

Medicinal effects of *Annona squamosa*

Santwana Palai^{1*}, Ritun Patra², Kautuk Kumar Sardar³

^{1*} Assistant Professor, Department of Veterinary Pharmacology & Toxicology

² Assistant Professor, Department of Veterinary Anatomy & Histology

³ Professor, Department of Veterinary Pharmacology & Toxicology

College of Veterinary Science and Animal Husbandry, Odisha University of Agriculture and
Technology, Bhubaneswar-751003, Odisha, India.

<https://doi.org/10.5281/zenodo.8270689>

Abstract

The *Annona squamosa* belongs to Annonaceae family that is widely utilised in traditional remedies around the world. *Annona squamosa* has a wide range of therapeutic qualities. It has traditionally been used to treat diabetes and hyperlipidemia. It also has hepatoprotective, anti-inflammatory, antiprotozoal, anticancer, antioxidant, antibacterial, and anticonvulsant effects. This review presents an in-depth examination of the botanical characteristics, ethnomedical applications, phytochemistry, and pharmacology of *Annona squamosa* as utilized in traditional medicine practices.

1. Introduction

Annona squamosa, popularly called as custard apple (English) and sharifa (Hindi), is a member of the Annonaceae family. It is an indigenous to Brazil, Bahamas, West Indies, Peru, Ecuador, Mexico, Bermuda, Egypt America. This plant is widely grown in India, particularly in Maharashtra, Madhya Pradesh, Uttar Pradesh, Tamil Nadu Chhattisgarh, Assam, Gujarat, Rajasthan, Andhra Pradesh and Bihar. The Indian Council of Agricultural Research reports a total cultivation area of 40,000 ha. It grows from a young sapling to 3.5 - 8.5 m tall tree having broad twigs and light brown to dark brown bark, thin leaves, and edible fruit (Figure 1). Its bark, seeds, and leaves all have unique pharmacological activities (Table 1). This plant has a variety of therapeutic qualities. The plant's roots, leaves, fruits, seeds, and bark have a variety of applications and are pharmacologically active. The fruit is delicious and creamy white in colour ^[1].

Table 1 Botanical Features of *Annona squamosa*

Plant name	Alternative name	Resident Names	Distribution	Reference
A. squamosa	A. squamosa f. Parvifolia Kuntze A. asiatica L.	Amritaphala Chirimoya Guanabanus Custard apple Sweetsop Gomez	Sudan, India, Pakistan, Costa Rica, China, Egypt, Thailand	[1, 2]



Figure 1: Parts of *Annona squamosa* exhibiting medicinal effects

2. Traditional Uses of *Annona squamosa*

Because of their vast occurrence, Annonaceae species are well-known and widely used in tropical regions. Traditional uses of the plant include leaves, twigs, bark, roots, seeds, fruit, and stem. Infusions, pastes, and decoctions are some of the procedures used to prepare it. *A. squamosa*, for example, has been used to cure ulcers. Antiparasitic actions of *A. squamosa* have been described. *A. squamosa* leaves are used as a cold remedy in the United States and as a dysentery remedy in India [2]. *A. squamosa* is also used to treat hyperthyroidism, as an antibiotic and insecticide, as a uterotonic, antiulcer, anti-inflammatory, abortifacient, antioxidant, antifertility, anticancer, antispasmodic,



analgesic, and for other disorders. The leaves have been shown to have anti-diabetic and hepatoprotective properties. Fruits are hemostatic, sedative, stimulant, and expectorant. Diabetes and hyperlipidemia have traditionally been treated using *A. squamosa*. The seeds have insecticidal properties and can be used to treat head lice [3].

Phytochemistry of *Annona squamosa*

Secondary metabolites like flavonoids, glycosides, essential oils, acetogenins, alkaloids, etc. are found, isolated, and described from practically every component of *A. squamosa* (Table 2). It contains flavonoids, glycosides, aporphine alkaloids, tetrahydroisoquinoline alkaloids, terpenes, and other chemicals, as well as an alkaloid called annonaine [4].

Minerals and vitamins present in *A. squamosa* genera include calcium, potassium, sodium, pantothenic acid B5, copper, riboflavin, phosphorus, zinc, iron, selenium, vitamin C, magnesium, thiamine, etc. Fruits are high in calories and a wonderful source of vitamins and minerals [5].

Table 2: Phytochemistry of different parts of *A. squamosa*

Sl. No.	Part	Phytochemicals	Type
1	Leaf	O-Methylarmepavine, Quercetin-3-O-glucoside, Anonaine, β -Caryophyllene, Bicyclogermacrene, β -Cedrene	Essential oils
2	Bark	2,4-cis-Mosinone A, Bullatacinone, Anoreticum-9-one, Bullatacin, 2,4-trans-Mosinone A, Squamone, Mosin B and C,	Acetogenin
3	Pulp fruit	α -Pinene, Sabinene, Limonene	Essential oils
4	Stem	11 ent-Kauranes, 16 α -Hydro-19-al-ent-kauran-17-oic acid, 17-Dihydroxy-ent-kauran-19-oic acid	Alkaloids
5	Seed	Dieposabadelin, Cyclosquamosin A-I, Annosquamins A, B and C, Squadiolin A-N, Squamostanin A-F, Neoannonin-B, Annosquatin A and B, Squamin A and B	Acetogenins

3. Pharmacological Activity of *A. squamosa*

A. squamosa shows various biological effects like antiulcer, antihyperglycemic, anti-inflammatory, antitumor, antiprotozoal, anthelmintic, antileishmanial, antimicrobial, antipyretic, antidiarrheal, antifungal antioxidant, antinociceptive, antimalarial, etc. through its fractions, whole extracts, or pure compounds of its different parts like bark, fruit, flower, etc [6] (Figure 1) (Table 2).



Table 2: Details of Pharmacological properties of *A. squamosa*

Distribution	Part Used	Traditional Usage	Pharmacological effects	Bioactive compounds
Asia, Australia, America	Stem Bark Seed Root	Digestive Headache Anthelmintic Analgesic Anti-inflammatory Antirheumatic Antimicrobial Carminative	Antibacterial Antigenotoxicity Antidiabetic Antilipidemic Antileishmanial Antimalarial Antioxidant	Monoterpenes: Limonene Acetogenins: Tetrahydrosquamone Squafosacin B, Bullatacinona, Squadiolins A and B, Squamona,

Antidiabetic and Antilipidemic effects

Young *Annona squamosa* leaves with black pepper (*Piper nigrum*) utilised as an anti-diabetic in northern Indian traditional medicine and are even used now a days. The aqueous leaf extract of *A. squamosa* in streptozotocin induced diabetic rats showed lower blood glucose along with higher serum insulin concentration. Combination of fruits of *Annona squamosa* and seeds of *Nigella sativa* is another ancient Indian medicine combination to be used against diabetes and cholesterol. Within 1 month, the polyherbal formulation lowered blood glucose in a dose-dependently and raised insulin in streptozotocin-induced diabetic rats @ 200 mg/kg demonstrating results like 250 mg/kg tolbutamide. These findings confirm the conventional usage of *Annona squamosa* in diabetes, implying that more research and longer-term clinical trials can establish it as antidiabetic and anti-cholesterol drug ^[7].

Antioxidant activity

The antioxidant action of ethanolic leaves extract of *A. squamosa* was established. The antioxidant action of 2,2-diphenyl-1-picrilhidrazil (DPPH), nitric oxide, and superoxide radical tests were used to investigate its antioxidant activity. At a concentration of 100g/mL, the antioxidant activity was 75.12%, 34.69%, and 10.29%, respectively ^[8].

Anti-inflammatory properties

Oral intake of *Annona squamosa* root extract @ 200 and 400 mg/kg provided considerable suppression with 25% and 48% inhibition in an acute carrageenan-persuaded rat paw edema model respectively than diclofenac sodium, which suppressed inflammation by 70% ^[9].



Antibacterial activity

Annona squamosa leaf extracts displayed antimicrobial effect against *Staphylococcus aureus* in both methanolic and ethanolic extracts, and this action was related to the incidence of alkaloids, flavonoids, etc. in the extract. The *A. squamosa* seed extracts in aqueous and methanolic solvent have been shown to be active against *Staphylococcus aureus* with MICs of 50 mg/mL and MBCs of 100 mg/ml. The action of *Annona squamosa* complexes identified from its leaves, such as 11-hydroxy-16-hentriacontanone, the fatty alcohol has been recorded as MIC ranging from 30 to 50 g/ml on Gram-negative and Gram-positive bacteria [10].

Antiviral effects

Several investigations employing entire extracts or purified components found *Annona squamosa* to have antiviral activity. For example, 16 β ,17-dihydroxy-ent-kauran-19-oic acid extracted from fruit of *A. squamosa* of show substantial effectiveness against HIV replication utilising a H9 lymphocyte cell assay with an EC₅₀ value of 0.8 μ g/ml. The seeds extract of *A. squamosa* in ethanol @ 0.15, 0.25 and 0.35 μ g/mL exhibit antiviral effect against the Avian influenza virus in a dose dependent manner showing 33.33%, 43.06%, and 59.72% of antiviral activity correspondingly. The leaves extract of *A. squamosa* was evaluated in Vero cells against dengue virus type-2 (DENV-2) using the viral ToxGLoTM method. Methanolic extracts of *A. squamosa* peels revealed antiviral efficacy against human viruses through non-radioactive immune/colorimetric assay [11].

6. Toxicity and interactions

The fruit of *A. squamosa* was tested for squamocin content using HPLC-MS, and the results showed that each fruit contained squamocin of about 13.5-36.4 mg, and that chronic use of *A. squamosa* fruit can be risky as it may lead to neurodegenerative illnesses. In addition, aqueous custard apple leaf extract and glipizide combination allowed for a dose reduction to half in rats with type 2 diabetes, lowering probability of need of insulin therapy. So, *Annona squamosa* could be used along with with diabetes medicines to maximise their efficacy and reduce normal dose [12].

7. Conclusions

The biochemistry of *Annona squamosa* reveals acetogenins, phenols, alkaloids, and essential oils as main ingredients. The leaves mostly contain alkaloids whilst acetogenins are mostly found in seeds and in minor amounts in leaves and pulp. Importantly, formulations including *Annona squamosa* components can be used in ethnoveterinary practises. The extraction procedures, pharmacological and phytochemical profiles will aid in the additional standardisation of *Annona squamosa* formulations in order to elicit likely therapeutic effects. The anti-diabetic and anti-cancer benefits of *Annona squamosa* should be studied further in order to establish it as a nutraceutical to aid in the treatment of diabetes and cancer.



Reference

1. Pandey, N., & Barve, D. (2011). Phytochemical and pharmacological review on *Annona squamosa* Linn. *International Journal of research in pharmaceutical and biomedical sciences*, 2(4), 1404-1412.
2. Singh, B., & Kumar, D. (2019). *Ethnobotanical aspects of Nagaur District, Rajasthan*. Lulu. com.
3. Vohora, S. B., Kumar, I., & Naqvi, S. A. H. (1975). Phytochemical, pharmacological, antibacterial and anti-ovulatory studies on *annona squamosa*. *Planta medica*, 28(05), 97-100.
4. Fatema, I. B., Chowdhury, N. S., Charu, T. K., & Islam, F. Phytochemical and Pharmacological Studies of the genus *Annona*: A.
5. Varadharajan, V., Janarthanan, U. K., & Krishnamurthy, V. (2012). Physicochemical, phytochemical screening and profiling of secondary metabolites of *Annona squamosa* leaf extract. *World Journal of pharmaceutical research*, 1(4), 1143-1164.
6. Marahatta, A. B., Aryal, A., Basnyat, R. C., & Marahatta, C. A. B. (2019). The phytochemical and nutritional analysis and biological activity of *Annona squamosa* Linn. *Int. J. Herb. Med*, 7, 19-28.
7. Dwivedi, C., & Daspaal, S. (2013). Antidiabetic herbal drugs and polyherbal formulation used for diabetes: A review. *J Phytopharmacol*, 2(3), 44-51.
8. El-Chaghaby, G. A., Ahmad, A. F., & Ramis, E. S. (2014). Evaluation of the antioxidant and antibacterial properties of various solvents extracts of *Annona squamosa* L. leaves. *Arabian Journal of Chemistry*, 7(2), 227-233.
9. Hemlatha, K., & Satyanarayana, D. (2015). Anti-inflammatory activity of *Annona squamosa* Linn. *Biomedical and Pharmacology Journal*, 2(1), 17-20.
10. Rani, K. B. Screening of Antibacterial, Antioxidant and Phytochemical of Leaf, Stem and Root extracts of *Annona squamosa* L. against Pathogenic Bacteria.
11. Chattopadhyay, D., & Bhattacharya, S. K. (2008). Ethnopharmacology: A new engine for the development of antivirals from naturaceuticals. *Handbook of ethnopharmacology*, 37(661), 2.
12. Chel-Guerrero, L.D., Sauri-Duch, E., Fragosó-Serrano, M.C., Pérez-Flores, L.J., Gómez-Olivares, J.L., Salinas-Arreortua, N., Sierra-Palacios, E.D.C. and Mendoza-Espinoza, J.A., 2018. Phytochemical profile, toxicity, and pharmacological potential of peels from four species of tropical fruits. *Journal of medicinal food*, 21(7), pp.734-743.

