the total GC peak area. Methyl butanoate, ethyl butanoate, and methyl hexanoate were the predominant esters, while α-pinene, β-pinene, (E)-ocimene, and germacrene D were the major terpenes. Other studies reported that monoterpene and sesquiterpene hydrocarbons accounted for up to 80% of the total volatiles, with α-pinene (70.4 ppm), limonene (44.2 ppm), and germacrene D (20.0 ppm) being the most abundant.[18] Additional research on immature fruits dried under various conditions showed that oven drying at 50 °C led to the highest number of volatile compounds identified, with monoterpenes and sesquiterpenes remaining the dominant classes. LC-MS/MS analysis of *A. atemoya* fruit revealed the presence of phenolic compounds such as epicatechin (211 µg/g-dw), catechin (38.6 µg/g-dw), and minor amounts of 3,4-dihydroxybenzoic acid, chlorogenic acid, and p-coumaric acid. Rutin, quercetin, caffeic acid, and ferulic acid were not detected in the tested samples. Although one study suggested the isolation of bullatacin from *A. atemoya* fruit, it is more likely derived from the seeds, as acetogenins have not been confirmed in the fruit pulp of this species. Overall, the fruits of both *A. squamosa* and *A. atemoya* are rich in volatile and non-volatile phytochemicals, making them valuable not only as nutritious fruits but also as potential sources of natural therapeutic agents.[17]

Phytochemical investigations of the seeds of Annona squamosa and Annona atemoya have revealed a rich and diverse profile of bioactive compounds, particularly annonaceous acetogenins, which are recognized for their potent cytotoxic, antitumor, pesticidal, and insecticidal properties. In A. squamosa, key acetogenins such as bullatacin, squamocin, annonacin, and cherimolin-1 have been isolated and shown to selectively inhibit cancer cell proliferation. These seeds also contain various alkaloids, flavonoids, saponins, tannins, and fixed oils rich in oleic, palmitic, and linoleic acids, enhancing their pharmacological and nutritional potential. Essential oils and certain toxic constituents have also been detected, some of which may affect the central nervous system, highlighting the importance of controlled dosage in therapeutic applications. Extraction of seed compounds is typically carried out using solvents like methanol, ethanol, hexane, and chloroform, followed by isolation and structural elucidation through techniques such as HPLC, GC-MS, NMR, and FTIR.[18]

In the case of A. atemoya, studies have similarly confirmed the dominance of acetogenins over phenolic and alkaloid compounds in the seeds. In one detailed study, seeds collected in Taiwan were extracted using ethyl acetate and further partitioned with chloroform, methanol, and hexane. Column chromatography and recrystallization yielded 17 distinct acetogenins, including squamostatin-A and -D, neoannonin, artemoin A–D, bullatacin, bullatanocin, bullatalicin, desacetyluvaricin, and isodesacetyluvaricin, whose structures were established using Kedde's reagent and other analytical methods. Another study on seeds collected in China used 95% ethanol for extraction, followed by chromatographic purification, leading to the isolation of a novel compound named Atemoyacin A. These findings underscore the chemical richness of Annona seeds and their potential as a source of novel anticancer and pesticidal agents. However, the presence of neurotoxic compounds necessitates careful pharmacological evaluation before clinical application.[17] Overall, the seeds of A. squamosa and A. atemoya offer significant promise for the development of natural therapeutic agents, particularly in oncology and agriculture.

PHARMACOLOGICAL ACTIVITIES OF *ANNONA SQUAMOSA*

- Antimalarial Activity
- Antioxidant Activity
- Antiulcer Activity
- Antidiabetic Activity
- Anti-inflammatory Activity
- Antimicrobial Activity
- Antibacterial Activity
- Antifertility Activity
- Wound healing Activity
- Anticancer Activity
- Insecticidal Activity
- Anti-headlice Activity
- Anti-fungal Activity
- Antithyroid Activity
- Anti-viral Activity
- Renoprotective Activity
- Vasorelaxant Activity
- Hepatoprotective Activity

Antimalarial Activity

Annona squamosa (custard apple), a medicinal plant widely recognized in traditional medicine, has shown significant antimalarial potential in both in vitro and in vivo studies. Various parts of the plant—particularly the leaves, seeds, and bark—contain a rich array of bioactive compounds such as acetogenins, alkaloids, flavonoids, and terpenoids, which are believed to contribute to its antiparasitic properties. Notable acetogenins, including bullatacin and squamocin, have demonstrated potent cytotoxicity against Plasmodium falciparum, the parasite responsible for the most severe form of human malaria. Crude extracts—especially chloroform, methanol, and ethyl acetate leaf extracts—have exhibited dose-dependent inhibition of both chloroquine-sensitive (D10) and chloroquine-resistant (Dd2).[23] P. falciparum strains. Among the important alkaloids isolated from A. squamosa, N-nitrosoxylopine, roemerolidine, and duguevalline have shown moderate antiplasmodial activity. These compounds were identified in both leaf and bark extracts, with the bark extract displaying an IC_{50} of 30 µg/mL against the blood-stage of P. falciparum, indicating significant inhibitory potential. The proposed mechanisms of action include disruption of mitochondrial function and interference with hems detoxification, both crucial to parasite survival. Additionally, the antioxidant properties of A. squamosa may contribute to reducing oxidative stress during malaria infection. While these findings strongly support the plant's traditional use in treating febrile and parasitic diseases, further pharmacological validation, toxicity studies, and clinical trials are necessary to establish its safety and efficacy. Nonetheless, Annona squamosa represents a promising natural source of novel antimalarial compounds, echoing the historical development of drugs such as quinine and artemisinin, which were also derived from plant sources.[13]

Antioxidant Activities

Annona squamosa, commonly known as custard apple or sugar apple, has demonstrated significant antioxidant activity due to its rich phytochemical composition. Various parts of the plant—including the leaves, fruit pulp, seeds, and bark—contain bioactive compounds such as flavonoids, phenolic acids, tannins, alkaloids, saponins, and acetogenins. Among these, flavonoids and phenolic compounds are primarily responsible for its antioxidant effects. Extracts prepared using solvents such as methanol, ethanol, and water have shown strong antioxidant potential, particularly those derived from the leaves and fruit pulp.[13] The antioxidant activity of *Annona squamosa* has been evaluated using several in

vitro assays, including DPPH (2,2-diphenyl-1-picrylhydrazyl), ABTS (2,2′-azinobis (3-ethylbenzothiazoline-6-sulfonic acid)), FRAP (Ferric Reducing Antioxidant Power), and hydroxyl radical scavenging tests. Methanolic leaf extracts have demonstrated high free radical scavenging activity, often comparable to standard antioxidants like ascorbic acid.[13] The fruit pulp, which is rich in vitamin C and phenolic compounds, also contributes significantly to antioxidant activity. Methanol and aqueous extracts of the pulp have shown scavenging effects on DPPH, lipid peroxidation, nitric oxide, superoxide, and hydroxyl radicals.[23]

Antiulcer Activity

The anti-ulcer activity of Annona squamosa has been extensively studied using various experimental models, including cold restraint, pyloric ligation, aspirin-, alcohol-, and histamine-induced gastric and duodenal ulcers. Twelve compounds isolated from the twigs of Annona squamosa were evaluated, showing significant protection against ulcer formation. The chloroform and hexane fractions of the plant demonstrated notable anti-secretory activity by reducing free and total acidity, pepsin content, and plasma gastrin levels. These effects were further confirmed through in vitro inhibition of H^+/K^+-K-ATPase activity.[13] Active constituents such as (+)-O-methylarmepavine, N-methylcorydaldine, and isocorydine possess potent antisecretory properties that help protect against peptic ulceration. Similarly, the leaf extract of Annona squamosa exhibited protective effects against aspirin-induced gastric ulcers, supporting its therapeutic potential as a natural anti-ulcer agent.[23]

Antidiabetic Activity

Annona squamosa (custard apple) possesses remarkable anti-diabetic and antihyperglycemic properties attributed to its rich content of bioactive compounds such as flavonoids, alkaloids, saponins, and tannins. Experimental studies on streptozotocin-induced diabetic male albino Wistar rats demonstrated that oral administration of the aqueous extract for 30 days significantly reduced blood glucose, urea, and uric acid levels, while enhancing insulin, C-peptide, and albumin concentrations. The extract also normalized various marker enzymes to near-control levels.[23] Extracts from the leaves, seeds, and roots of Annona squamosa exhibit potent hypoglycemic activity through multiple mechanisms, including stimulation of insulin secretion (secretagogue effect), inhibition of α-glucosidase, and modulation of insulin signaling pathways. At doses of 100 and 400 mg/kg, the hexane extracts elevated insulin levels and inhibited α-glucosidase activity in diabetic mice, showing effects comparable to standard drugs like glimepiride (1 mg/kg) and acarbose (10 mg/kg). Additionally, an acidic heteropolysaccharide (GASP3-3-I) isolated from the fruit pulp was identified as a key α-glucosidase inhibitor. Further studies revealed that the plant's antidiabetic effect is mediated through inhibition of protein-tyrosine phosphatase 1B and enhancement of insulin receptor-β, IRS-1 phosphorylation, and GLUT-4 expression, thereby improving glucose utilization and insulin sensitivity in peripheral tissues.[13] Quercetin-3-O-glucoside isolated from the leaves suppresses hepatic glucose-6-phosphatase activity, leading to reduced blood glucose levels. Moreover, Annona squamosa leaf extract effectively lowers serum triacylglycerol and total cholesterol levels in diabetic models. Combined therapy with Annona squamosa extracts and glipizide has also been shown to enhance glycemic control, enabling up to a 50% reduction in the required glipizide dose.[13]

Anti-inflammatory Activity

Annona squamosa (custard apple) demonstrates strong anti-inflammatory potential, attributed to its diverse phytochemical constituents such as flavonoids, alkaloids, saponins, and tannins. These compounds suppress inflammation by inhibiting the production of pro-inflammatory mediators, including prostaglandins, cytokines, and nitric oxide. Experimental investigations using animal models have shown that extracts of Annona squamosa leaves and seeds effectively reduce edema and inflammatory responses induced by carrageenan, a standard phlogistic agent used to evaluate anti-inflammatory activity. Carrageenan triggers the release of mediators like histamine and serotonin during the initial phase, kinins during the intermediate phase, and prostaglandins in the late phase, collectively contributing to the inflammatory process. Inflammation, characterized by cellular activation and cytokine release, underlies the pathogenesis of various diseases.[26] Different parts of Annona squamosa—including leaves, bark, pericarp, and seeds—contain active compounds with anti-inflammatory properties, some of which have been identified with defined mechanisms of action. Oral administration of the aqueous leaf extract (300 mg/kg for 30 days) in acetic acid-induced colitis in mice significantly decreased colonic malondialdehyde (MDA) levels while enhancing antioxidant enzymes such as glutathione (GSH), glutathione peroxidase (GPx), and catalase (CAT).Two novel cyclic peptides, fanlizhicyclopeptide A and fanlizhicyclopeptide B, isolated from the pericarp, were found to suppress the production of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in activated macrophages. Similarly, ethanolic extracts of Annona squamosa downregulated CD40 expression and inhibited the NF-κB signaling pathway, further reducing inflammatory responses.[3] Compounds such as 18-acetoxy-ent-kaur-16-ene and caryophyllene oxide, isolated from the bark, exhibited significant anti-inflammatory and analgesic effects at doses of 50 mg/kg and 12.5–25 mg/kg, respectively. Additionally, 16β,17-dihydroxy-ent-kauran-19-oic acid inhibited superoxide generation and elastase release in activated neutrophils by blocking calcium mobilization from intracellular stores. Seed-derived compounds, including cyclosquamosin D and cherimolacyclopeptide B, were also shown to inhibit the secretion of pro-inflammatory cytokines such as IL-6 and TNF-α in macrophages. Collectively, these findings suggest that

Annona squamosa exerts its anti-inflammatory effects through multiple mechanisms involving antioxidant defence enhancement, suppression of inflammatory mediator synthesis, and modulation of key cellular signaling pathways.[23]

Antimicrobial Activity

Annona squamosa L., commonly known as custard apple, has demonstrated significant antimicrobial potential, with various plant parts—particularly the stem bark, leaves, and seeds—exhibiting activity against a wide spectrum of microorganisms.[23] Methanolic extracts of the stem bark showed notable *in vitro* antibacterial activity against both Gram-positive (*Bacillus coagulans*, *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli*, *Vibrio alginolyticus*) bacterial strains. Flavonoids isolated from aqueous extracts not only exhibited antimicrobial effects against common microbial contaminants of pulses but also demonstrated 80% insecticidal activity against *Callosobruchus chinensis* at a concentration of 0.07 mg/mL. Further studies on four different solvent extracts of the leaves confirmed antimicrobial activity, with the methanolic extract showing the highest zone of inhibition against *Pseudomonas aeruginosa* (MIC: 130 µg/mL), followed by petroleum ether extract (MIC: 165 µg/mL) and methanolic extract against *E. coli* (MIC: 180 µg/mL). The antibacterial efficacy was evaluated using the agar diffusion method. Phytochemical analyses revealed the presence of bioactive compounds such as linalool, borneol, eugenol, farnesol, and geraniol, which contribute to the observed antimicrobial effects. In addition, volatile compounds and flavonoids present in *A. squamosa* were found to exhibit strong antibacterial activity, further supporting its potential use in developing natural antimicrobial agents.[3]

Antibacterial Activity

Annona squamosa (custard apple) exhibits notable antibacterial activity attributed to its diverse phytochemicals, including alkaloids, flavonoids, acetogenins, and tannins. Various plant parts—leaves, seeds, and bark—have been evaluated for their efficacy against both Gram-positive and Gram-negative bacteria commonly implicated in clinical and foodborne infections. Leaf extracts have demonstrated significant inhibitory effects against Bacillus cereus, Listeria monocytogenes, Staphylococcus aureus, Campylobacter jejuni, Klebsiella pneumoniae, Streptococcus pneumoniae, Enterococcus faecalis, Staphylococcus epidermidis, Vibrio alginolyticus, and Proteus species. Notably, Neisseria gonorrhoeae was also found to be susceptible, with activity comparable to standard antibiotics like penicillin and ciprofloxacin.[23] However, the antibacterial effect of leaf extracts is heat-labile and diminishes at high temperatures. Among the leaf constituents, 16-hentriacontanone (palmitone), a major cuticular wax component, exhibited superior antibacterial activity. Seed extracts, rich in bioactive compounds such as annotemoyin-1, annotemoyin-2, squamocin, and cholesteryl glucopyranoside, were effective against *Pseudomonas aeruginosa* and *Escherichia coli*. Methanol extracts of the bark showed strong activity, particularly against *Bacillus coagulans* and *E. coli*. Across studies, methanol extracts consistently displayed higher antibacterial potency compared to aqueous or petroleum ether extracts, likely due to better solubility of active constituents in organic solvents. Moreover, the extracts showed greater effectiveness against Gram-positive bacteria than Gram-negative strains, with *Bacillus subtilis*, *S. aureus*, and *S. epidermidis* being particularly sensitive. These findings underscore the potential of *Annona squamosa* as a natural source of antimicrobial agents, especially in light of rising antibiotic resistance.[13]

Anti-fertility Activity

Annona squamosa has shown potential antifertility effects, primarily attributed to its bioactive constituents such as acetogenins, flavonoids, and alkaloids. Ethanol extract of the seed powder demonstrated anti-ovulatory activity in rabbits, with one study reporting ovulation inhibition in 40% of subjects after administration of 200 mg/kg over two days. However, the effect was considered insufficient for therapeutic use.[4] The seed extract has also been investigated for post-coital antifertility activity, showing both anti-implantation and abortifacient effects in animal models, although a separate study in pregnant rats reported no significant impact on pregnancy outcomes. In male rats, oral administration of methanol extract from the bark resulted in significant contraceptive effects, which were reversible upon discontinuation. These findings suggest that *Annona squamosa* possesses both male and female antifertility potential, though further research is needed to validate its efficacy, safety, and mechanism of action for possible therapeutic applications.[13]

Wound Healing Activity

Annona squamosa has shown significant wound healing potential, primarily due to its rich content of flavonoids, tannins, alkaloids, and phenolic compounds, which contribute to its anti-inflammatory, antimicrobial, and antioxidant properties. Topical application of ethanolic extracts of A. squamosa leaves has been reported to enhance wound healing by promoting collagen and glycosaminoglycan synthesis, as well as increasing cellular proliferation at the injury site. These effects result in accelerated wound contraction, improved epithelialization, and greater tensile strength of the healed tissue in experimental models. Additionally, the extract helps reduce microbial load in infected wounds, supporting its traditional use in the treatment of wounds and ulcers. The superior efficacy of ethanol-based formulations is likely due to enhanced solubility and bioavailability of the active phytoconstituents. These findings underscore the potential of Annona squamosa as a natural agent for wound management, although further clinical research is required to confirm its therapeutic

value and establish standardized formulations for medical use.[23]

Anticancer Activity

Annona squamosa has shown significant anticancer potential, attributed to its rich array of bioactive compounds, particularly annonaceous acetogenins, flavonoids, alkaloids, and phenolic compounds. Among these, squadiolins A and B, isolated from the seeds, have demonstrated high cytotoxic activity against human Hep G2 hepatoma cells and MDA-MB231 breast cancer cells. Another potent acetogenin, squamotacin, extracted from the bark, exhibited selective cytotoxicity against PC-3 human prostate cancer cells, with a potency reportedly over 100 million times greater than that of Adriamycin. Additionally, bark extracts have shown chemoprotective effects by preserving cell surface glycoconjugates in a hamster buccal pouch model of carcinogenesis induced by 7,12-dimethylbenz(a)anthracene (DMBA). Oral administration of aqueous and ethanolic extracts (500 mg/kg and 300 mg/kg body weight, respectively) significantly reduced tumour incidence and normalized glycoconjugate levels in tumour-bearing animals. Further studies on defatted seed extracts revealed their ability to induce apoptosis in specific cancer cell lines, such as MCF-7 (breast cancer) and K-562 (leukaemia), through mechanisms involving reactive oxygen species (ROS) generation, glutathione depletion, Bcl-2 downregulation, and DNA fragmentation. However, these effects were selective, as COLO-205 colon cancer cells did not show similar responses, indicating a degree of specificity in the anticancer action.[23] These findings suggest that *A. squamosa* extracts exert their effects through oxidative stress-mediated apoptotic pathways, making them promising candidates for further development as selective anticancer agents. Nevertheless, comprehensive clinical studies are necessary to confirm their safety, efficacy, and therapeutic potential in humans.[21]

Insecticidal Activity

Annona squamosa has shown strong insecticidal potential, primarily due to the presence of bioactive compounds such as acetogenins (ACGs), alkaloids, tannins, phenolics, and glycosides. These compounds contribute to its effectiveness as a natural pesticide, offering an eco-friendly alternative to synthetic chemical agents. The ethanolic extract of *A. squamosa* has demonstrated significant insecticidal activity, particularly against *Sitophilus oryzae*, a common storage pest. In a study, the extract caused complete insect mortality at concentrations of 1% and 5% (w/v) within 39.6±1.4 and 14.5±1.1 minutes, respectively, with no mortality observed in control groups even after 100 hours. The extract also produced rapid knockdown effects, with KD_{50} values of 23.1 minutes and 11.4 minutes at the same respective concentrations.[13] Additionally, *A. squamosa* has been reported to inhibit the growth of *chrysanthemum aphid*, further supporting its potential as a botanical insecticide. The plant's insecticidal properties are not only potent but also biodegradable, selective, and environmentally safe, making it highly valuable in integrated pest management and preventive public health strategies. Continued research into formulation and field applications is essential to fully harness its commercial and agronomic potential.

Anti-headlice Activity

Annona squamosa, commonly known as custard apple, has demonstrated strong anti-head lice (pediculicidal) activity, particularly through its seed extracts. When combined with coconut oil in a 1:2 ratios, the seed extract achieved 98% lice mortality within two hours, significantly outperforming leaf extracts. In a study using the McCage method, active components isolated from the hexane extract of *A. squamosa* seeds caused 100% mortality of head lice within 30 to 62 minutes. Chromatographic and spectroscopic analysis revealed two major active compounds: oleic acid and a triglyceride with one oleate ester, with yields of 12.25% and 7.74% dry weight, respectively. These isolated compounds, as well as the crude hexane extract diluted with coconut oil (1:1), killed all tested head lice in 49, 11, and 30 minutes, respectively. The triglyceride ester, in particular, holds potential as a chemical marker for quality control of *A. squamosa* seed extracts in pediculicide formulations. These findings support the plant's traditional use for lice treatment and offer a promising, natural alternative to synthetic lice-control products, with the added benefits of being biodegradable, cost-effective, and less likely to induce resistance. Further clinical validation is recommended to establish standardized, safe formulations for human use.[3]

Antifungal Activity

Annona squamosa exhibits notable antifungal properties, which are primarily attributed to its diverse array of phytochemicals, including acetogenins, flavonoids, alkaloids, tannins, and phenolic compounds. Extracts from the leaves and seeds have demonstrated effective antifungal activity against several pathogenic fungi such as *Candida albicans*, *Aspergillus niger*, *Fusarium solani*, *Alternaria alternata*, and *Microsporum canis*. Both aqueous and organic extracts have shown efficacy, with organic solvents generally yielding higher antifungal potency due to better extraction of active constituents. Key antifungal compounds identified in the leaves include 16-hentriacontanone (palmitone) and 10-hydroxy-16-hentriacontanone, while the seeds contain squamocin A, squamocin G, and squamostatin A, which contribute to their antifungal activity. The proposed mechanisms include disruption of fungal cell wall integrity and inhibition of spore germination and enzyme systems. These findings support the traditional use of *A. squamosa* in managing fungal infections and indicate its potential as a natural source for developing antifungal agents.[13] However, further pharmacological research and clinical validation are required to fully establish its therapeutic applications and safety profile.

Antithyroid Activity

The compound 5,7,4'-trihydroxy-6,3'-dimethoxy-flavone 5-O-α-L-rhamnopyranoside (THDMF-Rha), isolated from the leaves of *Annona squamosa*, has demonstrated significant antithyroid activity. Oral administration of THDMF-Rha at a standardized dose for 15 days effectively reduced L-thyroxine-induced thyrotoxicosis in rats. The therapeutic effect was found to be comparable to that of propylthiouracil, a standard antithyroid drug.[13] The proposed mechanisms of action include suppression of thyroxine (T_4) synthesis and secretion, as well as inhibition of peripheral deiodinase activity, which is responsible for the conversion of T_4 to the more active triiodothyronine (T_3).

Antiviral Activity

Annona squamosa has demonstrated significant antiviral potential, largely attributed to its diverse range of bioactive compounds, including acetogenins, alkaloids, and flavonoids. Extracts from various parts of the plant—particularly the leaves, seeds, bark, and fruits—have shown inhibitory effects against several viruses in in vitro studies. One notable compound, 16β,17-dihydroxy-ent-kauran-19-oic acid, isolated from the fruits, exhibited potent anti-HIV activity in H9 lymphocyte cells, with an EC_{50} value of 0.8 µg/mL. These antiviral effects are believed to occur through mechanisms such as inhibition of viral replication, interference with viral entry, and disruption of protein synthesis. Preliminary evidence also indicates potential activity against herpes simplex virus (HSV) and hepatitis viruses. While these findings support the therapeutic potential of *Annona squamosa* as a natural antiviral agent, further detailed pharmacological and clinical studies are essential to fully understand its mechanisms of action, optimize dosage, and ensure safety and efficacy.[13]

Renoprotective Activity

The aqueous extract of *Annona squamosa* leaves has demonstrated significant renoprotective effects in various experimental models. Oral administration of 300 mg/kg of the extract for one month in streptozotocin-induced diabetic rats resulted in a marked reduction of elevated serum urea, creatinine, and uric acid levels, indicating improved kidney function. Although the exact mechanism is not fully understood, the antioxidant properties of the extract are believed to contribute to its nephroprotective action. In a separate study by Deshmukh et al., similar renoprotective effects were observed in a 5/6 nephrectomised animal model, where treatment with the same dose of *Annona squamosa* extract significantly increased renal superoxide dismutase (SOD) activity, suggesting enhanced oxidative stress defense. These findings are supported by additional studies showing that leaf and seed extracts can mitigate nephrotoxicity induced by agents like gentamicin and cisplatin. The protective effects are thought to be mediated through antioxidant, anti-inflammatory, and membrane-stabilizing mechanisms, helping to preserve renal structure and function. Histopathological evaluations confirm reduced glomerular and tubular damage in treated animals. Collectively, these results suggest that *Annona squamosa* holds therapeutic potential for the prevention and management of acute and chronic kidney injuries.[3] However, further pharmacological studies and clinical trials are required to validate its efficacy and safety in humans.

Vasorelaxant Activity

Annona squamosa has shown significant vasorelaxant activity, primarily due to its bioactive compounds such as flavonoids, acetogenins, and alkaloids. Studies using isolated rat aortic rings have demonstrated that extracts from the leaves and seeds induce dose-dependent relaxation of vascular smooth muscle. One specific compound, Cyclosquamosin B, isolated from the seeds, has been identified to mediate vasorelaxation by inhibiting calcium influx through voltage-gated calcium channels, thereby reducing vascular tone. The overall vasorelaxant effect is believed to involve both endothelium-dependent and independent mechanisms, potentially through the nitric oxide (NO pathway)-cGMP and alpha-adrenergic receptor modulation. These findings suggest that *Annona squamosa* holds potential in the treatment of hypertension and other cardiovascular disorders, although further studies are needed to fully elucidate its mechanisms and confirm its therapeutic efficacy.[13]

Hepatoprotective Activity

Annona squamosa has shown promising liver-protective effects, largely due to its abundance of flavonoids, acetogenins, phenolic compounds, and antioxidants. Studies in animal models have demonstrated that extracts from its leaves and seeds can safeguard the liver from damage caused by toxins such as carbon tetrachloride (CCl_4), paracetamol, and alcohol. Treatment with *Annona squamosa* extract helped normalize elevated liver enzymes—including ALT, AST, ALP, and bilirubin—reflecting improved liver function. Furthermore, microscopic examination of liver tissue showed reduced inflammation, cell death, and fat accumulation. These protective benefits are thought to arise from the plant's antioxidant, anti-inflammatory, and membrane-stabilizing properties, which shield liver cells from oxidative stress and injury. While these results highlight the potential of *Annona squamosa* as a natural treatment for liver disorders, more research and clinical trials are needed to confirm its safety and effectiveness in humans.[13]

CONCLUSION

Annona squamosa is a promising medicinal plant known for its wide range of pharmacological activities. It is rich in bioactive compounds such as alkaloids, flavonoids, and glycosides, which contribute to its therapeutic potential, including antimicrobial, anti-diabetic, anticancer, hepatoprotective, and immunomodulatory

effects. These diverse properties underscore its value as a natural resource for drug discovery and development. While preclinical studies have shown encouraging results, further rigorous clinical trials and safety assessments are essential to fully confirm its efficacy and ensure safe use in humans. Overall, Annona squamosa holds significant potential to advance modern medicine by integrating traditional knowledge with contemporary pharmacological research.

REFERENCES

1. Kaleem M, Asif M, Ahmed Q U, Bano B, Antidiabetic and antioxidant activity of Annona squamosa extract in streptozotocin-induced diabetic rats, Singapore Med J 2006; Rajsekhar Saha, Pharmacognosy and pharmacology of Annona squamosa: A review, International Journal of Pharmacy & Life Science, Oct: 2011; 2.
2. Neha Pandey, Dushyant Barve, Phytochemical and Pharmacological Review on Annona squamosa Linn, International Journal of Research in Pharmaceutical and Biomedical Sciences, Oct - Dec 2011; 2(4).
3. Dinesh K. Yadava, Neetu Singhb, Kapil Deva, Rolee Sharmac, Mahendra Sahaid, Gautam Palitb, Rakesh Maurya, Anti-ulcer constituents of Annona squamosa twigs, Fitoterapia, 2011; 82.
4. GhadirA. El-Chaghaby, Abeer F. Ahmad, EmanS. Ramis, Evaluation of the antioxidant and antibacterial properties of various solvents extracts of Annona squamosa L. leaves, King Saud University Arabian Journal of Chemistry, received 15 March 2011; accepted 13 June 2011 Available online: 14 July 2011.
5. Kapil Vyas, Hansraj Manda, Rahul Kumar Sharma, Gaurav Singhal, An Update Review On Annona Squamosa, International Journal of Pharmacy & Therapeutics, 2012; 3(2): 107-118,
6. Achara Dholvitayakhuna, Nathanon Trachooa, Uthai Sakeeb and T.P. Tim Cushniec, Potential Applications for Annona squamosa Leaf Extract in the Treatment and Prevention of Foodborne Bacterial Disease, Natural Product Communications, 2013; 8(3).
7. G. Vimala and F. Gricilda Shoba, A Review on Antiulcer Activity of Few Indian Medicinal Plants, International Journal of Microbiology, 2014.
8. Rasha YM Ibrahim, Amal I Hassan, Eithar K AL-Adham, The anti-ulcerative colitis effects of Annona squamosa Linn. leaf aqueous extract in experimental animal model, International Journal of Clinical and Experimental Medicine, 2015.
9. Anshuman Bhattacharya* and Raja Chakraverty, The pharmacological properties of Annona squamosa Linn: A Review, International Journal of Pharmacy and Engineering, A. Bhattacharja. et. al, June-2016; 4(2): 692-699.
10. Iqra Nishath, Evaluation of Anti-Ulcer and Analgesic Activity By Annona Squamosa Leaves, International Journal of Trends in Pharmacy and Life Sciences, 2016; 2(6): 993-1000.
11. Elizaˆngela Beneval Bento a, Francisco Elizaudo de Brito Ju´nior a, Dayanne Rakelly de Oliveira a, Cı´cera Norma Fernandes a, Gyllyandeson de Arau´jo Delmondes a, Francisco Rafael Alves Santana Cesa´rio a, Cristina Kelly de Sousa Rodrigues a, Valterlu´cio dos Santos Sales a, Francisco Rodolpho Sobreira Dantas No´brega de Figueiredo a, Izabel Cristina Santiago Lemos a, A´ lefe Brito Monteiro a, Irwin Rose Alencar de Menezes a, Jose´ Galberto Martins da Costa b, Marta Regina Kerntopf a, Antiulcerogenic activity of the hydroalcoholic extract of leaves of Annona muricata Linnaeus in mice, Saudi Journal of Biological Sciences, 13 January 2016.
12. Win Min Oo, Myat Mon Khine, Pharmacological Activities of Annona squamosa: Updated Review, International Journal of Pharmacy and Chemistry, 2017; 3(6): 86-93.
13. Biba Vikas, Akhil B S, Remani P, K Sujathan, Free Radical Scavenging Properties of Annona squamosa, Asian Pacific Journal of Cancer Prevention, 18, 201.
14. Ravindra Madhukar Katole, Jadhav Meghana Gautam, Dr. D. N. Mokat, Phytochemical study of-Annona squamosa L. and Annona reticulata L., International Journal of Research, April 2018; 05(12).
15. Anant Babu Marahatta, Aashish Aryal and Ram Chandra Basnyat, The phytochemical and nutritional analysis and biological activity of Annona squamosa Linn., International Journal of Herbal Medicine, 2019; 7(4): 19-28.
16. Diksha A. Narwade*, A. N. Aher, A Review On: Phytochemical and Pharmacological Study of Annona Squamosa, PharmaTutor, 2019.
17. Bassam S. M. Al Kazman, Joanna E. Harnett and Jane R. Hanrahan, The Phytochemical Constituents and Pharmacological Activities of Annona atemoya: A Systematic Review, Pharmaceuticals, 2020; 13: 269.
18. Manoj Kumar 1, Sushil Changan 2, Maharishi Tomar 3, Uma Prajapati 4, Vivek Saurabh 4, Muzaffar Hasan 5, Minnu Sasi 6, Chirag Maheshwari 7, Surinder Singh 8, Sangram Dhumal 9, Radha 10, Mamta Thakur 10, Sneh Punia 11, Varsha Satankar 12, Ryszard Amarowicz 13 and Mohamed Mekhemar 14, Custard Apple (Annona squamosa L.) Leaves: Nutritional Composition, Phytochemical Profile, and Health-Promoting Biological Activities, Custard Apple (Annona squamosa L.) Leaves: Nutritional Composition, Phytochemical Profile, and Health-Promoting Biological Activities, Biomolecules, 2021; 11: 614,
19. Maria Malik 1, Muhammad Aamir Iqbal 2,*, Mariam Malik 3, Muhammad Akram Raza 1, Wajeehah Shahid 4, Jeong Ryeol Choi 5,* and Phuong V. Pham 6,* Biosynthesis and Characterizations of Silver Nanoparticles from Annona squamosa Leaf and Fruit Extracts for Size-Dependent Biomedical Applications, Nanomaterials, 2022; 12: 616.

20. Arifia Safira1, Prasita Widayani1, Dhiya An-Najaaty1, Cinta Atsa Mahesa Rani1, Mela Septiani1, Yan Arengga Syah Putra1, Tridiganita Intan Solikhah1,*, Aswin Rafif Khairullah2, Hartanto Mulyo Raharjo3, A Review of an Important Plants: Annona squamosa Leaf, Pharmacognosy Journal, Mar-Apr, 2022; 14(2).
21. Fatma A. Mokhtar 1,*,†, Nabil M. Selim 2,*,†, Seham S. Elhawary 2, Soha R. Abd El Hadi 3, Mona H. Hetta 4, Marzough A. Albalawi 5, Ali A. Shati 6 , Mohammad Y. Alfaifi 6, Serag Eldin I. Elbehairi 6,7, Lamiaa I. Fahmy 8 and Rana M. Ibrahim 2, Green Biosynthesis of Silver Nanoparticles Using Annona glabra and Annona squamosa Extracts with Antimicrobial, Anticancer, Apoptosis Potentials, Assisted by In Silico Modeling, and Metabolic Profiling, Pharmaceuticals, 2022; 15.
22. D. Rama Bramha Reddy1*, K. Malleswari2, E. Naveen Kumar3, Phytochemicals and Pharmacological Activities of Annona squamosa, International Journal for Multidisciplinary Research, January-February 2023; 5(1).
23. Dharmendra Kumar Gautam a, Vishvajeet Singh b, Sachin Kumar Singh c, Pratik Tiwari d, Prabakaran S e, Sameer Verma a, Shivangi Tripathy f, Suraj luthra g and Ritik Chawla, Custard Apple (Annona squamosa L.): Exploring its Health Benefits and Medicinal Properties, European Journal of Nutrition & Food Safety, 2024; 16(10): 129-140.
24. Mohamed A. Abdel-Azeem1, Enas E. Eltamany2, Marwa S. Goda2, Jihan M. Badr2, Chemodiversity of Annona Squamosa Secondary Metabolites SINAI International Scientific Journal (SISJ), July 2024; 1(1).
25. Mohamed A. Abdel-Azeem1, Enas E. Eltamany2, Marwa S. Goda2, Jihan M. Badr2, Hanadi J. Al-Zubaidi1, Mohammed T. Mohammed2, Aoula Al-Zebeeby1 *, Azhar A. Alkaby1 and Wurood Razzaq Hassan3, Exploring the potential protective and anti-inflammatory effects of the crude ethanolic extract of Annona squamosa Linn fruit against Ethanol-mediated gastric erosion, Open Veterinary Journal, 2025; 15(2): 795-803.