



IJPPR

INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203




Human Journals

Review Article


June 2021 Vol.:21, Issue:3

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A Review on *Annona squamosa*L.: Pharmacognosy, Phytochemical Analysis, and Pharmacological Activities



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals



ISSN 2349-7203

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Submitted: 22 May 2021
Accepted: 29 May 2021
Published: 30 June 2021

Keywords: *Annona squamosa*, Custard Apple, Sitaphal, Annonaceae

ABSTRACT

Annona squamosa is commonly known as custard apple and Sitaphal, belonging to Annonaceae. This review deals with detailed Pharmacognostical, phytochemical, quantitative analysis and pharmacology of plant. Sitaphal is a multipurpose tree with edible fruits and an important source for medicine and industrial products. Researchers found that plant contains Alkaloids, Flavonoids, Carbohydrates, Tannins, Saponins and Steroids by performing the chemical test. TLC and HPTLC techniques used for qualitative determination and to detect a possible number of components in various extracts. Researchers used different spraying reagents to confirm phytochemicals. In GC/MS analysis, 15 compounds were detected from methanolic leaves extract. The total phenolic content of methanolic extract of leaves and bark was determined by Folin- Ciocalteu method. The total flavonoid content of methanolic extract of leaves and bark was determined by Aluminium chloride method. The researcher evaluated different plant extracts for Antidiabetic, anti-cancer, Insecticidal, Antimicrobial, Antioxidant, Anti-HIV as biological activities.



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INTRODUCTION:

Annona squamosa Linn. is commonly known as custard apple and sugar apple, the plant of Annonaceae family. Sugar apple is commonly found in forests and is now cultivated throughout India. Many components have been reported in previous years hence it had gained the attention of biochemists. Every part of plant has medicinal properties. Roots are used in depression and spinal disease. The bark is known powerful astringent. Ayurveda describes that fruit are good hair tonic, increases blood and strength of muscle. In this review, we summarize phytochemicals, qualitative and quantitative analysis and pharmacology of *Annona squamosa* Linn.

PLANT PROFILE:

Synonym: Sugar apple, Sitaphal, Custard apple.

Biological source: *Annona squamosa* is a small and well-branched tree belonging to *Annonaceae* that gives edible fruits known as sugar apple.

Habitat: Custard apple is originated from West Indies and South America. It is commonly cultivated in Thailand and India ⁽¹⁾.

TAXONOMY:

Kingdom- Plantae

Order- Magnoliales

Family- Annonaceae

Species- *Annona squamosa* ⁽²⁾.

BOTANICAL DESCRIPTION:

The height of tree is about 6 m. Leaves are oblong-lanceolate, subacute, globous above where lateral nerves 8 to 11 pairs, petioles are 12 mm long. Sepals are minute, triangular, and pubescent. Pubescent petals on both surfaces about 25×6 mm. Fruits are globose with a glaucous bloom on the surface, occurs yellowish-green when ripe and breaks easily. Seeds are smooth and brownish-black ⁽¹⁾.

Ecology: Sitaphal is widely distributed in tropics. In hot and dry climates trees grows well, at 30°C seedlings show high photosynthetic activity. Minimum temperature and high humidity (25°C and 70% RH) improve the pollination. Soil pH of 6 to 6.5 is optimal for custard apple (9).

CHEMICAL CONSTITUENTS:

Annona squamosa consist of alkaloids, phenolic compounds, flavonoids, saponins, tannins, phytosterols, carbohydrates, proteins and amino acids.

It also contains fixed oils, fats, gum and mucilage. Leaves contain anonaine, borneol, camphene, carvone, eugenol, geraniol, menthone, rutin and β - sitosterol.

Fruits consist of 28% of sugar, iron, calcium, carotene, thiamine, ascorbic acid. Root and stem give Borneol, Car-3-ene, Farnesol, Geraniol and Limonene (1).

TRADITIONAL USES:

Decoction of leaves is used to treat dysentery and infections in urinary tract, cough and cold. Crushed leaves are applied to wounds for healings. Seeds are responsible to treat digestive disorders. Seeds are used as insecticidal agent. Bark is helpful in diarrhoea. Fruits as a hair tonic (3).

THERAPEUTIC USES:

Leaves of *Annona squamosa* are used as antidiabetic. Aqueous leaf extract of custard apple is helpful against hyperthyroidism. Seed extract shows anti-fertility activity. Fruits have the capacity to enrich blood (4).

Preliminary Phytochemical Analysis:

Mona Agrawal et al., (2012) analysed different plant extracts for presence of alkaloids, flavonoid, steroids, carbohydrates, proteins, saponins and tannins. Researchers prepared plant extracts of Petroleum ether, Chloroform, Ethyl acetate, Acetone, Methanol. They performed different chemical test like the Liebermann-Burchard test, Foam test, Molisch's test, Mayers reagent, Biuret test and Shinoda test to detect the presence or absence of phytoconstituents. They reported that leaves of *Annona squamosa* contain Alkaloids, steroids, carbohydrates, flavonoids, saponins and tannins (10).

Thin Layer Chromatography :

Agarwal. M, et al., (2012) studied thin layer chromatography on pet ether, chloroform, ethyl acetate, acetone and methanol extracts of *Annona squamosa* by using different solvent systems. He used spray reagents such as, Dragendorffs, Liebermann- Burchard, 5% Ferric chloride and Anisaldehyde sulphuric acid were used to detect the presence of constituents. For petroleum ether, six spots were observed. For chloroform extract he observed 3 spots. For ethyl acetate extract he found four spots, having Rf values 0.02, 0.10, 0.18, 0.28. for acetone extract he observed five spots, for methanol extract he observed four spots having Rf values 0.05, 0.15, 0.22, 0.34⁽¹⁰⁾.

High-Performance Thin Layer Chromatography :

Yogesh Agrawal, et al., (2012) studied qualitative and quantitative analysis with help of HPTLC instrument (Camag), in which instrument contains TLC scanner connected with a PC WinCAT software, sample applicator (Linomat) and photo documentation (Reprostar III). The researcher used the concentration of 5µl of 1% solution from methanol, chloroform, pet ether, acetone and ethyl acetate extracts.

The researcher used Toluene:Ethylacetate:Diethylamine:Methanol:Chloroform (10:6:2:2:1) as a solvent system. The researcher used Dragendorffs Spray Reagent, Ferric Chloride Reagent, Liebermann- Burchard Reagent and Anisaldehyde Sulphuric Acid to detect the presence of alkaloids, flavonoids, steroids and sugars.

From petroleum ether extract , the researcher fingerprinted 17 compounds, from chloroform extract 5 compounds were fingerprinted, from ethyl acetate extract, 6 compounds were fingerprinted, from acetone extract, 9 compounds were fingerprinted, from methanolic extract, 11 compounds were fingerprinted. All Rf values was recorded¹⁸.

Further study of Jayashree Patel et al., HPTLC analysis reveals the presence of five known compounds namely, linalool, borneol, carvone, eugenol, farnesol and geraniol on basis of Rf values. At 200- 450 nm, no other component was overlap¹⁹.

Total Phenolic Content:

Marahatta Anant, et al., (2019) studied total phenolic content in plant extract by Folin-Ciocalteu method used Gallic acid as standard. For methanolic extract, the total phenolic

content of leaves and bark was calculated as 217.82 and 160.48 mg/g GAE. For hexane extract, total phenolic content for leaves and bark of *Annona squamosa* calculated as 200.98 and 29.98 mg/g⁽⁸⁾.

Total Flavonoid Content:

Aryal Ashish, et al., (2019) studied total flavonoid content for methanolic extract of leaves and bark by aluminium chloride assay method where he used quercetin as standard. For methanolic extract of leaves and bark of *Annona squamosa*, total flavonoid content was found to be 66.92 and 76.50 mg/g quercetin equivalent. For hexane extract of leaves and bark, total flavonoid content was estimated as 27.96 and 23.48 mg/g QE⁽⁹⁾.

GC/MS Analysis:

Marahatta Anant, et al., (2019) performed GC/ MS analysis on methanolic extract of leaves of *Annona squamosa*. He found 15 compounds as, Germecra-4 (15), 5, 10, (14)-trien-1- α -ol, Isospathunol, 6-Hydroxy-4, 4, 7a-trimethyl-5, 6, 7, 7a-tetrahydrobenzofuran-2 (4H)-one, Methyl hexadecanoate, Palmitic acid, Geranyl linalool, Methyl linoleate, Linolenic acid, Phytol, Caryophyllene (14-hydroxy-9 epi- Z), Naphthalactone, Elenodiol, Cedryl acetate, Pogostol, Nephytadiene⁽⁹⁾.

Pharmacological Activities:

Antimicrobial Activity

The plant extracts of petroleum ether, chloroform, methanol and water were tested for antimicrobial activity. *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus* were used as standard strains. The test bacterial strain was injected with A1% of the standard *inoculum* on Mueller Hinton Agar (MHA) using the pour plate method. Each well was filled with plant extracts and stand at room temperature for 1 hour to diffuse, then incubated for 24 hrs at 37°C. The zone of Prohibition Antibiotics was used to measure the diameter. The MIC was determined by cylinder agar diffusion method. Highest zone of inhibition was observed in methanol extract against *Ps. Aeruginosa* (MIC: 165). (Jayashree Patel et al.,2008)¹⁹.

Antiplasmodial activity

Methanolic extract of *A. Squamosa* was tested on chloroquine-sensitive strain 3D7 and chloroquine-resistant strain Dd2 of *p. falciparum* for antiplasmodial activity. It shows high

antiplasmodial activity with IC₅₀ values of 2 and 30 µg/ml on 3D7 and Dd2. Stem bark extract shows moderate activity with IC₅₀ values of 8.5 and 120 µg/ml on Dd2 (Ahir A et al., 1999)⁸.

Antiulcer Activity

Researchers isolate twelve compounds from *Annona squamosa* twigs and evaluated against cold restraint, aspirin, alcohol-induced gastric ulcer and histamine-induced duodenal ulcer models and confirmed through in vitro assay of H⁺ K⁺-ATPase activity and plasma gastrin level. Hexane and chloroform fraction of plant reduce ulcer formation in pyloric ligation, cold restraint and histamine model which is confirmed by in vitro inhibition of H⁺ K⁺-ATPase activity with an IC₅₀ value of 111.83, 60.98, and 88.42 µg/ml (Yadava et al., 2011)⁹.

Anti-head lice activity

Researcher used hexane seed extract and two major pure compounds for testing anti head lice activity and seven head lice collected from school girls. In petri dish hair were placed which contain solution of extract and pure compounds. He found that seed hexane extract of *Annona squamosa* in coconut oil at the ratio of 1:2 killed 98% of head lice within 2 hours (Interarongpai J, et al., 2006)²².

Antioxidant Activity

The ethanolic extract at 1000 µg/ml showed maximum scavenging of the radical cation 2, 2-azinobis- (3- ethylbenzothiazoline- 6-sulphonate) observed up to 99.07% followed by DPPH (89.77%) and nitric oxide radical (73.64%) at the same concentration. Polar extracts were found to be better free radical scavengers compared to less polar. Researcher analyzed the antioxidant effect of oral administration of aqueous extract of custard apple leaf on haemoglobin, blood glucose, glycosylated haemoglobin, an antioxidant enzyme, plasma insulin and lipid peroxidation in liver and kidney to streptozotocin-induced diabetic rats. After 30 days of oral administration, it significantly reduced the levels of blood glucose in diabetic rats but increased activities of plasma insulin and antioxidant enzymes (Shirwaikar A et al., 2004)²³.

Analgesic and anti-inflammatory activity

Caryophyllene oxide isolated from unsaponified petroleum ether extract from bark of *Annona squamosa* was studied. Caryophyllene oxide at dose 12.5 and 25mg/kg body weight and

unsaponified pet ether extract at dose about 50mg/kg body weight show a significant central and peripheral analgesic and anti-inflammatory activity. The researcher also found that 18-acetoxy-ent-kaur-16-ene which is isolated from petroleum ether extract of *Annona squamosa* exhibit analgesic and anti-inflammatory activity (Chavan et al., 2010, 2011)¹².

Antigenotoxic activity

Oral administration of ethanolic and aqueous bark extracts of *Annona squamosa* decreased the frequency of micronucleated polychromatic erythrocytes and chromosomal aberration in 7,12-dimethyl benzantracene treated hamsters. The researcher found that methanolic extract was more significant than aqueous extract (Suresh et al., 2010)²¹.

Antidiabetic Activity

Annona squamosa revealed that plant possess an antihyperglycemic effect. The study was done using Male albino Wistar rats. Diabetes was induced by using streptozotocin. Oral administration of aqueous extract of plant in diabetic rats for 30 days reduced blood glucose, urea, uric but increased the activities of insulin, c-peptide, albumin and restored all marker enzymes to near control levels (Kaleem M. et al., 2008)³⁵.

Antithyroid activity

Administration of *Annona squamosa* seed extract (200 mg/kg) to T (4) induced hyperthyroid animals for 10 days, reversed all these effects indicating their potential in the regulation of hyperthyroidism. Researcher found that leaf extract of plant exhibited thyroid inhibition in mice. At high concentration, it shows hepatotoxicity (Panda et al., 2007)¹³.

Vasorelaxant activity

A cyclic octapeptide, cyclosquamosin B which was isolated from the seeds of *Annona squamosa* was found to show a potential vasorelaxant effect on the rat aorta with high concentration potassium. It has moderately inhibitory effect on norepinephrine-induced contraction in the presence of nicardipine. From these results, it shows that the vasorelaxant effect by cyclosquamosin B may be attributed mainly to inhibition of calcium influx from extracellular space through voltage-dependent calcium channels (Morita H. et al., 2006)³³.

Antitumour Activity

The effect of aqueous and organic extracts from defatted seeds of *A. squamosa* was studied on a rat histiocytic tumour cell line AK-5. It caused significant apoptotic tumour cell death with enhancing caspase-3 activity. DNA fragmentation and annexin- V staining confirmed that extract induced apoptosis in tumour cells by oxidative stress. Aqueous extract of *A. squamosa* seeds has significant antitumor activity in vivo against AD-5 tumour. (Reddy, M. et al)

Antifertility activity

Researcher investigated seed extract of *Annona squamosa* for post coitus antifertility activity.

The seed extract of *A. squamosa* Linn shows anti-implantation and abortifacient activities. (Mishar A, et al., 1979)²⁸.

Insecticidal Activity

The ethanol extract of *Annona squamosa* produced significant Knockdown (KD50) in the concentration 1% w/v and 5% w/v tested 23.1 min and 11.4 min for respectively. The ethanolic *Annona squamosa* extract showed potent activity against *Sitophilus oryzae* pest. The reason for using new natural insecticides is that these are active at highly acceptable levels, biodegradable and do not leave toxic residues while the commonly used phosphorous and chlorinated insecticides contaminate the environment. (Kumar A. et al., 2010)³².

Pregnancy terminating effect

The contraceptive effect of methanolic extract of *Annona squamosa* stem bark was studied in male albino rats. The finding of the study supports the contraceptive alleges of *Annona Squamosa* however this contraceptive activity was reversible after withdrawal of the drug treatment. (Gupta et al., 2010)²⁴.

Stress and Depression

Sitaphal is a good source of Vit B complex which helps in colling the GABA neuron chemicals in the brain. It relaxes the mind and calm down stress, tension, depression and irritability. (Kaur R. et al., 2015)¹¹.

Anti-HIV

Annona squamosa extract shows the positive result when analysed for Anti- HIV screening. Saleem et al reported that the 14 isolated compounds in the study 16 β ,17-dihydroxy-ent-kauran-19-oic acid showed significant activity against HIV replication in H9 lymphocyte cells with an EC₅₀ value of 0.8 μ g/ml. (Saleem, T. et al., 2008)³¹.

CONCLUSION:

From the above review, preliminary phytochemical analysis of *Annona squamosa* extract shows the presence of alkaloids, flavonoids, carbohydrates, proteins, saponins, tannins and steroids. The researcher reported 5 components from HPTLC analysis namely Linalool, Borneol, Geraniol, Eugenol and Carvone. The researcher concludes that the total phenolic content for methanol extract of leaves of *Annona squamosa* is higher than that of plant, but the total flavonoid content is higher in extract of bark. From the GC/MS analysis of methanolic extract of leaves, phytol and geranyl linalool found as most abundant compounds. From antimicrobial activity the researcher found that methanol extract shows high zone of inhibition against *Ps. aeruginosa* (MIC: 165). The researcher concluded that aqueous extract of *Annona squamosa* is useful to control blood glucose level and beneficial in preventing diabetic complications from lipid peroxidation and antioxidant system in diabetic rats.

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