



COMPREHENSIVE REVIEW ON: PEELS OF *ANNONA SQUAMOSA* L.

Prakash Dabadi¹, Aishwarya K. S.², Chandana B. S.³, Mohammed Nasir Hussain⁴, Mohammed Shums Tabrij^{5*}, Hima Chaitra S.⁶

¹Associate Professor, Department of Pharmacology, Bapuji Pharmacy College, SS-Layout, Davangere-577004.

^{2,3,4,5,6}Department of Pharmacology, Bapuji Pharmacy College, SS-Layout, Davangere-577004.

Article Info

Article Received: 21 August 2026,
Article Revised: 11 September 2026,
Published on: 01 October 2026



*Corresponding author:

Mohammed Shums Tabrij

Department of Pharmacology, Bapuji
Pharmacy College, SS-Layout,
Davangere-577004.

<https://doi.org/10.5281/zenodo.23058547>

How to cite this Article: Prakash Dabadi¹, Aishwarya K. S.², Chandana B. S.³, Mohammed Nasir Hussain⁴, Mohammed Shums Tabrij^{5*}, Hima Chaitra S.⁶ (2026). Comprehensive Review On: Peels Of *Annona Squamosa* L.. World Journal of Advance Multidisciplinary Research, 3(9), 9-17. This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

Custard apple (*Annona squamosa* L.), a tropical fruit which has gained significant attention due to its rich nutritional composition and diverse pharmacological properties. This review summarizes the available scientific literature on the phytochemical constituents, nutritional value, traditional uses, and therapeutic potential of *A. squamosa*. Various parts of the plant, including the fruit, leaves, seeds, bark, and roots, contain rich bioactive compounds such as alkaloids, flavonoids, phenolics, Acetogenins, and vitamins. Experimental studies have demonstrated antioxidant, antidiabetic, antimicrobial, anti-inflammatory, hepatoprotective, anticancer, and wound-healing activities associated with these phytochemicals. The fruit is also recognized as a valuable source of carbohydrates, dietary fiber, minerals, and essential micronutrients, making it beneficial for human nutrition. Despite promising preliminary finding further clinical investigations and standardization of extracts are necessary to establish safety, efficacy, and therapeutic applications. This review highlights the medicinal significance of custard apple and emphasizes its potential as a source of natural bioactive compounds for future pharmacological activities.

KEYWORDS: Custard apple, antioxidant, antimicrobial, antidiabetic, anticancer.

INTRODUCTION

Custard apple (*Annona squamosa* L.) *Annonaceae*, popularly known as sugar apple or sweetsop, has high nutritional and medicinal value due to the presence of several secondary metabolites found in the epicarp of the fruit. Although it is indigenous to the tropics of America, the species is currently cultivated in many parts of the world, particularly in India. The plant is capable of adapting to dry and hot climate conditions and is widely grown in the Indian states of Karnataka, Maharashtra, Andhra Pradesh, Telangana, and Tamil Nadu.

It is a small, deciduous tree or shrub that usually grows to a height of 3-8 meters. It has thin, light brown bark, simple, lanceolate leaves, yellowish-green, fragrant flowers, and heart-shaped fruit having a knobbed and segmented appearance. The ripe fruit provides a sweet and creamy-white pulp, which contains several black seeds.

The plant parts, such as the leaves, bark, roots, seeds, fruit pulp, and epicarp (peel of the fruit), contain rich bioactive compounds like alkaloids, flavonoids, phenols, tannins, saponins, acerogenins, and terpenoids. The various phytochemical components provide several pharmacological actions, such as antioxidant, antimicrobial, anti-inflammatory, antidiabetic, and anticancer properties. This plant has been reviewed based on recent findings to direct future research activities.^[1]

TAXONOMIC CLASSIFICATION OF CUSTARD APPLE (*ANNONA SQUAMOSA* L.)^[2]

Taxonomic rank	Classification
➤ Kingdom	Plantae
➤ Subkingdom	Tracheobionata (Vascular plants)
➤ Family	<i>Annonaceae</i>
➤ Genus	<i>Annona</i>
➤ Species	<i>Annona squamosa</i>
➤ Common Name	Custard apple, sugar apple, sweetsop

GEOGRAPHICAL DISTRIBUTION^[2]

The *Annona squamosa* L. (custard apple) is a species belonging to the family *Annonaceae*. This species is believed to have originated from the tropical regions of America. At present, the plant is grown in many parts of the world as a result of its use as food and medicinal purposes.

This species is found in many countries such as India, Sri Lanka, Bangladesh, Pakistan, Thailand, Myanmar, Philippines, Vietnam, China, Brazil, Mexico, Peru, Australia, South Africa, and many other Caribbean countries. In India, the custard apple is grown almost in all the tropical and subtropical states.

The major states that produce custard apples include Maharashtra, Andhra Pradesh, Telangana, Karnataka, Madhya Pradesh, Chhattisgarh, Gujarat, Rajasthan, Tamil Nadu, Odisha, and Uttar Pradesh. The climate preferred by this species is warm and temperatures range between 20–35°C. The species is common in dry deciduous forests, wastelands, rocky areas, and orchards. The species grows well in sandy or loamy soil and is highly drought resistant. Because of its ability to withstand hot and arid climate, and also because of its ease of maintenance, *Annona squamosa* is one of the most cultivated species in the genus *Annona*.

MORPHOLOGICAL CHARACTER



Custard Apple tree

Habit: *Annona squamosa* L. is a small to medium-sized semi-deciduous tree or a large shrub belonging to the *Annonaceae* family. On average, the height of the plant is 3–8 meters; it has a wide crown with irregular branching.

Root: The plant has a strong and well-developed taproot system along with some lateral roots that serve for plant anchoring and nutrition.

Stem and Bark: The stem is a strong, erect and highly branched wood plant. The bark is thin, light brown to grey-brown in color, rough with small fissures in the adult plants. The young branches are green in color with very few hairs.

Leaves: The leaves are simple, alternate, exstipulate and short petiolate. The leaf shape is lanceolate or oblong lanceolate with an entire edge and an acute apex; it also gives off a strong aroma when the leaves are broken. The adaxial side of the leaf is smooth and dark green in color while the abaxial one is lighter.

Flowers: The flowers appear singly or in groups; they are greenish-yellow in color, have an aromatic smell and are bisexual. Every flower has three thick fleshy sepals and three small petals.

Fruit: The fruit is an aggregate (compound) berry; it is round, conical or heart-shaped, has a size of 5–10 cm in diameter. The surface of the fruit is green in color and covered with polygonal segments (scales); when the fruit matures, its color changes to yellowish-green and its flesh softens.

Pulp: The ripe fruit consists of soft, creamy-white and sweet-smelling pulp rich in carbohydrates, vitamins and minerals.

Seeds: There are numerous, shiny, glossy, hard and oblong or oval seeds in the range of dark brown to black color; there are many of them in the fruit pulp.

Epicarp (Fruit Peel): The epicarp is thick, green, rough, and segmented, becoming yellowish-green on ripening. It is rich in bioactive phytochemicals such as flavonoids, phenolic compounds, tannins, alkaloids, and Acetogenins, which contribute to its medicinal properties.

PHYTOCHEMICALS^[2]

The epicarp (fruit peel) of *Annona squamosa* L. is a rich source of bioactive phytochemicals that contribute to its medicinal properties, including antioxidant, antimicrobial, anti-inflammatory, anticancer, and anthelmintic activities. The major phytochemical constituents reported from the epicarp are as follows.

Table 01: Phytochemical & pharmacological significance of *Annona squamosa*^[2]

Phytochemical Class	Major Compounds Reported	Pharmacological Significance
Phenolic compounds	Gallic acid, Chlorogenic acid, Caffeic acid, Ferulic acid	Potent antioxidant and anti-inflammatory activities
Flavonoids	Quercetin, Kaempferol, Catechin, Epicatechin, Rutin	Antioxidant, antimicrobial, anti-inflammatory, anthelmintic
Tannins	Hydrolysable and condensed tannins	Anthelmintic, antimicrobial, astringent
Alkaloids	Anonaine, Liriodenine, Isocorydine	Antimicrobial, analgesic, cytotoxic

Acetogenins	Squamocin, Annonacin, Bullatacin, Squamostatin	Anticancer, insecticidal, antiparasitic
Terpenoids	α -Pinene, β -Pinene, Limonene, Caryophyllene	Antimicrobial, antioxidant, anti-inflammatory
Saponins	Triterpenoid saponins	Anthelmintic, antimicrobial, immunomodulatory
Glycosides	Various phenolic glycosides	Antioxidant activity
Steroids/Phytosterols	β -Sitosterol, Stigmasterol, Campesterol	Anti-inflammatory, hypocholesterolemic
Carbohydrates & Pectins	Cellulose, Hemicellulose, Pectin	Structural components; contribute to dietary fiber
Vitamins & Pigments	Vitamin C, Carotenoids	Antioxidant properties

THERAPEUTIC USES^[2-5]

Table 02: Therapeutic uses of *Annona squamosa*.

Plant part	Traditional use
Fruit	The ripe fruit is consumed as a nutritious food and is traditionally used for anaemia, diarrhoea and dysentery.
Unripe fruit	Traditionally used for diarrhoea and dysentery in some regions.
Leaves	Leaf decoction has traditionally been used as a vermifuge (anthelmintic), tonic, febrifuge and remedy for cold and dysentery.
Leaves/paste	Crushed leaves or leaf paste have been applied externally to boils, abscesses, wounds and ulcers.
Bark	Bark preparations have traditionally been used for diarrhoea and dysentery; bark and roots have also been reported as purgatives.
Roots	Root preparations have traditionally been used for dysentery and fever and as a purgative.
Seeds	Seeds have been traditionally used as an insecticidal agent and for controlling head lice.
Peel/fruit parts	Various parts of the fruit and plant have been included in traditional remedies for gastrointestinal complaints and inflammatory conditions.

PHARMACOLOGICAL ACTIVITY

1. Antimicrobial Screening

The antibacterial activity of four different extracts obtained from the leaves of Custard Apple (*Annona squamosa* L.) *Annonaceae* was investigated. The agar diffusion method was used to determine the antibacterial activity and the Phytochemical analysis was conducted by applying HPTLC (Camag system). The study used two gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*). The results indicated that the highest zone of inhibition was recorded in methanol extract against *P. aeruginosa* (MIC: 130 μ g/ml), followed by petroleum ether extract in the same bacterium (MIC: 165 μ g/ml) and methanol extract against *E. coli* (MIC: 180 μ g/ml). The study also revealed the presence of some phytochemicals in the extracts which provides the antibacterial property.^[6]

2. Evaluation of the Combinational Antimicrobial Effect of *Annona Squamosa*

This study investigated the antimicrobial properties of methanolic seed extracts of *Annona squamosa* (custard apple) and Phoenix dactylifera (date palm) against several pathogenic bacteria. With the rise of antibiotic resistance, researchers have begun to pay more attention to plant-

based antimicrobial agents due to their safety and efficacy. The methanolic extracts of the seeds were prepared and the agar disc diffusion method was used to determine the antimicrobial activities and the minimum inhibitory concentration (MIC) against both Gram-positive and Gram-negative bacteria. The microorganisms included *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, and *Pseudomonas aeruginosa*, with ampicillin-clavulanic acid serving as the control. The findings showed that the extracts had antibacterial properties, with *Annona squamosa* proving to have a greater impact than Phoenix dactylifera. Moreover, the combination of the extracts was found to have a significant synergistic effect against almost all bacteria except for *Pseudomonas aeruginosa* and *Salmonella paratyphi*. In addition, it was determined that the extracts have bactericidal properties against *Enterococcus faecalis* the 50 mg/mL concentration and 3×10^5 CFU/mL culture concentration, along with the finding of synergistic activities. Hence, this study shows that the seed extract of *Annona squamosa* can be an excellent natural antimicrobial agent.^[7]

3. Antioxidant Activity

The antioxidant potential of *Annona squamosa* fruit was determined through *in vitro* tests conducted on two

extracts: methanol and Aqueous water. The extract was analysed using the following methods: DPPH scavenging activity, lipid peroxidation, nitric oxide scavenging activity, superoxide scavenging activity, hydroxyl scavenging activity, total antioxidant capacity, and reducing power. According to the results, the methanolic extract shows higher inhibition of DPPH scavenging activity as compared to the aqueous extract (97.99% vs 94.15%), NO scavenging (70.96%), superoxide (78.68%), and hydroxyl (85.25%) radical scavenging activity, total antioxidant potential (206 mg α -tocopherol/g) and reducing capacity (56.0 mg ascorbic acid/g). The results indicated that the antioxidant potential of methanol extract is higher than the one of aqueous extract, which can be attributed to high content of phenolic and flavonoid compounds in the methanol extract.^[8]

4. Antifungal Activity

Antifungal Activity and antioxidant activities of organic and aqueous extracts of *Annona squamosa* Linn. Leaves show the study was conducted to assess the antifungal activity of *Annona squamosa* leaves extracts using by methanol, chloroform, and water. Due to the increasing popularity of natural products in the field of medicine thus, making this research study relevant. To evaluate the antifungal activity of the extracts, five fungal strains of *Alternaria alternata*, *Candida albicans*, *Fusarium Solani*, *Microsporum canis*, and *Aspergillus niger* were used. The study results showed that all extracts inhibited fungal activity in a dose-dependent pattern with the methanolic extract showing a maximum effect.

The antioxidant potential of all extracts was determined using DPPH, nitric oxide, hydrogen peroxide scavenging tests, and determination of reducing power. Similar to the antifungal activity of the extracts, antioxidant potentials significantly increased with concentrations, with methanolic extracts having the greatest ability to scavenge free radicals, as it is the case with chloroform and water extracts. Phytochemical studies depicted the presence of useful components such as flavonoids, phenols, tannins, glycosides, and saponins; The chloroform extract showed the lowest MIC of 200 μ g/mL against *Alternaria alternata*. In antioxidant assays, DPPH, H_2O_2 and nitric oxide scavenging activities showed IC_{50} values of 308.3, 242.7 and 185.2 μ g/mL, respectively, for the most active extracts. thus, making them useful in terms of antioxidant and antimicrobial activities.^[9]

5. Antioxidant Activity of Different Parts from *Annona Squamosa*

We extracted phenolics from *Annona squamosa* (leaves, bark, roots, and seedcake) and *Catunaregam nilotica* (leaves, bark, and seedcake) using methanol and assessed their antioxidant activity using different established *in vitro* methods.

The study was conducted using the plant materials *Annona squamosa* (leaves, bark, roots, and seedcake) and *Catunaregam nilotica* (leaves, bark, and seedcake).

Antioxidant activity was assessed using oxygen radical absorbance capacity (ORAC), MTT assay, and DPPH assay while the profile of polyphenols was determined using HPLC method.

The content of total phenolic compounds was determined by the Folin-ciocalteau method with the highest values being 171.5, 170.4, 169.5, and 167.9 g/kg plant extract, as GAE for *Annona squamosa* roots and *Annona squamosa* bark respectively. The extracts of the leaves of the two plants showed significant amounts of flavonoids content. The results also indicated that the extracts of *Catunaregam nilotica* and *Annona squamosa* exhibited antioxidant activities with IC_{50} values ranging between 7.81 and 62.5 and 7.81 and 125.0 μ g/ml respectively using DPPH assay. The extracts from different parts of the two plants showed strong antioxidant activity according to the ORAC method and MTT assay. These findings indicate that phenolic compounds from *Annona squamosa* and *Catunaregam nilotica* can possibly be used as natural antioxidants.^[10]

6. Antimicrobial activities

Antioxidant And Antimicrobial Activities from Raw Fruit Peel Crude Extracts of *Annona Squamosa* Linn of Plants have attained significance as medicinal elements due to their positive effects in the treatment of multiple diseases they further possess the ability to exhibit antioxidant as well as antimicrobial properties due to the presence of various metabolites. In the present research work, the extracts of *Annona squamosa* raw fruit peel have been chosen for the purpose of phytochemical analysis carried out to assess its potential as an antioxidant and antimicrobial agent. The findings of phytochemical analysis indicated that the extracts contain alkaloids, flavonoids, phenols, and saponins. The methanolic extract exhibited the highest DPPH radical-scavenging activity among the tested extracts, with an IC_{50} of 148 μ g/mL. The methanolic extract also showed maximum antibacterial activity against *Klebsiella pneumoniae* (21 mm) and antifungal activity against *Candida albicans* (23 mm) at 100. The study has concluded that the raw fruit peel of *Annona squamosa* has the potential to exhibit excellent antioxidant and antimicrobial properties.^[11]

7. Antibacterial and Wound Healing Activity

Antibacterial and Wound Healing Activity of the Leaves of *Annona squamosa* Linn. Medicinal plants' natural sources have proved to be both effective and safe solutions for wound recovery. In traditional medicine literature suggests that *Annona squamosa* leaves have been used across the globe as medications for wounds. Methanol-dried extracts of *Annona squamosa* leaves were produced using various solvents including petroleum-ether, ether, chloroform, alcohol, and chloroform-water according to their polarity. Each extract underwent an antibacterial assessment based on the methods developed in microbiology. According to antibacterial screening results, maximum inhibitory effects were displayed only in the petroleum ether, alcoholic, and chloroform-water extracts of

Annona squamosa leaves because these extracts were used for observation of wound recovery properties. It is necessary to state that the administration of *Annona squamosa* leaves using petroleum ether method in the dose of 300 mg/kg b.w. orally had successful results in all tests. Wound contraction values after 18 days were assessed as (91.12 ± 0.62 , $p < 0.05$) for excision wound test. Wound breaking strength values during the incision wound test were (299.83 ± 5.446 grams, $p < 0.05$), while granuloma breaking tests showed (378.56 ± 5.520 $p < 0.05$). All the outcomes gained in each test of the wound healing method were statistically reliable compared to control values. The basic elements of the studied extracts including sterols, flavonoids, and tannins have been confirmed.^[12]

8. Antibacterial Activity Against Some Respiratory Tract Isolates

Screening of *Annona squamosa* extracts for antibacterial activity against some respiratory tract isolates. Ethanolic extract was obtained from leaves of *Annona squamosa* by percolation and after that, the extract was partitioned in chloroform and distilled water in the ratio of 1:1 using 30ml of solvent. The extract were tested against clinical isolates of *Klebsiella pneumoniae*, the species of *Proteus*, *Pseudomonas* as well as *Staphylococcus aureus*, *Streptococcus pneumoniae* and α -haemolytic *Streptococci*, using disc diffusion and micro-broth dilution methods. The ethanolic extract and fraction(s) were screened for plant secondary metabolites according to standards. The results of the performed antibiotic susceptibility tests shows that chloroform extracts were effective against *Staphylococcus aureus* and *Streptococcus pneumoniae* (10 mm) at 50µg/disc and ethanolic extract exhibited efficacy against *Klebsiella pneumoniae*, *Streptococcus pneumoniae* and species of *Proteus* at 200µg/disc having zone diameter of *Klebsiella pneumoniae* (11 mm) larger than the one obtained as a result of the action of a standard Augmentin disc (06 mm).^[13]

8. Anti-Inflammatory Activity

Anti-Inflammatory Effect of Fruit Peel Extracts of *Annona squamosa* L. On Mouse Models of Rheumatoid Arthritis is a type of autoimmune disorder caused by the exposure of the body to several antigenic substances leading to arthritis. Several herbs have been researched and used for their ability to stall the progress of the arthritis disease, such as artichoke tea, honey and bee venom. The current research provided an experimental model of induction of rheumatoid arthritis by means of Freund's Complete Adjuvant (FCA) in mice and the regulatory effect of fruit peel extract of the custard apple, so-called *Annona squamosa* Linn (AS). After 10 weeks, the mice were administered with a high dosage of 400mg/kg/day of AS peel extract, as a result, the body weight of the mice increased from 31.56g to 38.00g, while the number of white blood cells decreased from 8.38 to 5.23 ($\times 10^3$ cells/mm³). Moreover, the diameter of the ankle joint decreased from 4.63 to 3.95 (mm). The findings of the study have shown that the treatment with AS fruit peel extract leads to decreased infiltration of immune cells into

the joint, reduced formation of the Fibers, and restoration of the cartilage structure of the synovial membrane.^[14]

9. Analgesic and Anti-Inflammatory Activity

Caryophyllene oxide was extracted from a methanolic extract of bark of *Annona squamosa* and was evaluated for analgesic and anti-inflammatory effects. Caryophyllene oxide at 12.5 and 25 mg/kg body weight as well as methanol extract at 50 mg/kg body weight produced significant analgesic effects both centrally and peripherally along with anti-inflammatory effects. These effects produced by caryophyllene oxide are comparable with the standard drug Pentazocine (50 mg/kg body weight) for Anti-inflammatory effects and Aspirin (100 mg/kg body weight) for analgesic effects used in the respective experiments.^[15]

10. Anti-Ulcer and Analgesic Activity

Evaluation of Anti-ulcer and analgesic activity by *Annona squamosa* Leaves encompass the analytical, phytochemical and pharmaceutical studies of the medicinal shrub *Annona squamosa* (Family *Annonaceae*). Natural products are regarded as a better option given its low damaging effects on both the environment and the non-target species. The Annonaceous acetogenins are the emerging class of prospective long chain fatty acids derivatives that observed solely in the species of the family *Annonaceae* to which they initially belonged. The compounds gained the worldwide attention because of their impressive anti-tumor and other pesticidal activities. The pharmacological purposes of the above mentioned plant include the normalization of hyperthyroidism and lipid-peroxidation. It also has analgesic, anti-inflammatory, anti-microbial, cytotoxic, antioxidant, hypolipidemia, anti-ulcer, molluscicidal, genotoxic, vaso-relaxant, anti-neoplastic, hepatoprotective and larvicidal properties among other characteristics. The various parts of the plant including its leaves, roots and seeds contain different medicinal characteristics and use 62.43% anti-ulcer protection at 100 mg/kg and 87.37% reduction in writhing at 100 mg/kg, because these clearly demonstrate the dose-dependent activity.^[16]

11. Anthelmintic Activity

It has been shown that extracts of *Annona squamosa* seeds have an anthelmintic effect against *Haemonchus contortus*, the principal nematode in sheep and goats in Northeast Brazil. A compound numbered 1 was isolated from the ethyl acetate extract and was found to inhibit the larval hatching of *H. contortus* at a concentration of 25 mg/ml. Measurements were performed using different spectroscopic techniques; the results allowed researchers to establish the structure of compound and the methanolic bark extract of *Annona squamosa* at 50 mg/kg and isolated caryophyllene oxide at 12.5 and 25 mg/kg body weight exhibited significant central and peripheral analgesic and anti-inflammatory activities. The activities were compared with aspirin (100 mg/kg) and pentazocine (50 mg/kg) as standard drugs.^[17]

12. Evaluation Of Gastric Antiulcer and Antioxidant Activities in Aqueous Extracts of *Annona Squamosa* and *Achyranthes Aspera* in Rats

The study examined the efficacy of aqueous extracts from *Annona squamosa* and *Achyranthes aspera* on rats using both pyloric ligation and aspirin-induced gastric ulcers. The study also evaluated the extracts' antioxidant activity through nitric oxide scavenging and lipid peroxidation inhibition assays. The results indicated that both extracts given at a dose of 200 mg/kg produced a significant reduction ($p < 0.01$) of the ulcer index in comparison to the control group. The antioxidant activity results also indicated that the extracts were effective with a significant inhibition of nitric oxide scavenging and lipid peroxidation activity ($p < 0.01$) as compared to control and $53.5 \pm 0.23\%$ nitric oxide scavenging at 100 $\mu\text{g/mL}$ and $61.6 \pm 0.06\%$ lipid peroxidation inhibition at 50 $\mu\text{g/mL}$, along with the 200 mg/kg antiulcer dose. The study confirmed the antiulcer ability of the aqueous extracts of *Annona squamosa* and *Achyranthes aspera* through reduction in the pH, acidity and volume of gastric juices.^[18]

13. Antiviral Activity

Dengue virus infection is a prevalent viral infection transmitted by mosquitoes and it can cause dengue hemorrhagic fever or dengue shock syndrome. Nevertheless, dengue is a serious disease that has no specific antiviral therapy or vaccine. Thus, we aimed to test the efficacy of *Annona squamosa* leaf extract against DENV2 strain isolated from Surabaya, Indonesia in 2013 (NCBI accession number: KT012509). Methods: In this study, we assessed the antiviral activity of *Annona squamosa* leaf extract against DENV2 in Vero cells using Viral ToxGlo™ assay. Furthermore, we used CellTiter-Glo® Luminescent Cell Viability Assay to determine the viability of Vero cells in cell culture based on ATP quantification. Findings: ASLE inhibit DENV-2 replication in Vero cells with IC50 of 73.78 $\mu\text{g/mL}$ and SI of 4.49 when cells were treated after two days of virus infection, while its CC50 for cytotoxic effects on Vero cells is 331.54 $\mu\text{g/mL}$. Interestingly, this is the first study showing the effect of ASLE on DENV-2. Conclusion: In summary, ASLE showed antiviral activity against DENV-2 with minimal toxicity, hence it may be potentially used as a drug candidate.^[19]

14. Composition, Extraction Technologies, and Food Applications

The article examines the nutritional makeup, plant compounds, ways to extract useful components, food uses, safety aspects, and future potential of custard apple seeds and peels. It stresses the value of turning fruit waste into useful items, which supports environmental sustainability and reduces waste. The piece covers traditional extraction techniques like solvent extraction, Soxhlet extraction, and maceration, as well as modern eco-friendly methods such as ultrasound-assisted extraction, microwave-assisted extraction, and supercritical fluid extraction. It also outlines different food uses for custard apple by-products, including their role as natural preservatives, functional food

components, edible coatings, biodegradable films, and sources of edible oils and proteins and *Annona squamosa* peel contains 28.771 ± 0.008 mg GAE/g total phenolics and 81.27 ± 1.74 μg QE/g total flavonoids. Different extraction techniques produced higher phenolic recoveries, including 94.08 mg GAE/g by maceration, 96–98 mg GAE/g by microwave-assisted extraction, and 109.38 mg GAE/g by supercritical-fluid extraction.^[20]

15. Physico-Chemical Properties of Custard Apple

The study examines the physical and chemical features of both ripe and unripe *Annona squamosa* fruits. This study aims to aid in the development of post-harvest processing equipment and products that add value. It looks at several key factors including the weight and size of the fruit, its firmness, the amount of pulp obtained, moisture levels, pH, total soluble solids, sugar content, and ascorbic acid. The findings offer dependable data that can be used in food processing and storage. Despite its usefulness, the study mainly covers engineering and quality-related aspects, and it doesn't go into much detail about phytochemical content, biological effects, or potential industrial uses and custard apple contained 51.50% peel in ripe fruits and 59.29% in unripe fruits, with moisture contents of 68.42% and 64.75%, respectively. The ripe fruit pulp showed 30.7 °Brix total soluble solids, 15.6 g/100 g total sugar and 13.65 mg ascorbic acid. As a whole, it serves as a useful resource for researchers working in post-harvest technology and food engineering.^[21]

16. Effect of Drying Methods on Physicochemical Properties, Bioactive Compounds, and Application

The study looks at using custard apple peel as a sustainable ingredient in functional food. The study compares tray drying and vacuum drying methods and shows that vacuum drying better keeps rich bioactive compounds intact. Ultrasound-assisted extraction with a 60:40 water–ethanol ratio produced the highest total phenolic content of 1245.12 ± 0.17 mg GAE/100 g. Structural characterization using FTIR, XRD and SEM confirmed the functional and structural characteristics of the peel powder and water mix produced the highest phenolic content. Additionally, adding 4% peel powder resulted in cream biscuits that had good sensory acceptability. Overall, the study is well-designed and showcases a new way to turn fruit waste into safe, nutritious, and valuable food products.^[24]

17. Bioactive Effect of Custard Apple By-Products by *In Vitro* Assays

The article looks into the health benefits of custard apple seed and peel extracts through various lab tests. The study shows that both by-products have significant antioxidant, free radical scavenging, enzyme-inhibiting, and antiplatelet effects. Generally, seed extracts have higher phenolic content and stronger biological effects compared to peel extracts. These findings indicate that these agro-industrial by-products could be valuable in the food, pharmaceutical, and cosmetic industries. The peel extract showed a total phenolic content of 28.771 ± 0.008 mg GAE/g dry extract,

with antioxidant capacities of 0.27 ± 0.01 mmol Fe^{2+} /g DE (FRAP), 130.0 ± 0.4 μ mol TE/g DE (TEAC) and 0.324 ± 0.009 mmol TE/g DE (ORAC). The peel also exhibited nitric oxide-scavenging activity with an IC_{50} of 11.8 ± 0.3 mg/L, indicating its potential as a source of phenolic compounds and antioxidant bioactive constituents. However, more studies in living organisms and clinical trials are needed to confirm their health benefits and safety.^[22]

18. Antioxidant, Anticancer and Antibacterial Properties of *Annona squamosa* Leaf Extracts

This research article discusses the chemical composition and biological effects of *Annona squamosa* leaf extracts. Using GC-MS, the study found many rich bioactive compounds, like germacrene-D and trans-caryophyllene, that fight free radicals, bacteria, and cancer. The extracts proved to be strong free radical scavengers, killed bacteria, and greatly reduced the growth and migration of colon cancer cells in the laboratory. The methanolic extract showed the highest total phenolic content of 282.1 ± 11.2 mg GAE/g, whereas the acetone extract exhibited the highest total flavonoid content of 7.1 ± 0.9 mg quercetin/g. Among the antioxidant assays, the acetone extract showed the strongest DPPH radical-scavenging activity with an IC_{50} of 33.9 ± 4.8 μ g/mL, while the water extract showed the strongest hydrogen peroxide-scavenging activity with an IC_{50} of 110 ± 14.1 μ g/mL. The methanolic extract also demonstrated antibacterial activity, producing inhibition zones of 16.5 ± 0.5 mm against *Staphylococcus aureus* and 18.3 ± 0.6 mm against *Pseudomonas aeruginosa*. GC-MS analysis identified several bioactive constituents, with germacrene-D (22.01%) and trans-caryophyllene (12.12%) among the major compounds. Overall, the study proves that *Annona squamosa* leaves can be used therapeutically, and that they should be used in future research.^[23]

19. Antimicrobial Potential of Nanomaterials Synthesized with Extracts from *Annona* Plants

This article is a good summary of green synthesis of nanomaterials from *Annona* species and their biomedical applications. It talks about how alkaloids, phenolics, terpenoids, and acetogenins help nanoparticles form and stay together. The article highlights the antibacterial, antioxidant, anti-cancer, anti-diabetic and anti-parasitic activities of these nanomaterials with silver nanoparticles. Among the 74 studies analysed, *Annona squamosa* accounted for 27.63%, while silver nanoparticles were the most frequently reported nanomaterial (48.64%). The authors also reported that stirring was the most commonly used synthesis method (62.43%). In one reported study, CdS nanoparticles synthesized using *A. muricata* leaf extract showed a spherical morphology with a particle size of 3.42 nm and exhibited antimicrobial activity against *Staphylococcus aureus* and antifungal activity against *Aspergillus niger*. It also highlights the need for standardized synthesis protocols, and more *in vivo* toxicity studies, before using in humans. Overall, the article is informative and useful for researchers in nano and natural product.^[24]

20. Anticancer Activity

Research shows the nutritional content and biological activities of different fruit parts, including peel, pulp, and seeds. Study shows that seed extracts contain the most phenolic compounds, antioxidants, antibacterial properties, and anti-cancer activity against various human cancer cell lines. The peel extracts demonstrated considerable antimicrobial activity, with *Annona h.* peel producing inhibition zones of 14.70 ± 1.07 mm against *Klebsiella pneumoniae* and 16.10 ± 1.25 mm against *Salmonella senftenberg*. The peel extracts also exhibited cytotoxic activity against selected cancer cell lines. The *Annona S.* peel showed IC_{50} values of 30.69 ± 0.35 μ g/mL against Caco-2, 15.28 ± 0.67 μ g/mL against HepG-2, 15.17 ± 0.17 μ g/mL against MCF-7, and 14.36 ± 0.35 μ g/mL against PC-3. Overall, this study is useful science supporting the use of custard apple peels for nutraceuticals and pharmaceuticals, but we need more studies on the safety and effectiveness of using these in the living body.^[25]

21. Antimicrobial, Anticancer, Apoptosis Potentials, Assisted by In Silico Modelling, and Metabolic Profiling

The research article "Green Biosynthesis of Silver Nanoparticles Using *Annona* Fruit Extracts" looks into how we can make nanoparticles in a way that is good for the environment. This is done by using extracts from the *Annona squamosa* and *Annona glabra* fruits. The silver nanoparticles that are made this way are then carefully checked using tools like UV-visible spectroscopy and others. When we test these nanoparticles, we find that they are very good at fighting off bad microbes like *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*. Silver nanoparticles also show that they can help fight cancer in the lab, which's very promising. This is seen when they are tested on cells like PC3, SKOV3 and HeLa and UPLC-QTOF-MS/MS profiling tentatively identified 114 compounds, including 77 acetogenins, 20 diterpenes and 17 miscellaneous compounds. The synthesized *A. squamosa*-silver nanoparticles had an average particle size of 6.63 nm and showed a UV-Visible absorption maximum at 414 nm. The ethanolic *A. squamosa* extract exhibited cytotoxic activity against PC3 cells with an IC_{50} of 3.5 ± 0.1 μ g/mL, while the corresponding silver nanoparticles showed stronger activity with an IC_{50} of 1.7 ± 0.4 μ g/mL. The extract also induced apoptosis in PC3 cells ($79.63 \pm 3.3\%$) and demonstrated significant biological activity against the tested cancer cell lines. The study also uses something called docking to see how well the silver nanoparticles can fight cancer. The results from this are also very positive. So, this study shows that making nanoparticles from *Annona* species in a green way can have many good uses in medicine. The silver nanoparticles made from *Annona* species are very promising for use, in medicine.^[26]

22. In Vitro Cytotoxicity of *Annona squamosa* L. Pulp Extract as a Mouthwash

This study was conducted the cytotoxicity of ethanolic pulp extract of *Annona squamosa* as a potential herbal

mouthwash for children using human dermal fibroblast neonatal (HDFn) cells. Its cytotoxicity was compared to 0.12% chlorhexidine, the standard mouthwash. The extract was tested at concentrations ranging from 6.25 to 400 µg/mL. Cell viability was $94.41 \pm 0.48\%$ at 6.25 µg/mL and decreased to $66.71 \pm 3.28\%$ at 400 µg/mL, demonstrating a concentration-dependent cytotoxic effect. The IC₅₀ value of *A. squamosa* extract was 235.4 µg/mL, whereas chlorhexidine showed an IC₅₀ of 97.8 µg/mL, indicating comparatively lower cytotoxicity of the *A. squamosa* extract. The results showed that the *Annona squamosa* extract had much lower cytotoxicity, with an IC₅₀ value of 235.4 µg/mL, while chlorhexidine had a value of 97.8 µg/mL. At lower concentrations, the extract showed minimal toxicity and maintained high cell viability. These findings suggest that *Annona squamosa* pulp extract is biocompatible and could be a safer natural option compared to chlorhexidine for children's oral care. However, more *in vivo* and clinical studies are needed before it can be widely used in practice.^[27]

CONCLUSION

Annona squamosa L. (custard apple) is a valuable medicinal and nutritional plant containing a wide range of bioactive phytochemicals, including phenolic compounds, flavonoids, tannins, alkaloids, acetogenins, terpenoids, saponins, and phytosterols. The review indicates that the fruit peel, which is often considered a waste material, contains several biologically active constituents with significant pharmacological potential. Studies have reported antioxidant, antimicrobial, anti-inflammatory, anthelmintic, anticancer, and other therapeutic activities associated with different parts of the plant, particularly the fruit peel and seeds.

The reported antioxidant activity of custard apple extracts is associated mainly with their phenolic and flavonoid content, while antimicrobial and antiparasitic effects may be related to the combined action of tannins, alkaloids, saponins, terpenoids, and annonaceous acetogenins. Research on raw fruit peel extracts has demonstrated promising antioxidant and antimicrobial properties, supporting the possibility of utilizing the peel as a source of natural bioactive compounds rather than treating it solely as fruit waste. The anthelmintic potential of *Annona squamosa* has also been demonstrated in experimental studies, particularly against *Haemonchus contortus*, indicating its possible importance in the development of plant-based antiparasitic agents.

Recent studies further highlight the potential of custard apple peels and other by-products for applications in pharmaceutical, nutraceutical, food, and cosmetic fields. Valorization of the peel could provide an economical and sustainable approach for converting fruit-processing waste into useful bioactive products. However, most of the available evidence is based on *in-vitro* and experimental studies. Therefore, further research involving standardized extracts, identification and isolation of active compounds,

toxicity evaluation, *in-vivo* studies, pharmacokinetic investigations, and well-designed clinical trials is necessary to establish their safety, efficacy, and therapeutic applications. Overall, *Annona squamosa* L. peel represents a promising natural source of bioactive compounds and deserves further systematic investigation for the development of safe and effective herbal therapeutic products.

REFERENCE

1. Rajesh K, Suganya G, Anitha P. Phytochemical and pharmacological profile of *Annona squamosa* Linn.: A review. *International Journal of Pharmaceutical Sciences and Research*, 2014; 5(11): 4557–4567.
2. Ma C, Chen Y, Chen J, Li X, Chen Y. A review on *Annona squamosa* L.: phytochemicals and biological activities. *The American Journal of Chinese Medicine*, 2017; 45(5): 933–964.
3. Moussa AY, et al. Phytochemical constituents, bioactivities, and applications of custard apple (*Annona squamosa* L.): A narrative review. *Food Chemistry*, 2024; 459: 140363.
4. Coria-Téllez AV, Montalvo-González E, Yahia EM, Obledo-Vázquez EN. *Annona muricata*: A comprehensive review on its traditional medicinal uses, phytochemicals, pharmacological activities, mechanisms of action and toxicity. *Arabian Journal of Chemistry*, 2018; 11: 662–691.
5. Singh RP, Pattnaik AK, Rudrapal M, Bhattacharya S. *Annona squamosa* Linn.: A Review of Its Ethnobotany, Pharmacology, Phytochemistry, Toxicity, and Conservation Needs. *Pharmacognosy Magazine*, 2025; 21(2): 403–412.
6. Gutiérrez-Pinzón Y, Martínez-Preciado AH, Velázquez-López JM, Pech-Jiménez C, Zúñiga-Mayo VM, Guevara-Martínez SJ, et al. antimicrobial potential of nanomaterials synthesized with extracts from *Annona* plants. *Antibiotics (Basel)*, 2025; 14(8): 748.
7. Javed A. Evaluation of the combinational antimicrobial effect of *Annona squamosa* and *Phoenix dactylifera* seeds methanolic extract on standard microbial strains. *Int Res J Biol Sci*, 2013; 2(5): 68–72.
8. Nandhakumar E, Indumathi P. *In vitro* antioxidant activities of methanol and aqueous extract of *Annona squamosa* (L.) fruit pulp. *J Acupunct Meridian Stud*, 2013; 6(3): 142–148.
9. Kalidindi N, Thimmaiah NV, Jagadeesh NV, Nandeep R, Swetha S, Kalidindi B. Antifungal and antioxidant activities of organic and aqueous extracts of *Annona squamosa* Linn. leaves. *J Food Drug Anal*, 2015; 23(4): 795–802.
10. Mariod AA, Abdelwahab SI, Elkheir S, Ahmed YM, Fauzi PN, Chuen CS. Antioxidant activity of different parts from *Annona squamosa* and *Catunaregam nilotica* methanolic extract. *Acta Sci Pol Technol Aliment*, 2012; 11(3): 249–258.
11. Kaladhar DSVGK, Duddukuri GR, Yarla NS. Phytochemical analysis, antioxidant and antimicrobial activities from raw fruit peel crude extracts of *Annona*

- squamosa* Linn. *World J Pharm Pharm Sci*, 2014; 4(1): 1373–1380.
12. Shenoy C, Patil MB, Kumar R. Antibacterial and wound healing activity of the leaves of *Annona squamosa* Linn. (Annonaceae). *Res J Pharmacogn Phytochem*, 2009; 1: 44–50.
13. Yusha'u M, Taura DW, Bello B, Abdullahi N. Screening of *Annona squamosa* extracts for antibacterial activity against some respiratory tract isolates. *Int Res Pharm Pharmacol*, 2011; 1(9): 237–241.
14. Nguyen TT, Tran PN, Phan HT. Evaluation of anti-inflammatory effect of fruit peel extracts of *Annona squamosa* L. on mouse models of rheumatoid arthritis. *J Microbiol Biotechnol Food Sci*, 2021; 11(2): e2075.
15. Singh TP, Singh RK, Malik P. Analgesic and anti-inflammatory activities of *Annona squamosa* Linn. bark. *J Sci Innov Res*, 2014; 3: 60–64.
16. Nishath I. Evaluation of anti-ulcer and analgesic activity by *Annona squamosa* leaves, 2016; 2(6): 993–1000.
17. Souza MM, Bevilacqua CM, Morais SM, Costa CT, Silva AR, Braz-Filho R. Anthelmintic acetogenin from *Annona squamosa* L. seeds. *An Acad Bras Cienc*, 2008; 80(2): 271–277.
18. Alluri R, Sagi AK, Pasala PK. Evaluation of gastric antiulcer and antioxidant activities in aqueous extracts of *Annona squamosa* and *Achyranthes aspera* in rats. *Int J Phytopharmacol*, 2011; 2(2).
19. Ansori ANM, Fadholly A, Proboningrat A, Antonius Y, Hayaza S, Susilo RJ, et al. Novel antiviral investigation of *Annona squamosa* leaf extract against Dengue Virus Type-2: *In vitro* study. *Pharmacogn J*, 2021; 13(2): 456–462.
20. Mamayabay MA. Valorization of custard apple (*Annona squamosa*) seeds and peels: composition, extraction technologies, and food applications. *Sustain Food Technol*, 2026; 4.
21. Kaur J, Mittal A, Singh S, Baghel DS. A comprehensive review on custard apple (*Annona squamosa*).
22. Redasni A, Mondal S, Pawase P, Saleem F, Chavan R, Ameer K, et al. Valorization of custard apple (*Annona squamosa* L.) peel waste: Effect of drying methods on physicochemical properties, bioactive compounds, and application in functional cream biscuits. *Food Chem Adv*, 2026; 12: 1013.
23. Rojas-García A, Rodríguez L, Cádiz-Gurrea MDL, García-Villegas A, Fuentes E, Villegas-Aguilar MDC, et al. Determination of the bioactive effect of custard apple by-products by *in vitro* assays. *Int J Mol Sci*, 2022; 23(16): 9238.
24. Al-Nemari R, Al-Senaidy A, Semlali A, Ismael M, Badjah-Hadj-Ahmed AY, Ben Bacha A. GC-MS profiling and assessment of antioxidant, antibacterial, and anticancer properties of extracts of *Annona squamosa* L. leaves. *BMC Complement Med Ther*, 2020; 20: 296.
25. Gutiérrez-Pinzón Y, Martínez-Preciado AH, Velázquez-López JM, Pech-Jiménez C, Zúñiga-Mayo VM, Guevara-Martínez SJ, et al. antimicrobial potential of nanomaterials synthesized with extracts from *Annona* plants: A review. *Antibiotics*, 2025; 14(8): 748.
26. Shehata MG, Abu-Serie MM, Abd El-Aziz NM, El-Sohaimy SA. Nutritional, phytochemical, and *in vitro* anticancer potential of sugar apple (*Annona squamosa*) fruits. *Sci Rep.*, 2021; 11: 6224.
27. Vyas K, Manda H, Sharma RK, Singhal G. An update review on *Annona squamosa*. *Int J Pharm Ther*, 20123; (2): 107–118.
28. Mokhtar FA, Selim NM, Elhawary SS, Abd El Hadi SR, Hetta MH, Albalawi MA, et al. 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 (Basel)*, 2022; 15(11): 1354.
29. li SH, Jafar ZJ. *In vitro* cytotoxic effect of *Annona squamosa* pulp extract as a mouthwash for children on human normal cell line. *J Baghdad Coll Dent*, 2022; 34(1): 60–66.