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Review Paper

Phytochemistry and Pharmacological Activities of Annona squamosa Extracts: A Comprehensive Review

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ABSTRACT

Annona squamosa L. (family Annonaceae) is a tropical plant that is generally known as custard apple or sugar apple and is of considerable medicinal importance in traditional medicine. Various parts of the plant—such as the leaves, fruit, seeds, bark, and roots—have been used traditionally to treat diabetes, diarrhea, dysentery, fever, skin disorders, parasitic infections, and inflammatory conditions. The plant contains a variety of bioactive phytochemicals, including alkaloids, flavonoids, phenolic compounds, tannins, terpenoids, saponins, and annonaceous acetogenins, all of which account for its wide range of biological effects. Experimental studies have shown that A. squamosa has significant antioxidant, antimicrobial, anti-inflammatory, antidiabetic, hepatoprotective, anticancer, anthelmintic, and insecticidal properties. The seeds, in particular, contain a large amount of acetogenins and cyclopeptides which have considerable pharmacological potential. Apart from its medical uses, A. squamosa also has important roles in the food, cosmetic, agricultural, and nutraceutical industries. This review gives a brief summary of the botanical features, geographical distribution, phytochemical components, traditional medicinal applications, pharmacological actions, and possible therapeutic uses of Annona squamosa, emphasizing its value as a promising natural source of bioactive compounds for future pharmaceutical development.

INTRODUCTION

Herbal medicine remains one of the oldest and most widely practiced systems of healthcare worldwide. Approximately 75–80% of the global population still depends on herbal medicine for primary healthcare needs, particularly in developing countries where traditional medicinal systems continue to play a vital role[8]. Herbal medicines are generally regarded as readily

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accessible, affordable, and culturally acceptable therapeutic options. They are often considered a valuable alternative for the management of various diseases in cases where conventional synthetic drugs fail to provide adequate relief or produce undesirable side effects such as lethargy and other adverse reactions[5]. In many parts of the world, herbal medicine continues to serve as a fundamental component of the healthcare system, and traditional herbal practitioners have long been recognized for their knowledge of indigenous medicinal plants used in the treatment of a wide range of disorders.

Traditional medicine employs herbal remedies prepared in various forms, including infusions, decoctions, powders, extracts, and tinctures. Medicinal preparations are derived from different parts of plants such as bark, leaves, fruits, seeds, roots, and flowers, which contain numerous phytoconstituents including alkaloids, tannins, saponins, sterols, fixed oils, glycosides, proteins, phenols, flavonoids, quinones, and terpenoids[29]. The processing of medicinal plants plays several important roles, including reducing toxicity and adverse effects, protecting active constituents, enhancing biological activity, and improving the ease of administration[14]. Both synthetic pharmaceuticals and traditional herbal medicines have originated from natural products, highlighting the significance of plants as a source of therapeutic agents [7].

Different data shows that *A. squamosa* seeds be potential for the new products discovery process based on a survey mainly focused on nutritional, phytochemical and biological properties. There is a potential for this plant species, A. squamosa seeds, to be used as an ingredient in the nutraceutical and food/nutrition industry (e.g., anticancer drugs and dietary supplements blockers against antitumoral) with beneficial effects on health [30].

1. PLANT PROFILE

Annona squamosa L., commonly referred to as custard apple, sugar apple, or sweetsop, is a fruit-bearing plant of medicinal significance within the family Annonaceae[1]. This species has been utilized extensively in traditional and folk medicine worldwide and is widely distributed in Myanmar, the West Indies, India, and other tropical and subtropical regions. Although its precise origin is debated, it is generally considered native to tropical America [2,3,30]. Annona squamosa is a member of the genus *Annona*, which includes more than 120 species known for their edible fruits and medicinal properties [9]. The Annonaceae family is among the largest in the order *Magnoliales*, comprising approximately 135 genera and over 2,300 species [21,22,28]. The genus name *Annona* is derived from the Latin word *anon*, meaning "yearly produce," which refers to the annual fruit-bearing characteristic of these species [10,24,25].

Figure 1. *Annona squamosa* fruit

Figure 2. *Annona squamosa* Seed

2.1 Biological Source

Custard apple (*Annona squamosa* L.) is a tropical tree or shrub belonging to the family Annonaceae. It is believed to be native to the Amazon rainforest and is widely cultivated in tropical and subtropical regions because of its edible fruits and medicinal value [17]. Although the exact origin of *A. squamosa* remains uncertain, the species is extensively cultivated in tropical countries, particularly in warm climatic conditions such as the Brazilian semi-arid region [16].

2.2 Taxonomical Classification

Table No 1: Taxonomical Classification of *Annona squamosa* [10, 21,35,36]

Taxonomic Rank	Classification
Kingdom	Plantae
Subkingdom	Tracheobionta
Division	Magnoliophyta
Superdivision	Spermatophyta
Class	Magnoliopsida (Dicotyledons)
Subclass	Magnoliidae
Order	Magnoliales
Family	Annonaceae
Subfamily	Maloideae
Genus	*Annona* ; *Annona* L.
Species	*A. squamosa*; *Squamosa*; *reticulata*
Tribe	Abreae

2.3 Vernacular Names

Table No 2: Vernicular Name of *Annona squamosa*

Language	Vernacular Name
Odia	Ata
Hindi	Sharifa [2,4]; Sitafal[5]
Arabic	Gishta[2]
English	Sweetsop, Custard apple, Sugar apple [3,4,5]; sweet apers[4]
Myanmar	Aw-za[3]
Telugu	Sitaphal[4]; Seethaphalam[5]; Seetha phalam[25]
Gujarati	Sitafal[9]
Marathi	Sitaphal[11]
Indonesian	Srikaya[13]
Urdu	Sharifa[14]
Egyptian	Keshta[23]
Bengali	Ata [25]
Malayalam	Aathappazham, Seetha pazham[25]
Middle East	Qishta, Ishta, or Ashta[26]
French	Corossolier cailleux; Pommier cannelle[27]

2.4 Botanical Description

Annona squamosa is a small to medium-sized semi-evergreen tree or shrub that typically reaches a height of 3 to 8 meters, with a broad, open crown and irregularly spreading branches[22,24]. It is widely cultivated across India for its nutritious fruits,

which generally mature between September and October[4,12]. The fruit is green, cone-shaped, and characterized by scaly segments, while the edible pulp is creamy white, sweet, aromatic, and rich in vitamins A and C[10,11,22]. Fruits usually measure 6 to 10 centimeters in diameter and contain 20 to 38 smooth, glossy black or dark-brown seeds[17,22]. The leaves are simple, lanceolate, and measure approximately 6 to 17 centimeters in length and 3 to 5 centimeters in width[22].

This species thrives in dry tropical climates, tolerates mild frost, and grows optimally in well-drained soils, despite having a relatively shallow root system [10].

2.5 Geographical Distribution

Annona squamosa is widely cultivated across tropical and subtropical regions worldwide[2,28]. Native populations in the Andes first cultivated the species, and it was introduced to California in 1871[24]. It is considered native to the West Indies and is extensively grown in the Philippines, India, and Thailand[7,25,27]. The species is also botanically associated with Jamaica, and its origin is linked to the West Indies and South America[25,27].

In the seventeenth century, *A. squamosa* was introduced to southern China, Queensland (Australia), Polynesia, Hawaii, tropical Africa, Egypt, and the lowlands of Palestine[21]. The plant was likely introduced to Brazil as "fruta do conds" and later spread to the Philippines and other parts of Asia via the West Indies[21].

Although its precise origin is uncertain, *A. squamosa* is widely cultivated in tropical regions, especially in areas with high temperatures such as the Brazilian semi-arid zone[16]. It thrives in lowland tropical climates across southern Mexico, tropical Africa, Australia, Central and South America, Hawaii, the United States, Polynesia, Florida, and the Antilles[17].

The species is cultivated in tropical South America, southern Florida, Puerto Rico, Jamaica, Barbados, and dry regions of Australia. Historical records show its presence in Indonesia since the seventeenth century, after which it became established in southern China, tropical Africa, Egypt, and the lowlands of Palestine[5].

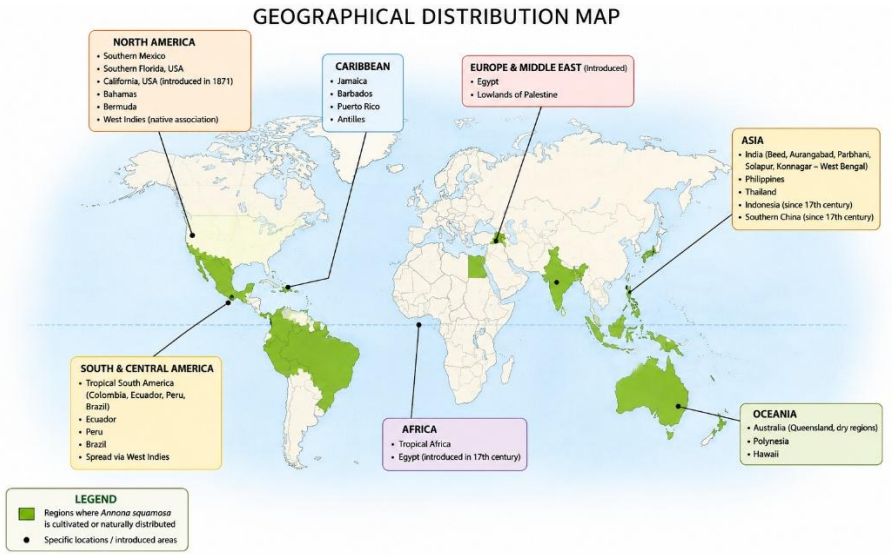

Figure No 3: Geographical Distribution Map

Annona squamosa is cultivated in Paukkhaung Township of the Bago Region[3], Konnagar (West Bengal)[7], Kabama Layout, Sabon Gari, Zaria[11], tropical South America, southern Mexico, and

soAnnona squamosa is cultivated in Paukkhaung Township (Bago Region)[3], Konnagar (West Bengal)[7], Kabama Layout (Sabon Gari, Zaria)[11], tropical South America, southern Mexico, and southern Florida[21]. In India, it is extensively grown in Beed, Aurangabad, Parbhani, and Solapur districts[12]. The species is considered native to the New World tropics, especially northern South America, including Colombia, Ecuador, and Peru[24]. ted across the West Indies, South and Central America, Ecuador, Peru, Brazil, India, Mexico, the Bahamas, Bermuda, and Egypt[15,30].

2.6 Nutritional and Phytochemical Characteristics

The increased consumption of custard apple is attributed to its nutritional value, pleasant flavor, and medicinal properties [26]. The seeds provide essential minerals such as potassium, phosphorus, calcium, sulfur, iron, manganese, zinc, and copper[3]. The fruit is a rich source of vitamins A, B, C, E, and K, as well as antioxidants, polyunsaturated fatty acids, and essential minerals[2]. Various parts of the plant contain glycosides, alkaloids, saponins, flavonoids, tannins, carbohydrates, proteins, phenolic compounds, phytosterols, and amino acids. These constituents are responsible for a broad spectrum of biological activities, including antifeedant, antimalarial, cytotoxic, immunosuppressive, anti-HIV, and antiplatelet aggregation effects[26,27].

The seeds of *A. squamosa* consist of a seed coat (32.4%) and a seed kernel (67.7%), with a crude fatty oil content of approximately 22.2% on a dry weight basis. These seeds are particularly rich in alkaloids, flavonoids, phenolic compounds, annonaceous acetogenins, and cyclopeptides, which contribute to diverse pharmacological activities[30]. Experimental studies have shown that the seeds exhibit antibacterial, antioxidant, hepatoprotective, and antitumor or anticancer properties. Additionally, more than 400 bioactive compounds have been isolated from various parts of *A. squamosa*[30]. As a result, the fruit, leaves, bark, roots, and seeds are widely used in traditional medicine and are increasingly recognized for their medicinal, pharmaceutical, and nutraceutical applications [24].

3. Phytochemical Constituents

The majority of volatile oils in *Annona squamosa* have been reported from the fruit pulp and leaves[21]. Different parts of the plant contain a wide variety of bioactive phytochemicals, including acetogenins, alkaloids, flavonoids, phenolic compounds, tannins, terpenoids, steroids, saponins, glycosides, cyclopeptides, and fatty acids, which contribute to its diverse pharmacological properties.

Fruit:

The unripe fruit contains acetogenins, glycosides, alkaloids, flavonoids, phytosterols, steroids, saponins, volatile compounds, cyclic ketones, long-chain fatty acids, terpenoids, tannins, phenols, verbenone, and borneol[33]. In addition, the fruit has been reported to contain twelve known kaurane derivatives and two new kaurane diterpenoids, namely annosquamosin-A and annosquamosin-B [33].

The n-hexane fraction of the fruit pod contains several compounds, including 5-(propan-2-ylidene)cyclopenta-1,3-diene, 9,10-dehydro-isolongifolene, 6-((benzyloxy)methyl)-2,3,4-trimethylcyclohexyl formaldehyde, 2-methyloct-5-yn-4-yl-3-fluorobenzoate, methyl palmitate, n-hexadecanoic acid, trans-13-octadecenoic acid, octadecanoic acid, 3-(1,1-dimethylallyl)-scopoletin, 2-[(1,2-dimethylpiperidin-3-yl)methyl]-3H-indol-3-one, andrographolide, and nordextromethorphan.

Similarly, the dichloromethane (DCM) fraction of the fruit pod has been reported to contain

spathulenol (1,1,7-trimethyl-4-methylene decahydro-1H-cyclopropa[e]azulen-7-ol), methyl palmitate, n-hexadecanoic acid, oleic acid, androsterone, kaur-16-ene, 2,3,4,6-tetramethyl-benzoic acid, and methyl-4,11-dimethyl-8-methylenetetradecahydro-6a,9-methanocyclohepta[a]naphthalene-4-carboxylate[22].

Leaves:

The leaves are a rich source of alkaloids [21]. Isoquinoline alkaloids have been isolated from the leaves, and approximately 59 chemical compounds have been identified from the leaf essential oil. The leaf oil is particularly rich in terpenes and sesquiterpenes, including β-caryophyllene (31.1%), δ-cardinene, α-muurolene (5.5%), and α-cadinol (4.3%). Two acetogenins, annoreticulin and isoannoreticulin, isolated from the leaves, have demonstrated selective cytotoxic activity against certain human tumor cell lines[33].
The leaves also contain anonaine, benzyltetrahydroisoquinoline, borneol, camphene, camphor, car-3-ene, carvone, β-caryophyllene, farnesol, geraniol, 16-heptatriacontanone, hexacontanol, higenamine, isocorydine, limonene, linalool acetate, menthone, methyl anthranilate, methyl salicylate, methyl heptenone, p-(hydroxybenzyl)-6,7-(2-hydroxy,4-hydroxy)isoquinoline, n-octacosanol, α-pinene, β-pinene, rutin, stigmasterol, β-sitosterol, thymol, and n-triacontanol [24,27,23].

Root:

Root extracts have been reported to contain anolobine, liriodenine, norushinsunine, reticuline, anonaine, and isocorydine [27]. Other constituents identified from the roots include borneol, camphene, camphor, carvone, β-caryophyllene, eugenol, geraniol, 16-heptatriacontanone, hexacontanol, higenamine, isocorydine, and limonene [33].

Stem:

Diterpenoids are commonly isolated from the stem and bark of *A. squamosa*[21]. The stem contains annosqualine, bullatacin, bullatacinone, annosquamosins A, and annosquamosins B[27]. In addition, six new ent-kaurane diterpenoids—annomosin A, annosquamosin C, annosquamosin D, annosquamosin E, annosquamosin F, and annosquamosin G—have been isolated from the stem [27,33].

Bark:

The bark is also rich in diterpenoids[21]. Reported constituents include acetogenins, squamone, 4-deoxyannoreticulin, cis-4-deoxyannoreticulin, (2,4-cis and trans)-squamoxinone, (2,4-cis and trans)-Mosinone A, Mosin B, Mosin C, squamotacin, molvizarin, (2,4-cis and trans)-squamolinone, (2,4-cis and trans)-9-oxoasimicinone, and bullacin B[24,27]. Additional compounds such as N-nitrosoxylopine, roemerolidine, and duguevalline have also been isolated from the bark, along with bullatacin [33].

Seeds:

The seeds contain annotemoyin-1, annotemoyin-2, squamosin, and cholesteryl glucopyranoside[3]. Phytochemical investigations have indicated that flavonoids are among the major constituents present in the seeds[5], while acetogenins and cyclopeptides are reported to occur predominantly in the seed fraction [21].
The n-hexane extract of the seeds contains o-xylene, (E)-hept-2-enal, nonanal, 9-methyl-undec-1-ene, 1-dodecanol, (2E,4E)-deca-2,4-dienal, (E)-oct-2-enal, 8-heptadecene, methyl palmitate, n-hexadecanoic acid, 2-chloroethyl linoleate, (E)-

methyloctadec-9-enoate, (E)-octadec-9-enoic acid, and palmitic anhydride [22].

Other compounds isolated from the seeds include acetogenin, samaquasine, annonacin, annonastatin, Cyclosquamosins A–I, Squamtin A, and Annosquamosin A[24,27]. The seeds are also reported to contain polyketides, annonaceous acetogenins (neurotoxins), cyclopeptides, carbohydrates, proteins, lipids, oleic acid, and linoleic acid [30].

Table 3: Phytochemical Constituents of Different Parts of Annona squamosa

Plant part	Major phytochemical constituents	Reference
Whole plant	Acetogenins, alkaloids, flavonoids, phenolic compounds, tannins, terpenoids, steroids, saponins, glycosides, cyclopeptides, and fatty acids	21
Fruit (unripe)	Acetogenins, glycosides, alkaloids, flavonoids, phytosterols, steroids, saponins, volatile compounds, cyclic ketones, long-chain fatty acids, terpenoids, tannins, phenols, verbenone, borneol	13
Fruit	Kaurane derivatives; annosquamosin-A and annosquamosin-B	33
Fruit pod (n-hexane fraction)	5-(Propan-2-ylidene)cyclopenta-1,3-diene, 9,10-dehydro-isolongifolene, methyl palmitate, n-hexadecanoic acid, trans-13-octadecenoic acid, octadecanoic acid, andrographolide, nordextromethorphan, etc.	22
Fruit pod (DCM fraction)	Spathulenol, methyl palmitate, n-hexadecanoic acid, oleic acid, androsterone, kaur-16-ene, tetramethyl-benzoic acid derivatives	22
Leaves	Rich in alkaloids; isoquinoline alkaloids; essential oil containing ~59 compounds	21, 33
Leaf essential oil	β-Caryophyllene, δ-cardinene, α-muurolene, α-cadinol (terpenes and sesquiterpenes)	33
Leaves	Annoreticulin, isoannoreticulin, anonaine, higenamine, isocorydine, limonene, geraniol, camphor, camphene, α-pinene, β-pinene, rutin, stigmasterol, β-sitosterol, thymol, n-triacontanol	24,27,33
Roots	Anolobine, liriodenine, norushinsunine, reticuline, anonaine, isocorydine	27
Roots	Borneol, camphene, camphor, carvone, β-caryophyllene, eugenol, geraniol, higenamine, limonene, hexacontanol	33
Stem	Diterpenoids	21
Stem	Annosqualine, bullatacin, bullatacinone, annosquamosins A and B	27
Stem	Ent-kaurane diterpenoids: annomosin A, annosquamosins C-G	27,23
Bark	Diterpenoids	21
Bark	Acetogenins, squamone, 4-deoxyannoreticulin, squamoxinone, Mosin A-C, squamotacin, molvizarin, squamolinone, 9-oxoasimicinone, bullacin B	24,27
Bark	N-Nitrosoxylopine, roemerolidine, duguevalline, bullatacin	33
Seeds	Annotemoyin-1, annotemoyin-2, squamosin, cholesteryl glucopyranoside	3
Seeds	Flavonoids, acetogenins, cyclopeptides	5,21
Seed (n-hexane extract)	o-Xylene, (E)-hept-2-enal, nonanal, 1-dodecanol, methyl palmitate, n-hexadecanoic acid, linoleate derivatives, oleic acid derivatives, palmitic anhydride	22
Seeds	Acetogenin, samaquasine, annonacin, annonastatin, Cyclosquamosins A-I, Squamtin A, Annosquamosin A, polyketides, proteins, lipids, carbohydrates, oleic acid, linoleic acid	24,27,30

4. Traditional Uses

Traditionally, *A. squamosa* has been used to alleviate numerous health conditions[51]. Different

parts of the plant are employed in folk medicine for the management of cardiac disorders, diabetes, hyperthyroidism, and cancer. The plant has also been traditionally used in the treatment of epilepsy, dysentery, worm infestation, constipation, hemorrhage, dysuria, fever, thirst, ulcers, and as an abortifacient[4,5]. Crushed seeds are commonly used in folk medicine for their insecticidal and antiparasitic activities, particularly for the treatment of head lice and dandruff infestations[3,7].

Different parts of the plant are traditionally used as follows[7]:

- **Roots:** Used as a purgative and for the management of mental depression.
- **Fruits:** Used as a blood tonic, cooling agent, sedative, antiemetic, antitussive, and for strengthening muscles; they are also traditionally used in the management of malignant tumors.
- **Seeds:** Used as an abortifacient and for destroying lice in hair.
- **Bark:** Used as a tonic.
- **Leaves:** Crushed leaves are applied to ulcers and wounds, while leaf decoctions are used in the treatment of dysentery.

5. Pharmacological Activities

The plant *Annona squamosa* L. has a wide range of pharmacological properties because of the many bioactive phytoconstituents it contains, such as annonaceous acetogenins, alkaloids, flavonoids, phenolic compounds, terpenoids, cyclopeptides, and essential oils. Various parts of the plant, for example the leaves, seeds, bark, roots, and fruits, have shown important biological activities in both in vitro and in vivo studies[34,35] . The main pharmacological activities of A. squamosa are set out below.

5.1 Antioxidant Activity

The leaves, fruits and seeds of *A. squamosa* have a strong antioxidant activity due to their high level of phenolic compounds, flavonoids, tannins and proanthocyanidins. Extracts from the leaves have demonstrated powerful free-radical scavenging activity in the DPPH, ABTS, FRAP and reducing power tests[37]. They reduce lipid peroxidation and protect cellular components against oxidative damage by boosting endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx)[38]. It is regarded as one of the main reasons for the hepatoprotective, antidiabetic and anticancer effects of A. squamosa[39].

5.2 Antidiabetic Activity:

The young leaves of A. squamosa have traditionally been used in diabetes management. Experimental studies show that both aqueous and alcoholic leaf extracts significantly reduce blood glucose levels in streptozotocin- and alloxan-induced diabetic animal models[40]. These extracts improve glucose tolerance, increase plasma insulin levels, decrease glycated hemoglobin, and normalize altered lipid profiles. The antidiabetic effects are mainly due to flavonoids, alkaloids, and acetogenins. These compounds enhance insulin secretion, improve insulin sensitivity, inhibit intestinal carbohydrate-digesting enzymes, and reduce oxidative stress linked to diabetes[41].

5.3 Antimicrobial Activity

The antimicrobial activity of extracts obtained from the leaves, seeds, bark, and fruit of *A. squamosa* has been found to be significant against a wide variety of Gram-positive and Gram-negative bacteria as well as several fungal pathogens. Extracts made using methanol, ethanol, acetone, and hexane have demonstrated inhibitory effects on *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella*

pneumoniae, and the *Candida* species[42]. This antimicrobial effect is mainly due to acetogenins, alkaloids, terpenoids, and phenolic compounds, which act by disrupting microbial cell membranes, interfering with enzyme systems, and inhibiting the synthesis of nucleic acids. The extracts from the seeds are especially known for their powerful insecticidal and antiparasitic properties[43].

5.4 Hepatoprotective Activity

Several studies have found that extracts from the leaves of A. squamosa have a hepatoprotective effect concerning chemically induced liver damage. Administration of these extracts results in a significant decrease in the elevated levels of serum liver biomarkers, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin, together with the restoration of normal liver histology[44]. This hepatoprotective action is mainly due to antioxidant and membrane-stabilising mechanisms, which prevent lipid peroxidation and help to maintain hepatocellular integrity. Flavonoids and phenolic compounds are seen as the main factors responsible for this activity[45].

5.4 Anticancer and Cytotoxic Activity

Annona squamosa is especially famous for its potential against cancer, a property attributable to the presence of annonaceous acetogenins such as squamocin, bullatacin, annonacin, and annosquamosins[46]. These substances show selective cytotoxicity towards a number of human cancer cell lines, such as those from the breast, colon, liver, pancreas, and lungs. The acetogenins inhibit mitochondrial complex I (NADH: ubiquinone oxidoreductase), which results in a depletion of ATP, the induction of apoptosis, cell-cycle arrest, and the suppression of tumor cell proliferation. Moreover, experimental studies have demonstrated the chemopreventive and antilipid-peroxidative effects of extracts from the bark and seeds in animal models of carcinogenesis[47].

5.4 Anti-inflammatory Activity

The leaf and bark extracts of *A. squamosa* have been shown to exhibit considerable anti-inflammatory activity in experimental studies[48]. They prevent protein denaturation, membrane lysis, and the production of inflammatory mediators such as prostaglandins and nitric oxide[49]. The flavonoids, alkaloids and terpenoids found in the plant exert their anti-inflammatory effect by influencing cyclooxygenase (COX), lipoxygenase (LOX) and pro-inflammatory cytokines. These results back the traditional practice of using crushed leaves for the treatment of wounds, ulcers, boils and inflammatory skin conditions[50].

5.5 Anthelmintic and Antiparasitic Activity

The seeds of A. squamosa have long been used in traditional medicine to treat intestinal worms, lice infestation, and external parasites[51]. Seed extracts show pronounced anthelmintic activity against several helminth species by causing paralysis and death of the worms[52]. Acetogenins and cyclopeptides are the principal antiparasitic constituents. Due to their strong insecticidal activity, seed preparations have also been used as natural pesticides and insect repellents[53].

5.6 Antihypertensive and Cardioprotective Activity

Traditional systems of medicine regard preparations made from the fruit and leaves of A. squamosa as substances which have a calming effect on the heart and act to reduce blood pressure[54]. Experimental studies indicate that extracts from the leaves might have a vasodilatory

and hypotensive effect, possibly by means of modulating calcium channels, causing vascular relaxation through nitric oxide and via antioxidant mechanisms. The improvement of the lipid profile together with a decrease in oxidative stress may also play a part in the cardioprotective effects of the plant[55].

5.7 Neuroprotective Activity

Recent investigations show that the bioactive compounds in *A. squamosa*, especially flavonoids and acetogenins, might have a neuroprotective effect by decreasing oxidative stress, neuroinflammation, and neuronal apoptosis. Experimental studies have also indicated possible advantages in cases of memory impairment, neurodegeneration, and cerebral oxidative damage. Nevertheless, since some annonaceous acetogenins can show neurotoxicity when given in high doses, further toxicological and clinical studies are needed before the substances can be used therapeutically[56,57].

6. Industrial and Therapeutic Uses

Different parts of *Annona squamosa* are used in the pharmaceutical, agricultural, cosmetic, and food industries.

- Can be conjugated with targeting ligands and used as immunotoxins for killing cancer cells [1]
- Seed oil has been utilized for biodiesel production and can be used as an energy source in agriculture, industry, and transportation [3]
- Fruits are used in the preparation of ice creams, milk beverages, and sorbets [5,17,28]
- Seed oil is used in the paint industry [9]
- Seeds are used to treat head lice because of their insecticidal properties [9]
- Used as a biopesticide and as an alternative agent for pest control [9]
- Seed oil may be used as a cooking oil after detoxification to remove toxic alkaloids [9,30]
- The fruit is recommended for weight gain because it provides approximately 104 kcal per 100 g of edible portion [10]
- Seeds are used as fish poison and pesticides [10]
- Used as an insect repellent and weedicide [10]
- Seeds are employed for pest control because of their insecticidal activity [12]
- Used in biodiesel production [12]
- Seed oil is used in cosmetic industries for the manufacture of shampoos and soaps that enhance hair strength and shine [17]
- Traditionally used in the treatment of anemia and burning sensations [22]
- Extensively used in the preparation of candies [28]
- Used in the manufacture of soap in the soap industry [9,30]

CONCLUSION

Annona squamosa L. is a valuable medicinal plant with a rich phytochemical profile and many pharmacological activities. Alkaloids, flavonoids, phenolic compounds, terpenoids, and annonaceous acetogenins contribute to its antioxidant, antimicrobial, anti-inflammatory, antidiabetic, hepatoprotective, and anticancer effects. Traditional medicinal uses of different plant parts are increasingly supported by experimental evidence, especially the therapeutic potential of the seeds. Due to its medicinal, nutritional, and industrial importance, *A. squamosa* is a promising source of natural bioactive compounds. Further phytochemical characterization, toxicological evaluation, and clinical studies are needed to validate its therapeutic efficacy and support the development of standardized phytopharmaceutical and utraceutical products.

Conflict of Interest Declaration

The authors declare that there was no conflict of interest in this study. This study contains no research involving animals or humans.

REFERENCES

1. Dhanraj, S. R., Vennila, J. J., & Dhanraj, M. (2020). Pharmacological investigation of ribosome inactivating protein (RIP) – like protein extracted from Annona squamosa L. seeds. Journal of King Saud University – Science, 32(7), 2982–2988. https://doi.org/10.1016/j.jksus.2020.08.002
2. Mohammed Adam Yahya Abdualrahman, Haile Ma, Cunshan Zhou, Abu ElGasim Ahmed Yagoub, Ali Osman Ali, Haroon Elrasheid Tahir, Asif Wali,Postharvest physicochemical properties of the pulp and seed oil from Annona squamosa L. (Gishta) fruit grown in Darfur region, Sudan,Arabian Journal of Chemistry,Volume 12, Issue 8,2019,Pages 4514-4521,ISSN 1878-5352, https://doi.org/10.1016/j.arabjc.2016.07.008
3. Ye Min Htet, Maung Maung Khin, Hnin Hnin Aye. Determination of the elemental content of the seed and physicochemical properties of the seed oil of annona squamosa l. (aw-za). J. Myanmar Acad. Arts Sci. 2019 Vol. XVII. No.1B,
4. Sanjay Prasad Gupta, Manager Rajdeo Singh, Iliyas Ahemad. Evaluation of antimicrobial activity of seed extracts of Annona squamosa L. and Azadirachta indica . J Med Plants Stud 2019;7(4):282-284.
5. Biswas, Souvik & Das, Arijit & Chattopadhyay, Souvik & Nag, Mrinmoy & Roy, Dipan & Chandra, Pallakhyi & Sen, Amartya. (2023). ANTIMICROBIAL ACTIVITY IN METHANOLIC SEED EXTRACT OF ANNONA SQUAMOSA. International Journal of Pharmaceutical Sciences and Research. 14. 5340-5348. 10.13040/IJPSR.0975-8232.14(11).5340-48.
6. Sivakumar, R., Sri Renganathan, P., Mary Helan, H., & Rajachandrasekar, T. (2019). Removal of copper ion from aqueous solution using seeds of sugar apple (Annona squamosa L.)1. RJLBPCS, 5(2), 1117-1135. doi:10.26479/2019.0502.85
7. Bhattacharya, A. & Debnath, Sujit & Dey, M. & Kar, D.. (2012). Phytochemical and pharmacological evaluation of the seeds of Annona squamosa Linn. International Journal of Pharmacy and Pharmaceutical Sciences. 4. 92-94.
8. Rajpoot, V. S., Sharma, M., Singh, A., & Jain, S. (2020). Isolation, characterization and comparative study of insecticidal compound from seeds of Annona squamosa. World Journal of Pharmaceutical Research, 9(5), 2260-2269. doi:10.20959/wjpr20205-17484
9. Shah, Kamlesh & Pathak, Jignesh & Suthar, Ramchandra. (2021). Identification of Phytochemicals from Seed Extract of Custard Apple, Annona squamosa. Bioscience Biotechnology Research Communications. Vol 14 No. 397-402. http://dx.doi.org/10.21786/bbrc/14.1/56
10. Neha, Tanya, & Dutta, A. K. (2022). Beneficial Aspects of Custard Apple (Annona squamosa): A Perspective Review. International Journal for Research in Applied Science & Engineering Technology (IJRASET), 10(1). https://doi.org/10.22214/ijraset.2022.40000
11. Aliyu, N., & Duniya, V. A. (2023). Effect of Custard Apple (Annona squamosa L.) Seeds Extracts on In-Vitro Activity of Malassezia globosa. Journal of Chemical Engineering and Industrial Biotechnology (JCEIB), 9(1), 13-19. https://doi.org/10.15282/jceib.v9i1.9283
12. Phatak, S., Chitale, S., Karadkar, N., & Karkhanis, D. (2023). Phytochemical

characterization, antioxidant and antimicrobial testing of ethanolic and ISO-propanolic extracts of Annona squamosa seeds. International Journal of Phytology Research, 3(4), 1-4. Retrieved from www.dzarc.com/phytology

13. Wahyuni, D., Waluyo, J., & Purwanto, R. G. (2020). The Toxicity of Srikaya Seed Granules (Annona squamosa L.) with Different Heating Temperatures Against the Larva of Aedes aegypti L. Bioedukasi, 18(1), 1-7.
14. APA: Alaqeel, N.K., Almalki, W.H., Binothman, N., Aljadani, M., Al-Dhuayan, I.S., Alnamshan, M.M., Almulhim, J., Alqosaibi, A.I., Ajmal, M.R., Alammar, D.M., & Tarique, M. (2022). The inhibitory and anticancer properties of Annona squamosa L. seed extracts. Brazilian Journal of Biology, 82(e268250). https://doi.org/10.1590/1519-6984.268250
15. Mahmoud, M. A. A., & Hassan, A.-N. T. (2022). Insecticidal Activity of Seed Extracts of Annona squamosa L., Against the Cotton Leafworm Spodoptera Littoralis (Boisd.). Egypt. J. Chem., 65(6), 73-80. DOI:10.21608/EJCHEM.2021.85993.4205
16. Leite, D.O.D.; Camilo, C.J.; Nonato, C.d.F.A.; Carvalho, N.K.G.d.; Salazar, G.J.T.; de Morais, S.M.; Costa, J.G.M.d. Chemical Profile and Evaluation of the Antioxidant and Anti-Acetylcholinesterase Activities of Annona squamosa L. (Annonaceae) Extracts. Foods 2021, 10, 2343. DOI:10.3390/foods10102343
17. Baskar, G., Nithica, S., Pravin, R., & Renuka, V. (2023). Extraction, characterization and kinetics of ultrasonic assisted extraction of biooil from Annona squamosa seeds. Indian Journal of Chemical Technology, 30(2), 217-222. https://doi.org/10.56042/ijct.v30i2.68816
18. Ilakkia, M., Premalatha, K., Vellaikumar, S., Shanmugam, P. S., Harish, S., & Nelson, J. (2023). Laboratory Studies on Chromatographic Profile, Toxicity and Repellent Activity of Custard Apple (Annona squamosa L.) Seed Extract. International Journal of Environment and Climate Change, 13(10), 2949-2955. https://doi.org/10.9734/IJECC/2023/v13i102961
19. Irwan, Z., Kamarudin, W. F. W., Korish, U. A. S. A., Z, N. A., Rusli, A. S., & Sallehuddin, S. (2021). Effectiveness of Annona Squamosa and Annona Muricata Seed Extracts as Ingredients in Bio-pesticides Spray IOP Conference Series: Materials Science and Engineering, 1176(1), 012007. IOP Publishing. https://doi.org/10.1088/1757-899X/1176/1/012007
20. Yunita, M. N., Raharjo, A. P., Wibawati, P. A., & Agustono, B. (2019). Antiviral Activity of Ethanolic Extract of Srikaya Seeds (Annona squamosa L.) Against Avian Influenza Virus. The Indian Veterinary Journal, 96(09), 26-29. Retrieved from https://www.researchgate.net/publication/341398418
21. Yassin, S., Elsohafy, S. M., Darwish, F. A., & Amer, M. E. (2024). Annona squamosa L.: A promising herbal remedy – insights into its biological activities and phytochemical composition. Journal of Applied Pharmaceutical Science, 1(1), 82-95. ISSN: 3009-7061.
22. Adesanwo, J. K., Akinloye, A. A., Otemuyiwa, I. O., & Akinpelu, D. A. (2021). Chemical Characteristics and Biological Activities of Annona squamosa Fruit Pod and Seed Extracts. Journal of Exploratory Research in Pharmacology, 6(1), 5–15. https://doi.org/10.14218/JERP.2020.00019

23. Shehata, M. G., Abu-Serie, M. M., Abd El-Aziz, N. M., & El-Sohaimy, S. A. (2021). Nutritional, phytochemical, and in vitro anticancer potential of sugar apple (Annona squamosa) fruits. Scientific Reports, 11(6224). https://doi.org/10.1038/s41598-021-85772-8
24. Singh, Y., Bhatnagar, P., & Thakur, N. (2019). A review on insight of immense nutraceutical and medicinal potential of custard apple (Annona squamosa Linn.). International Journal of Chemical Studies, 7(2), 1237-1245. Retrieved from https://www.researchgate.net/publication/332329163
25. Saha, R. (2011). Pharmacognosy and pharmacology of Annona squamosa: A review. International Journal of Pharmacy & Life Sciences, 2(10), 1183-1189
26. Eshra, D. H., Shehata, A. R., Ahmed, A. N., & Saber, J. I. (2019). Physicochemical Properties of the Seed Kernels and the Oil of Custard Apple (Annona squamosa L.). International Journal of Food Science and Biotechnology, 4(4), 87-93. doi: 10.11648/j.ijfsb.20190404.12
27. Pandey, N., & Barve, D. (2011). Phytochemical and Pharmacological Review on Annona squamosa Linn. International Journal of Research in Pharmaceutical and Biomedical Sciences, 2(4), 1404-1411.
28. Hagr, T. E., Adam, I. A., Almain, A. A., & Mohammed, M. M. (2019). Phytochemical Screening, GC-MS Analysis, Antibacterial and Antioxidant Activity of Seeds Oil of Annona Squmosa L. Sudanese Medicinal Plant. Open Science Journal of Pharmacy and Pharmacology, 7(1), 1-6. Retrieved from http://www.openscienceonline.com/journal/osjpp
29. Khare, R. K., Das, G., Kumar, S., Gautam, V., Nath, S., Verma, R., … & Yadav, N. (2022). Phytochemical analysis of custard apple (Annona squamosa) and Karanja (Pangamia pinnata) seed extracts. The Pharma Innovation Journal, SP-11(1), 480-484.
30. Kumari, N., Prakash, S., Kumar, M., Radha, Zhang, B., Sheri, V., Rais, N., Chandran, D., Dey, A., Sarkar, T., et al. (2022). Seed Waste from Custard Apple (Annona squamosa L.): A Comprehensive Insight on Bioactive Compounds, Health Promoting Activity and Safety Profile. Processes, 10(11), 2119. https://doi.org/10.3390/pr10102119
31. Kumar, Y., Chandra, A. K., Dubey, A., & Gajera, H. P. (2018). Fruit Morphology and Quality Parameter Studies of Global Custard Apple (Annona squamosa) Germplasms. International Journal of Current Microbiology and Applied Sciences, 7(10), 1297-1311. https://doi.org/10.20546/ijcmas.2018.710.146
32. Momin, R.K., & Kadam, V.B. (2011). Biochemical Analysis of Leaves of some Medicinal Plants of Genus Sesbania. Journal of Ecobiotechnology, 3(2), 14-16. Retrieved from https://www.researchgate.net/publication/261885600
33. Reddy, D. R., Malleswari, K., & Kumar, E. N. (2023). Phytochemicals and Pharmacological Activities of Annona squamosa. International Journal for Multidisciplinary Research (IJFMR), 5(1), 1-9. Retrieved from www.ijfmr.com
34. Kazman, B. S., Harnett, J. E. & Hanrahan, J. R. (2022). Traditional Uses, Phytochemistry and Pharmacological Activities of Annonacae. Molecules 27(11). https://doi.org/10.3390/molecules27113462
35. 35. Scholar, S. G. & Kamidi, S. (2023). Phytochemistry, Pharmacological Activities, and Applications of Annona squamosa L.: Review Article. Journal of Pharma Insights

and Research. https://doi.org/10.69613/zk3ptk98

36. Leite, D. O., Camilo, C. J., Nonato, C. d., Carvalho, N. K., Salazar, G. J., Morais, S. M. & Costa, J. G. (2021). Chemical Profile and Evaluation of the Antioxidant and Anti-Acetylcholinesterase Activities of Annona squamosa L. (Annonaceae) Extracts. Foods 10(10). https://doi.org/10.3390/foods10102343
37. Vikas, B., S, A. B., P, R. & Sujathan, K. (2017). Free Radical Scavenging Properties of Annona squamosa. Asian Pacific Journal of Cancer Prevention 18(10). https://doi.org/10.22034/APJCP.2017.18.10.2725
38. Leite, D. O., Camilo, C. J., Nonato, C. d., Carvalho, N. K., Salazar, G. J., Morais, S. M. & Costa, J. G. (2021). Chemical Profile and Evaluation of the Antioxidant and Anti-Acetylcholinesterase Activities of Annona squamosa L. (Annonaceae) Extracts. Foods 10(10). https://doi.org/10.3390/foods10102343
39. Leite, D. O., Camilo, C. J., Nonato, C. d., Carvalho, N. K., Salazar, G. J., Morais, S. M. & Costa, J. G. (2021). Chemical Profile and Evaluation of the Antioxidant and Anti-Acetylcholinesterase Activities of Annona squamosa L. (Annonaceae) Extracts. Foods 10(10). https://doi.org/10.3390/foods10102343
40. Rajesh Kumar Gupta, Achyut Narayan Kesari, P.S. Murthy, R. Chandra, V. Tandon, Geeta Watal, (2005). Hypoglycemic and antidiabetic effect of ethanolic extract of leaves of Annona squamosa L. in experimental animals. Journal of Ethnopharmacology 99(1), pp. 75-81. https://doi.org/10.1016/j.jep.2005.01.048
41. Ansari, P., Flatt, P. R., Harriott, P. & Abdel-Wahab, Y. H. (2020). Evaluation of the Antidiabetic and Insulin Releasing Effects of A. squamosa, Including Isolation and Characterization of Active Phytochemicals. Plants (Basel) 9(10). https://doi.org/10.3390/plants9101348
42. 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 Oct 6;20(1):296. doi: 10.1186/s12906-020-03029-9. PMID: 33023568; PMCID: PMC7541211.
43. Ramalingum, N. & Mahomoodally, M. F. (2014). The Therapeutic Potential of Medicinal Foods. Advances in Pharmacological and Pharmaceutical Sciences 2014. https://doi.org/10.1155/2014/354264
44. Yahya, M., Ginting, B., Saidi, N., Riski, C. D., Purnama, A., Auliansyah, T. I. & Gunana, T. Z. (2026). Antioxidant activities and toxicity of dichloromethane and n-hexane extracts of Annona squamosa L. leaves. Journal of Advanced Pharmaceutical Technology & Research 17(1), pp. 24-30. https://doi.org/10.4103/JAPTR.JAPTR_231_25
45. Zahid, M., Arif, M., Rahman, M. A. & Mujahid, M. (2020). Hepatoprotective and antioxidant activities of Annona squamosa seed extract against alcohol-induced liver injury in Sprague Dawley rats. Drug Chem Toxicol 43(6), pp. 588-594. https://doi.org/10.1080/01480545.2018.1517772.
46. Ma, C., Li, Y., Lu, J., Wang, M., Li, X., Chen, J., Chen, Y. & Ju, W. (2024). Three new cytotoxic annonaceous acetogenins from the seeds of Annona squamosa. Natural Product Research 38(7), pp. 1135-1139.

https://doi.org/10.1080/14786419.2022.2134362

47. Akatsuka, A., Kojima, N., Okamura, M. & Dan, S. (2016). A novel thiophene-3-carboxamide analog of annonaceous acetogenin exhibits antitumor activity via inhibition of mitochondrial complex I. Pharmacology Research & Perspectives 4(4). https://doi.org/10.1002/prp2.246
48. Ito, C. N., Procopio, E. d., Balsalobre, N. d., Machado, L. L., Silva-Filho, S. E., Pedroso, T. F., Lourenço, C. C., Oliveira, R. J., Arena, A. C., Salvador, M. J. & Kassuya, C. A. (2024). Analgesic and Anti-Arthritic Potential of Methanolic Extract and Palmatine Obtained from Annona squamosa Leaves. Pharmaceuticals 17(10). https://doi.org/10.3390/ph17101331
49. Ito, C. N., Procopio, E. d., Balsalobre, N. d., Machado, L. L., Silva-Filho, S. E., Pedroso, T. F., Lourenço, C. C., Oliveira, R. J., Arena, A. C., Salvador, M. J. & Kassuya, C. A. (2024). Analgesic and Anti-Arthritic Potential of Methanolic Extract and Palmatine Obtained from Annona squamosa Leaves. Pharmaceuticals 17(10). https://doi.org/10.3390/ph17101331
50. Khan, A. D., Singh, M. K., Lavhale, P. M., Yasir, M. & Singh, L. (2024). Exploring the wound healing activity of phytosomal gel of Annona squamosa and Cinnamomum tamala leaves ethanolic extracts with antioxidant and antimicrobial activities in S aureus infected excision wound model. Journal of Biomaterials Science 35(16), pp. 2447-2468. https://doi.org/10.1080/09205063.2024.2382540
51. Tiangda, C. H., Gritsanapan, W., Sookvanichsilp, N. & Limchalearn, A. (2000). Anti-headlice activity of a preparation of Annona squamosa seed extract. Southeast Asian J Trop Med Public Health 31, pp. 174-177. https://doi.org/10.1142/S0192415X17500501
52. Souza, M. M., Bevilaqua, C. M., Morais, S. M., Costa, C. T., Silva, A. R. & Braz-Filho, R. (2008). Anthelmintic acetogenin from Annona squamosa L. Seeds. An Acad Bras Cienc 80(2), pp. 271-277. https://doi.org/10.1590/s0001-37652008000200005
53. Ma, C., Li, Y., Lu, J., Wang, M., Li, X., Chen, J., Chen, Y. & Ju, W. (2024). Three new cytotoxic annonaceous acetogenins from the seeds of Annona squamosa. Natural Product Research 38(7), pp. 1135-1139. https://doi.org/10.1080/14786419.2022.2134362
54. Singh, R. P., Pattnaik, A. K., Rudrapal, M. & Bhattacharya, S. (2024). Annona squamosa Linn.: A Review of Its Ethnobotany, Pharmacology, Phytochemistry, Toxicity, and Conservation Needs. Journal of Ethnopharmacology 300. https://doi.org/10.1177/09731296241281422
55. Loretizo, K. D., Alegado-Bagaoisan, D. O., Acosta, P. C., Chua, F. G., Delaganar, G. B., Carandang, R. R. & Miranda, K. J. (2026). Evaluation of Anti-angiogenic Activity of the Acetone Leaf Extract of Annona squamosa Linn. (Annonaceae). Acta Medica Philippina 60(4), pp. 71-78. https://doi.org/10.47895/amp.vi0.10294
56. Leite, D. O., Camilo, C. J., Nonato, C. d., Carvalho, N. K., Salazar, G. J., Morais, S. M. & Costa, J. G. (2021). Chemical Profile and Evaluation of the Antioxidant and Anti-Acetylcholinesterase Activities of Annona squamosa L. (Annonaceae) Extracts. Foods 10(10). https://doi.org/10.3390/foods10102343
57. Bonneau, N., Baloul, L., Ndob, I. B., Sénéjoux, F. & Champy, P. (2017). The fruit of Annona squamosa L. as a source of

environmental neurotoxins: From quantification of squamocin to annotation of Annonaceous acetogenins by LC-MS/MS analysis. Food Chemistry 226, pp. 32-40. https://doi.org/10.1016/j.foodchem.2017.01.042

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