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# Phyto-pharmacological review of *Annona squamosa* Linn.

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## ABSTRACT

*Annona squamosa* L. (Family: Annonaceae), commonly known as custard apple, is cultivated throughout India, mainly for its edible fruit. The plant is traditionally used for the treatment of epilepsy, dysentery, cardiac problems, worm infestation, constipation, hemorrhage, antibacterial infection, dysuria, fever, and ulcer. It also has antifertility, antitumor and abortifacient properties. Ethanolic extracts of leaves and stem are reported to have an anticancerous activity. In this review, we have explored the Phyto-pharmacological properties of the *A.squamosa* plant and compiled its vast pharmacological applications to comprehend and synthesize the subject of its potential image of multipurpose medicinal agent.



## KEYWORDS

*Annona squamosa*;
Acetogenin;
Flavonoids;
Medicinal plant;
Anti-diabetic activity.

## INTRODUCTION

Plants have always been a common source of medicament either in the form of traditional preparations or pure active principles. In survey done by WHO it has been estimated that 80% of more than 4,000 million inhabitants of the worlds rely on traditional medicines for their primary health care needs and it can safely be presumed that a major part of traditional therapy involves use of plant extracts or their active principles[1]. There is a growing interest in herbal remedies because of their effectiveness, minimal side effects in clinical experience and relatively low costs. Herbal drugs or their extracts are prescribed widely, even when their Biological active compounds are unknown. Even the World Health Organization (WHO) approves the use of plant drugs for different diseases.

The plant *Annona squamosa (Annonaceae)* is commonly called Custard Apple in English and Sharifa or Seetaaphal in Hindi in India[2]. *A.squamosa* is a multipurpose tree with edible fruits and is a source of medicinal and industrial products[2]. This plant is reputed to possess varied medicinal properties[3]. Ayurvedic practitioners use stem and leaf extracts as indigenous uterotonic drug[4].

The plant *A.squamosa* is a large, evergreen, straggling shrub or small tree, 7 m in height, introduced into India, found wild and cultivated in various parts, up to an altitude of 900m. The leaves are somewhat hairy when young, oblong, and 8 to 15 centimeters in length with petiole 1 to 1.5 centimeters long. The flowers occur singly in the axils of the leaves and are about 2.5 centimeters long. They are pendulous, hairy, three-angled, and greenish-white or yellowish. The fruit is large, somewhat heart-shaped, and 6 to 9 centimeters in length. The outside of the fruits are marked by polygonal tubercles. When the fruit is ripe, it is a light yellowish green. The flesh is white, sweet, soft and juicy,

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The Whole Plant


Leaves


Fruits


Flowers

and has a mild very agreeable flavor[5]. The figures show the various parts of the plant *A.squamosa.*

## Phytoconstituents from *Annona squamosa*

Phytochemical studies showed that the *A.squamosa* contained a high amount of flavonoids like rutin and hyperoside[6,7]. From the leaves of *A.squamosa*, a tetrahydroisoquinoline alkaloid with cardio tonic activity[8] and a new bioactive acetogenin from its bark[9] have been isolated. Some workers have isolated flavonoids from leaves[10], Aporphine alkaloids[11, 12], terpine derivatives[13], glycoside[14] and a novel diazepine, squamolone[15] were isolated from this plant.

Some workers have isolated 11-hydroxy-16-hentriacontanone from the leaf cuticular wax of *A.squamosa* along with its known isomer 10-hydroxy-16-hentriacontanone in a ratio of 67:33[16]. The volatile constituents of *A. squamosa* bark were identified from the essential oil obtained by steam distillation and studied by GC/MS. Six major components were identified as 1H-Cycloprop(e)azulene (3.46%), germacrene D (11.44%), bisabolene (4.48%), caryophyllene oxide (29.38%), bisabolene epoxide (3.64%) and kaur-16-ene (19.13%)[17]. Discovery of three new Annonaceous acetogenins, (2, 4-cis and Trans)-squamolinone, (2, 4-cis and Trans)-9-oxoasimicinone, and bullacin B was done by some workers[18]. The bark extracts of *A. squamosa* yielded a new bioactive acetogenin, squamotacin, and the known compound, molvizarin, which is new to this species[19]. Annotemoyin-1, Annotemoyin-2, squamocin and cholesteryl gluco pyranoside were isolated from the seeds of *A. squamosa*[20]. A phytochemical investigation on the stems of *A.squamosa* led to the isolation of six new ent-kaurane diterpenoids, annomosin A (16beta-hydroxy-19-al-ent-kauran-17-yl 16beta-hydro-19-al-ent-kauran-17-oate), annosquamosin C (16alpha-hydro-17-hydroxy-19-nor-ent-kauran-4alpha-ol), annosquamosin D (16beta-acetoxy-17-hydroxy-19-nor-ent-kauran-4alpha-ol), annosquamosin E (16beta-hydroxy-17-acetoxy-19-nor-ent-kauran-4alpha-formate), annosquamosin F (16beta-hydroxy-17-acetoxy-18-nor-ent-kauran-4beta-hydroperoxide), and annosquamosin G (16beta,17-dihydroxy-18-nor-ent-kauran-4beta-hydroperoxide), along with 14 known ent-kaurane diterpenoids[21].

Phytochemical analysis of the fruits of *A.squamosa* yielded 12 known kaurane derivatives and two new kaurane diterpenoids, which have been named annosquamosin (16 beta-hydroxy-17-acetoxy-ent-kauran-19-al) and annosquamosin (19-nor-ent-kaurane-4 alpha,16 beta,-17-triol)[22].

Some worker has isolated twelve compounds from *A.squamosa*. Their structures were identified as liriodenine, moupinamide-(-)-kauran-16 alpha-ol-19-oic acid, 16 beta, 17-dihydroxy-(-)-kauran-19-oic acid, anonaine, 16 alpha, 17-dihydroxy-(-)-kauran-19-oic acid, (-)-isokaur-15(16)-en-17,19-dioic acid, squamosamide, 16 alpha-methoxy-(-)-kauran-19-oic acid, sachanoic acid, (-)-kauran-19-al-17-oic acid, daucosterol[23].

## Pharmacological studies of *Annona squamosa*

### Antifungal activity

Crude and methanol extracts of the leaves of *A. squamosa* were found to possess antifungal activity against *Alternaria alternate* (Fr.) Keissler, *Colletotrichum demantrium* (Pers. ex Fr.) Grove, *C.gloeosporioides* (Peniz) Sacc., *Curvularia lunata* (Wakker) Boedijn, *Drechslera specifera* (Bain) v.Arx, and Myrothecium *roridum* Tode ex Fr[5].

Antimicrobial activity: Antimicrobial activity of the isomeric hydroxy ketones from *A.squamosa* was tested against selected Gram-positive and Gram-negative bacterial strains, and some selected fungal strains, and com-

pared with palmitone[24,25].

**Antioxidant property**

Free radical scavenging potential of ethanolic extracts of leaves of *A.squamosa* by using different antioxidant models of screening was reported, the extract showed only moderate scavenging activity of superoxide radicals and anti-lipid peroxidation potential, which was performed using rat- brain homogenate[26].

**Anti-headlice activity**

The petroleum ether extract of *A.squamosa* seeds prepared as a cream (stable for at least 12 months) and reported as anti-headlice activity. The custard apple cream may be, therefore, suitable for use as an alternative therapy against headlice[27].

**Antidiabetic activity**

Some workers reported that the *A.squamosa* extract supplementation is useful in controlling the blood glucose level, improves the plasma insulin, lipid metabolism and is beneficial in preventing diabetic complications from lipid peroxidation and antioxidant systems in experimental diabetic rats; therefore, it could be useful for prevention or early treatment of diabetes mellitus [28-30]. *A.squamosa* leaves extract lowered blood glucose with a simultaneous increase in the plasma insulin and C-peptide levels. In addition, *A.squamosa* extract could influence protein metabolism and marker enzymes in STZ-induced diabetic rats[31].

**Mosquitocidal activity**

The Methanolic extract of leaves of *Annona squamosa* tested for mosquitocidal effect against *C.quinquefasciatus*. The results suggest the potential mosquitocidal effect of *A.squamosa* on *C.quinquefasciatus*[32].

**Antiandrogenic and antispermatogenic activities**

Some workers evaluated antiandrogenic activities of (methanol stem bark extract) *A.squamosa* with their respective reversibility in male albino rats. The stem bark extract feeding caused a marked reduction in the number of spermatocytes and spermatids in the testis[33].
Cytotoxic activity: Compounds acetogenins isolated from the bark of *A. squamosa* showed selective cytotoxic activity against the human pancreatic tumor cell line, PACA-2, with potency 10-100 times that of Adriamycin[19,33].

**Antifertility activity**

Postcoital antifertility activity of *A. squamosa* was reported in the seed extract, while aerial parts are inactive[34].

**Hepatoprotective activity**

The hepatoprotective activity of leaves of *A.squamosa* was reported against isoniazid-rifampicin induced hepatotoxicity. The alcoholic and aqueous extracts of leaves of plant tested against isoniazid-rifampicin induced hepatotoxicity. Both the extracts showed significant effect against toxicity of these drugs[35].

**Anthelmintic activity**

*An A.squamosa seed extracts* showed anthelmintic activity against *Haemonchus contortus*, the main nematode of sheep and goat in Northeastern Brazil. A compound 1 was isolated from ethyl acetate extract and inhibited the egg hatching of *H.contortus* at 25 mg $ml^{-1}$[36].

## CONCLUSION

The therapeutic efficacy of *A.squamosa* extensively used in Indian System of Medicine has been established through modern testing and evaluation (pre-clinical and clinical trials) in different disease conditions. These studies place this indigenous drug a novel candidate for bioprospection and drug development for the treatment of such diseases as cancer, diabetes, male and female infertility and some infections. The medicinal applications of this plant, countless possibilities for investigation still remain in relatively newer areas of its function. Hence, phytochemicals and minerals of these plants will enable to exploit its therapeutic use.

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