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### AN UPDATE REVIEW ON *ANNONA SQUAMOSA*

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#### ABSTRACT

*Annona Squamosa*, a multipurpose, drought resistant evergreen tree commonly known as “Custard apple” belonging to family Annonaceae, is gaining lot of importance for its therapeutic potentials. Various part of tree has been used in traditional folkloric medicine. The crushed leaves are sniffed to overcome hysteria and fainting spells; they are also applied on ulcer and wounds and a leaf decoction is taken in case of dysentery. Before exploiting any plant for medicinal purpose it is imperative to have complete information about its biology, chemistry, and all other applications so that the potential of plant could be utilized maximally. The taxonomy, botanical description of the plant, its distribution and ecological requirement are discussed in this paper. The possibilities of potential of plant for various pharmacological activities have been summarized. Overall, this paper gives an overview on covering the biology, chemistry, and various commercial and therapeutic applications

**Keywords:** *Annona squamosa*, Ecological requirement, Pharmacological, Commercial, Therapeutic applications.

#### INTRODUCTION

The genus name ‘Annona’ is from the Latin word ‘anon’ meaning ‘yearly produce’, (referring to the production of fruits of the various species in this genus) contains approximately 2300 known species (Audrey Leatemala J, 2004). Species name *squamosa* refers to the knobbly appearance of the fruit. Annona, a drought resistant tree or shrub, is widely distributed throughout the tropics and do well in hot and relatively dry climates such as those of the low-lying interior plains of many tropical countries (Agroforestry Database 4.0). The species *squamosa* cultivated mainly because of their edible fruits, commonly known as sweet sop, is heart shaped weighing about ~150g, with a very bumpy skin. When ripe, pulp is creamy, very sweet and pleasantly flavoured (Mysore N. et al., 2008) the custard apple, by definition, is a small tree or large shrub, which can reach a height of three to five

meters, but under favorable conditions it can attain a height of 6 or 8 meters. Various parts of the plant are of medicinal value, leaves are used as vermicide. Root is a drastic purgative (Yu-Liang Yang et al., 2008) and scrapings of root bark are used for toothache. Unripe fruit is astringent and ripe fruit is beneficial in malignant tumors, the fruit has sizeable number of seeds. The seed yield about 30% oil. The extraction of the oil can be done by the process of solvent extraction. Annona seed oil contains acetogenins that are toxic to insects. Pesticides derived from plants like *Annona Squamosa* can play a major role in pest management in sustainable agriculture. They have renewable character, are nonpersistent in the environment, and are relatively safer to the natural enemies, non-target organisms, and human beings. The purpose of this review is to provide information about current development in the field of Annona research.

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#### Taxonomical classification

Kingdom: Plantae  
Division: Magnoliophyta  
Class: Magnoliopsida (Dicotyledons)

Subclass: Magnoliidae  
 Order: Magnoliales  
 Family: Annonaceae (Custard-apple family)  
 Subfamily: Maloideae  
 Tribe: Abreae  
 Genus: *Annona* L.  
 Species: *Annona squamosa* L.

### Botanical description of *Annona squamosa*

*Annona squamosa* or custard apple is a well branched shrub or small tree with thin gray bark. Its botanical description is given in figure-1. The crown is spherical or a flattened ball. It has green leaves 10-15 cm long and 3-5 cm wide, sharp or blunt at the tip and round or widely wedge shaped at the base. The leaves are arranged alternately. Dormancy is induced by fluctuations in rainfall and temperature/light. But not all trees respond simultaneously. The plant is monoecious and flowers are bisexual. The flowers are in clusters of 2 to 4, and the length of each flower is about 2.5 cm, the outer petals are oblong and green and purplish at the base. Inner petals reduce to minute scales, or are absent. Nitidulid beetles are the important pollinators with wind and self-pollinating being low. After pollination berries tubercled with prominent scales formed. Fruits with white pulp are edible, round or heart shaped with many round protuberances, and has a sweetly aromatic taste. Each carpel holds on oblong, smooth, shiny blackish or dark brown seed, ranging in length from 1.3 to 1.6 cm, with a pale swelling at the hilum or albumen filled with numerous transverse, brown lines of clefts.

**Leaves** Leaves are oblong –lanceolate, 10-15 cm long and 3-5 cm wide, alternately arranged on short petioles, young leaves are slightly hairy, solitary and clustered crystals occur in epidermal cells (Dinesh Kumar *et al.*, 2005).

**Flowers** The trees are semi-deciduous, Flowering occurs during spring to early summer, and in permanently humid regions, flowering occurs throughout the year. Inflorescences are supra-axillary. The flowers are bracteate, pedicillate, actinomorphic, protogynous (Vithanage, 1983) (pistils are mature before pollen is liberated from anthers), spirocyclic and bisexual. Flower is 2-4 cm long and contains three degenerated sepals and six petals. The six petals are arranged into two whorls with three each and the petals of the inner whorl are degenerated into small scales or completely disappear. The multiple pistiles grow on the conical receptacle, in the centre of the flower with a number of stamens at the periphery. Flowers are pollinated by nitidulid beetles (George *et al.*, 1992).

**Stem** Irregular branches with thin gray bark contain N-Nitrosoxylopin, roemerolidine and duguevalline antimalarial alkaloid (Johns Tylor *et al.*, 2012).

**Fruits** Trees start to bear fruit when 3-4 year old. In India fruits are produced in July-august. Sugar apple, as the name says it all, is sweet as sugar. The flesh nearest to the rind, tastes like sugar crumbs too. It is usually conical in shape but sometimes, it may be almost round. It is easy to tell when it is ready to eat. The rind is thick with knobby segments but will turn soft and crack open, releasing a sweet aroma when it ripens. Normal ripening occurred at temperature between 15-30 °C (Broughton *et al.*, 1981).

**Roots** Branched tap root (verma, 2010).

**Seeds** Seeds are black or dark brown in colour. There are 30-40 seeds in an average fruit. The *Annona squamosa* is a diploid species with 2n=14 (Carlos, 2005).

### DISTRIBUTION

The original home of custard apple is unknown. It is a native semi-deciduous tree in tropical America and the West Indies. It was planted in Puerto Rico as fruit trees in 1626, spreading from cultivated areas to roadside and valleys. The Spanish probably carried seeds from the new world to the Philippines, and the Portuguese are assumed to have introduced it to southern India before 1590 (Julia *et al.*, 1987) Today it is cultivated in almost all tropical and subtropical countries (Yung-Yen Tien *et al.*, 2004).

### ECOLOGY AND CLIMATE REQUIRED FOR DEVELOPMENT

The *Annona squamosa* is probably the most droughts tolerant among other species of Annonaceae family as it grows and produces poorly where rains are frequent. It grows well with more than 700 mm of rainfall per year (Agroforestry Database 4.0). Temperature is a limiting factor, with frost killing young trees, but older trees show some tolerance. Seedlings have high photosynthesis activity at 30°C and show vigorous shoot growth (Higuchi *et al.*, 1998). Poor pollination is a frequent problem under high temperatures (>30°C) and low humidity (<60% relative humidity (RH)), even with hand pollination. Lower temperature (25°C) and higher humidity (70% or higher RH) greatly improves pollination (Crane *et al.*, 1994). The optimal soil pH for custard apple is 6.0-6.5. It is capable of growing in a wide range of soil types, from sandy soil to clay loams (Reddy *et al.*, 2010).

### USES OF ANNONA SQUAMOSA

Uses of different parts of *Annona squamosa* plant are given in table 1. Custard apple has a number of medicinal and non-medicinal uses. The pulp of the ripe

fruit is eaten fresh or utilized as flavouring for ice-cream and milk beverages (Vanitha *et al.*, 2010). Delicious products such as jam and squash can also be made from the pulp (Haq N and Hughes A, 2002). It can also be used to make wine (Leal, 1990). The superior quality oil can be extracted from the seeds, contains fatty acids like oleic, linoleic, palmitic, and stearic (Mariod Abdalbasit adam *et al.*, 2010). These acids find use in the preparation of soap and plasticizer industry as well as in alkyd manufacturing (Ahmad Sharif *et al.*, 2006). Nonedible seed oil is used as insect repellent (Khan *et al.*, 1983) and the seed cake can be used as manure (Kamble and Soni, 2010). The tree is also a good source of firewood and is grown in gardens as ornamental tree (Agroforestry Database 4.0). Alkaloidal extract of the plant was found to possess corrosion inhibition efficiency of c38 steel in normal hydrochloric acid medium (Lebrini *et al.*, 2010).

### PHYTOCHEMISTRY OF *ANNONA SQUAMOSA*

The curative properties of medicinal plants are perhaps due to the presence of various secondary metabolites. The extraction of different parts of *Annona squamosa* in different solvents revealed the presences of alkaloids, flavonoids, phenols, carbohydrate, saponin, sterols and tannins (Agrawal *et al.*, 2012; Ashok *et al.*, 2010). Chemical composition of various parts of *Annona squamosa* is given in table 2. Phytochemical analysis of fruits yielded 12 kaurane derivatives and two new kaurane diterpenoids Annosquamosin A and Annosquamosin B among these 16 beta, 17-dihydroxy-ent-kaurane-19-oic acid showed anti-Hiv activity (Wu *et al.*, 1996), same compound isolated from the stem also showed anti-inflammatory activity (Yeh *et al.*, 2005). Flavonoids isolated from aqueous extract of *Annona squamosa* have been showed antimicrobial activity (Kotkar *et al.*, 2002). Podophyllptoxin (a non-alkaloid toxin lignan compound) and its demethyl derivative 4'-demethylpodophyllotoxin, lirioidenine and (-)-kaur-16-en-19-oic acid were also isolated from the branches (Hatano *et al.*, 2002). GC analysis of fatty acid methyl esters (FAMES) of seed oil revealed the presence of saturated fatty acids like Hexadecanoic acid (Palmitic acid), Octadecanoic acid (Stearic acid), and unsaturated fatty acids like Octadecenoic acid (Oleic acid), Eicosanoic acid (Gondoic acid) (Alassane *et al.*, 2004). acetogenins are present in bark (Chao-Ming *et al.*, 1997, Hopp *et al.*, 1998). An alkaloid higenamine found in leaves is a cardiotoxic active principle (Wagner *et al.*, 1980) seeds contain saponin, haemolyses red blood cells and is a fish poison (Saluja *et al.*, 1990).

### PHARMACOLOGICAL POTENTIAL OF PLANT

#### Antithyroidal activity

Administration of *Annona squamosa* seed extract (200 mg/kg) or quercetin (10 mg/kg) simultaneously to T(4)-induced hyperthyroid animals for 10 days, reversed all these effects indicating their potential in the regulation of hyperthyroidism (Panda *et al.*, 2007). Further research revealed that *Annona squamosa* leaf extract exhibited thyroid inhibitory effects in mice, but altered hepatic LPO in a dose dependent manner. At low concentration it appeared to be anti-thyroidic as well as antiperoxidative, whereas, higher concentration showed antithyroidic effect but hepatotoxicity (indicated by enhanced LPO) suggesting the unsafe nature of the highest dose (Panda *et al.*, 2003).

#### Antidiabetic activity

Antihyperglycemic effect of aqueous extract of root of *Annona squamosa* at a dose of 250 mg/kg and 500 mg/kg body weight was studied. The study resulted dose dependant reduction of blood glucose levels 6 hour after oral treatment (Mujeeb Mohd *et al.*, 2009).

#### Vessels relaxation effect (vasorelaxant activity)

Cyclosquamosin B isolated from the seeds of *Annona squamosa*, showed inhibition effect on vasoconstriction of depolarized rat aorta with high concentration potassium, but moderately inhibitory effect on norepinephrine-induced contraction in the presence of nicardipine. These results showed 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 *et al.*, 2006).

#### Anticancer activity

Seeds contain Squadiolins A and B showed high potency against human Hep G2 hepatoma cells and significant cytotoxic activity against human MDA-MB-231 breast cancer cells (Liaw *et al.*, 2008). Yet another study revealed that acetogenin squamotacin from the bark of *Annona squamosa* showed selective cytotoxicity for PC-3 (human prostate tumour cell line) with a potency greater than 100 million times that of Adriamycin (Hopp *et al.*, 1996). Further investigation have provided that bark extracts protected the cell surface glycoconjugates during 7,12-dimethyl benz(a)anthracene (DMBA) induced hamster buccal pouch carcinogenesis. Oral administration of aqueous and ethanolic extracts at a dose of 500 mg/kg b.w. and 300 mg/kg b.w reduced the total number of tumours and normalized the levels of glycoconjugates in tumour-bearing animals (Suresh *et al.*, 2010).

**Antimicrobial activity**

Methanolic extract of stem bark of *Annona squamosa* possesses the invitro antimicrobial activity against *Bacillus coagulans* and *Escherichia coli* bacteria of gram-positive and gram-negative strain (Kachhawa *et al.*, 2012). Antibacterial potential of plant against *Bacillus subtilis*, *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Vibrio alginolyticus* showed positive results (Padhi *et al.*, 2011).

**Analgesic and Anti-inflammatory activity**

Unsonified petroleum ether extract of *Annona squamosa* bark extract at a dose of 50 mg/kg b.w. and carophyllene oxide isolated from the bark of *Annona squamosa* at the doses of 12.5 and 25 mg/kg b.w. exhibited significant central as well as peripheral analgesic activity, along with anti-inflammatory activity (Chavan *et al.*, 2010). Another study showed that 18-acetoxy-ent-kaur-16-ene isolated from petroleum ether extract of custard apple bark exhibited analgesic and anti-inflammatory activity (Chavan *et al.*, 2011).

**Antigenotoxic activity**

Oral administration of aqueous and ethanolic bark extracts of *Annona squamosa* significantly decreased the frequency of micronucleated polychromatic erythrocytes and chromosomal aberration in 7,12-dimethyl benz(a)anthracene (DMBA) treated hamsters. The effect of ethanolic extract was found to be more significant than the aqueous extract (Suresh *et al.*, 2008).

**Anti-head lice activity**

Extract of *Annona squamosa* seeds in coconut oil

at the ratio of 1:2 killed 98% of head lice within two hours, while the leaf extract had less potency (Intaranongpai *et al.*, 2006).

**Antioxidant activity**

Ethanolic extract of the bark of *Annona squamosa* showed significant antioxidant activity using in vitro antioxidant models like DPPH radical scavenging activity, hydroxyl radical scavenging activity, superoxide radical scavenging activity (Pandey *et al.*, 2011).

**Pregnancy terminating effect**

Contraceptive effect of methanolic extract of *Annona squamosa* stem bark was studied in male albino rats. The findings of the study support contraceptive allege of *Annoa squamosa* however this contraceptive activity was reversible after withdrawal of the drug treatment (Gupta *et al.*, 2010).

**Antiulcer activity**

Anti-ulcer activity of twelve compounds isolated from *Annona squamosa* twigs was evaluated against cold restraint, pyloric ligation, aspirin, alcohol induced gastric ulcer and histamine induced duodenal ulcer models and further confirmed through in vitro assay of H<sup>+</sup> K<sup>+</sup>-ATPase activity and plasma gastrin level. *Annona squamosa* and its chloroform and hexane fraction attenuated ulcer formation in cold restraint, pyloric ligation, histamine model and displayed anti-secretory activity in vivo through reduced free, total acidity and pepsin in pyloric ligation, confirmed by in vitro inhibition of H<sup>+</sup> K<sup>+</sup>-ATPase activity with corresponding decrease in plasma gastrin level (Yadava *et al.*, 2011).

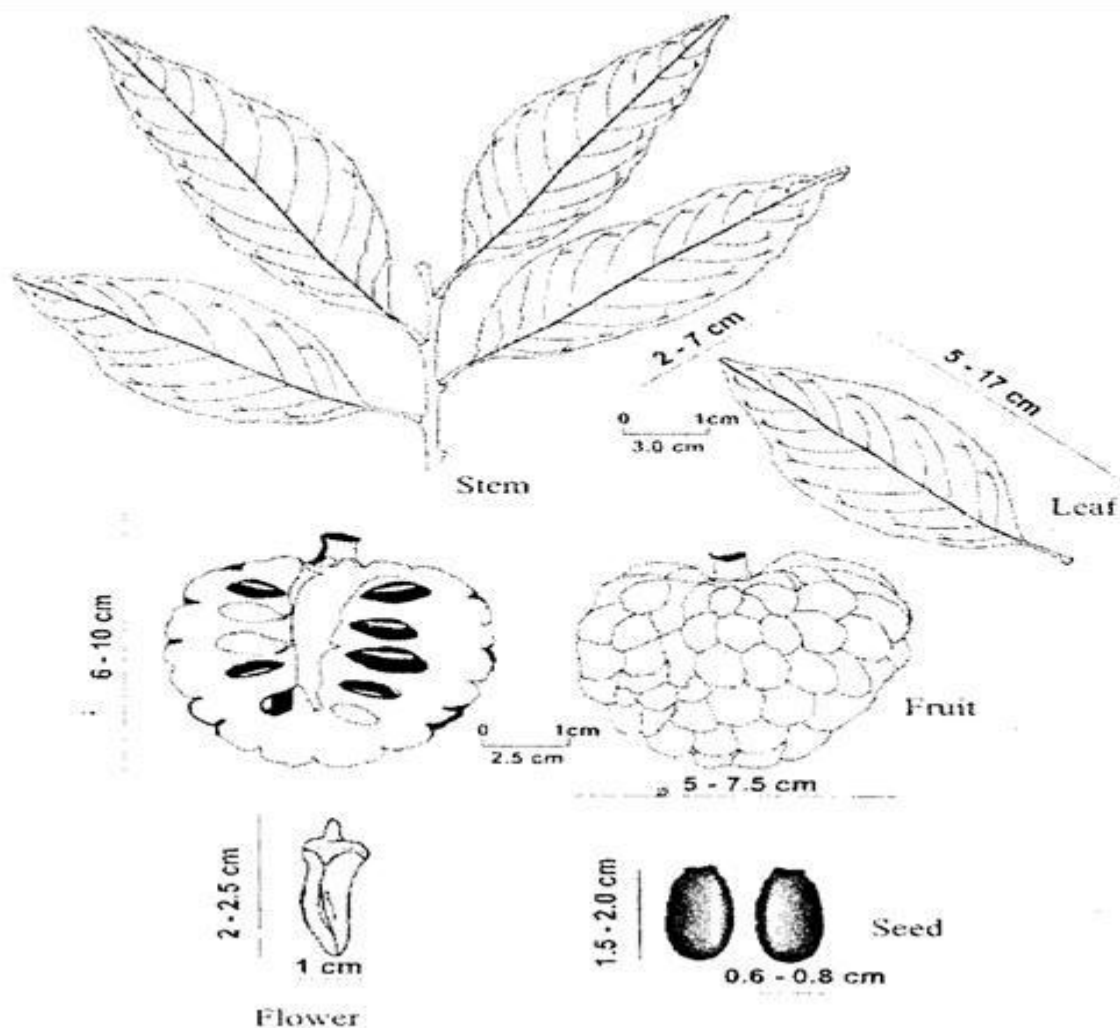
**Table1: Uses of different parts of *Annona squamosa* in medicines** (Gupta *et al.*, 2005; Yusha'u *et al.*, 2011; Mujeeb Mohd *et al.*, 2009; Rahman *et al.*, 2008; Chao-Ming *et al.*, 1997; Agrawal *et al.*, 2012; Vanitha *et al.*, 2011; Yang *et al.*, 2007; Saluja *et al.*, 1994).

Plant part used	Uses
Leaves	Antidiabetic, to treat hysteria and fainting spells, swelling, anal prolapse.
Root	Purgative, in the treatment of dysentery, antidiabetic, spinal marrow disease.
Fruit	Astringent, haematinic, cooling, expectorant, useful in treating anemia and burning sensation.
Bark	Bark decoction to prevent diarrhoea, anticancer.
Seeds	Anti-inflammatory, hypotensive, extract of defatted seeds showed antitumor and central analgesic activity, haemolyses red blood cells and is a fish poison.

**Table2: Chemical composition of different parts of *Annona squamosa*** (Nonfon *et al.*, Leal *et al.*, Saluja *et al.*, 1990; Bhakuni *et al.*, 1972; Hopp *et al.*, Chao-Ming *et al.*, 1997; Hopp *et al.*, 1996; Hopp *et al.*, 1998; Bhakuni *et al.*, 1972; Yang *et al.*, 1970; Oliver-Bever *et al.*, 1986; Beena and Remani, 2007).

Various parts	Chemical composition
Seeds	Annonastatin, asimicin, squamocin, essential oils like $\beta$ farnesene, $\beta$ -pirene, $\alpha$ pirene, limorene etc.
Leaves	Alkaloids like Aporphine, roemerine, norisocoryline etc., rhamnoside, quercetin-3-o-glucoside.
Bark	Acetogenins like 4-deoxyannoreticuline, annoreticuline-9, annosquamosins A,B cyclopeptides, squamone, squamotacin, 2,4 cis and trans squamoxinone.
Roots	Liriodenine, norcorydine, isocorydine, Norushinsunine etc.
Fruit	kaurane-type diterpenes, (-)-ent-kaur-16-en-19-oic acid and 16 $\alpha$ ,17-dihydroxy-ent-kauran-19 oic acid.

Figure 1: Important parts of *Annona squamosa*.



## CONCLUSION AND FUTURE PROSPECTS

The above review is a sincere effort to provide the updated information regarding botany, phytochemistry, ecological needs, pharmacological and commercial potential of *Annona squamosa* a medicinal plant used in the Indian system of medicine. *Annona* possesses terrific medicinal properties, attributed by its diverse group of secondary metabolites. The usage of herbs to treat a variety of different ailments is universal,

and exists in every human culture on Earth. Research on phytoconstituent has gained a special attention in recent time as several of phytoconstituent found in *Annona squamosa* show promising activity like anti-cancer, anti-inflammatory, antidiabetic, antimicrobial and many more. It may thus be considered an important gift from Ayurveda to mankind and requires right scientific and systematic approach for better exploitation in future.

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