Chapter 12
Annona squamosa: Phytochemical Constituents, Bioactive Compounds, Traditional and Medicinal Uses

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12.1 Introduction

From early time plants have been one of the basic sources of medications. The interest of using medicinal plant in treatment of many aliments is increased, this because of the emergence of multidrug resistant of many microbes and the harmful side effects of the synthetics drugs this beside its high cost. Numerous lifesaving drugs utilized in the armamentarium of current prescription are given by herbs (Goyal et al. 2007) *Annona squamosa* Linn which belong to the family Annonaceae is one of the fundamental therapeutic plants, ordinarily called "custard apple". It has been accounted for to have numerous pharmacological exercises and is utilized in customary applications (Raj et al. 2009). Therefore a lot of research was done on the different parts of the plant because of the occurrence of precious annonaceous acetogenins, which are generally utilized for the treatment of numerous illnesses (Kaleem et al. 2008). It is known with different names in the different language like Custard apple in English and Sharifa in Hindi, it is distributed in all over India and other tropical countries (Morton 1987).

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12.2 Botanical Description

Annona squamosa Linn is also known with other various names such as common-seureuba, sugar apple, gishta, sweet apple, sweetsop (Wunderlin and Hansen 2008). *Annona squamosa* is a little tree that grows up to 3–8 m, with wide, sporadically branches of light dark colored bark having flimsy leaves that happen independently, estimating 5–17 cm long and 2–6 cm in width (Pandey et al. 2014). Flowers are greenish-yellow, on slim bristly stalks, sepals pointed, bushy, green, around 16 mm long; 3 external petals elliptical, thick and adjusted at the tips, yellow-green, somewhat hairy, inside light yellow and keeled with a purplish or ruddy spot at the thin, stamens various, white, under 16 mm long; ovary light green, styles white on the raised axis (Orwa et al. 2009). The round or heart-molded greenish yellow, matured fruit is pendulous on a thickened stalk. The pulp is white-tinged yellow, palatable, and sweetly fragrant. Every carpel contains an elliptical, gleaming and smooth, dull dark colored, 1.3–1.6-cm seed (Pandey et al. 2014). Stem is cylindrical with characteristic odour and bitter taste. Outer side thick cork cells are found upon maturation (Anshuman and Raja 2016; Bhattacharya, and Chakraverty 2016) (Fig. 12.1).

Fig. 12.1 Mature *Annona squamosa* tree with fruits. (https://commons.wikimedia.org)

12.3 Plant Distribution

Annona squamosa (sugar apple) is constantly developed in tropical South America yet not regularly in Central America, in all respects as often as possible in southern Mexico, West Indies, Bahamas, Bermuda and once in a while southern Florida just as in Jamaica, Puerto Rico, Barbados and in dry locales of Australia. It was developing in Indonesia from the get-go in the seventeenth century and has been generally received in southern china, tropical Africa, Egypt and marshes of Palestine. Development is most broad in India where the tree is exceedingly prominent. The sugar apple is a standout amongst the most essential organic products in the inside of Brazil (Morton 1987). It is traditionally cultivated in north eastern parts of Thailand (Intaranongpai et al. 2006).

12.4 Biochemical Analysis

Anuragi et al. (2016) studied the proximate analysis of Annona, they reported 73.9% moisture content, 1.4% ash content, 23.2% total carbohydrates, 16.6% total soluble sugars, 7.8% reducing sugars, 3.3% fiber content, 1.9% protein content, 0.3% phenol content, 0.22% titratable acidity, 31.5% ascorbic acid content, and 25.5% seed oil content. Andrade et al. (2001) investigated the Brazilian *Annona squamosa* fruit pulp chemical composition they reported the amounts of sugars as 58% of dry mass. They reported very low triglyceride and a considerable amount of 0.25% for diterpenoid compound kaur-16-en-18-oic acid detected in the lipid fraction. These authors investigated the essential oil of the fruit pulp and they confirmed the major compounds as α-pinene (25.3%), sabinene (22.7%) and limonene (10.1%).

12.5 Medicinal Uses

12.5.1 Antibacterial Activity

The emergence of multidrug resistance by many organisms and the side effects of the synthetic antibiotics triggered the search for antimicrobial agents from the plant source to control microbial infections. All the distinctive pieces of the plant demonstrated affectability to numerous life forms. The Leaves of *Annona squamosa* are utilized in local prescription for disease treatment and aversion and they have been appeared to have antibacterial activity in ongoing investigations (Dholvitayakhun et al. 2016). Vohra et al. (1975) reported that seed extracts of *A. squamosa* show antibacterial action. Oil of *A. squamosa* also showed a clear

sensitivity against *Bacillus subtilis* and *Staphylococcus aureus* (Chavan et al. 2006). Many studies disclosed that the solvents which is used in the extractions of phytochemicals from *Annona squamosa*, affect its efficiency as antimicrobial. A study by Padhi et al. (2011) investigated three extracts (methanol, petroleum, and aqueous) of the leaf of *A. squamosa* and *A. reticulate* against three Gram-positive bacteria and five Gram-negative bacteria, by using agar cup and broth dilution methods. It was shown that *B. subtilis, S. epidermidis, S. aureus* and *V. alginolyticus* were most susceptible to the extracts among the tested bacteria. But, *S. typhi* didn't depict any zone of inhibition. Therefore, the methanol extract revealed the highest inhibition zone to bacterial growth then came petroleum ether and aqueous extracts for both *A. squamosa* and *A. reticulata* leaf solvent ether, chloroform water, petroleum ether, chloroform and alcohol leaves extracts were subjected to antibacterial screening, the three late extracts reveal the greatest zone of inhibition. Within these extracts the petroleum ether extracts showed significant results. Therefore comparing to the control group all the outcomes was critical for various parameters in wound healing activity (Shenoy et al. 2009). Another study assessed the antibacterial activity of different solvent extracts of *A. squamosa* against different Bactria spp. four of the species showed weak activity (El-Chaghaby et al. 2014). *Annona squamosa* bark is also active against bacteria *Bacillus coagulans* and *Escherichia coli* are more sensitive to methanol extract of stem bark than other bacteria (Kachhawa et al. 2012). It was found that *Neisseria gonorrhoeae*, *Campylobacter jejuni*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Bacillus cereus*, and *Listeria monocyto-genes* were susceptible to the *A. squamosa* leaf extract in vitro. This has been confirmed by Shokeen et al. (2005), and Yusha'u et al. (2011) using *A. squamosa* leaf extract. Salman and Senthilkumar (2015) reported that, *S. sobrinus* is more susceptible to the *A. squamosa* bark extract than *S. mutans,* but there is no much differences within the species. They also found that *S. mutans* and *S. sobrinus* are susceptible to 5–50 mg/ml concentration of the bark extract of *A. squamosa.* The susceptibility of *S. mutans* and *S. sobrinus* to A. squamosa bark extract made its useful as antibacterial agent and it can be used to prevent dental caries, this lead to suggestion of addition of the extract to the tooth paste or mouth wash so as to prevent the tooth decay. Number of *A. squamosa* phytochemical compounds showed antibacterial activity, such as linalool, borneol, eugenol, farnesol, geraniol, tannins, phenolic compounds, polyphenols, annotemoyin-1, annotemoyin-2, squamocin and cholesteryl glucopyranoside, and flavonoids, which showed strong antibacterial activity. In addition to silver nanoparticles (AgNPs) that biologically synthesized from *A. squamosa* (Bulut and Rapid 2009), has antibacterial action (Patel and Kumar 2008). The antibacterial activity of *A. squamosa* leaf extracts suggested by Dholvitayakhun et al. (2016) to be due to disrupting cell wall formation. The change in shape of *B. cereus* after treated with inhibitory concentrations of *A. squamosa* extract, strongly supported the suggestion of the cell wall disruption by the plant (Dholvitayakhun et al. 2016).

12.5.2 Antidiabetic

Demand of diabetic patients to utilize natural products has increased as the result of the adverse impacts of insulin and oral hypoglycaemic drugs (Kameswara and Appa 2001). The extracts of *Annona squamosa* leaves, seeds and roots were found to have antidiabetic and hypoglycaemic effects (Tomar and Sisodia 2012; Gupta et al. 2005). A few clans in India take a blend of 4–5 recently risen youngleaves alongside five grains of dark pepper (*Piper nigrum*) promptly in the first part of the day for the treatment of diabetes. Proceeded with treatment with this mixture ensured up to 80% positive results (Topno 1997). Supplementation with the aqueous extract of *A. squamosa* is helpful in controlling the blood glucose level, improves the plasma insulin, lipid digestion and is valuable in keeping diabetic complexities from lipid peroxidation and cancer prevention agent frameworks in exploratory diabetic rats. Panda and Kar (2007) investigated the effect of ethanolic extract of *A. squamosa* L. in the Alloxan induced diabetic control rats. They found a considerable decrease in blood glucose level when compared to diabetic control group. However, the addition of *A. squamosa* (300 mg/kg) water extract orally to diabetic rats for 30 days reduced blood glucose, urea, uric acid and creatinine significantly; nevertheless, they elevated the actions of insulin, C -peptide, albumin, albumin/globulin ratio beside restoring all marker enzymes nearly to the control levels (Kaleem et al. 2008). *A. squamosa* leaf extract was also found to decrease blood triacylglycerol and total cholesterol levels in diabetic animals (Gupta et al. 2008). Kalidindi et al. (2015) reported that the leaves extract of *A. squamosa* possesses anti-diabetic action because it induces the insulin release from the pancreatic islets, raises the consumption of glucose in muscle, as well as inhibits the glucose productivity from the liver. This effect comes from the fact that this plant contains quercetin which has antidiabetic action. Shirwaikar et al. (2004) suggested that the critical antidiabetic action of A. squamosa water concentrate is because of the presence of flavonoids and adhesive in the plant. Additionally, quercetin-3-O-glucoside segregated from *A. squamosa* leaf was found to restrain glucose 6 phosphatase action in the liver and to bring down blood glucose level (Panda and Kar 2007). The mechanism by which *A. squamosa* brings about its hypoglycemic action in diabetic rat was suggested by (Shirwaikar et al. 2004) to be by potentiating the insulin impact of plasma by expanding either the pancreatic secretion of insulin from the current beta cells or by its discharge from the bound structure.

12.5.3 Antimalarial Activity

The different parts of *Annona squamosa* exhibits antimalarial activities. In vitro *Annona squamosa* leaf methanol extract delineated the strong hindrance against the chloroquine-sensitive strain 3D7 and chloroquine-resistant strain Dd2 of threatening plasmodium, additionally its stem skin methanol concentrate had

moderate inhibitory impact against Dd2 (Johns et al. 2011). Kamaraj et al. (2012) also reported that the bark extract displayed IC50 of 30 µg/ml against blood stage of Plasmodium falciparum. The N-Nitrosoxylopine, Roemerolidine and Duguevalline separated from *Annona squamosa* leaf extricate are known alkaloids in charge of antimalarial properties (Johns et al. 2011). The noteworthy activity appeared by the concentrates of *Annona squamosa* suggested that the plant may had emphatically kill insects especially mosquitoes, in this manner giving a promising source of larvicidal agents. Brazilian plant demonstrated larvicidal impact against *Aedes adopictus* and *C. quinquefascinits* and against *Anopheles stephensi*. Present larvicidal action result underpins the reports and exhibited that concentrate of Annona species are potential anti-mosquito agents (Magadula et al. 2009.

12.5.4 Therapeutic Potentials of Annona squamosa Linn

The plants are essential wellsprings of drugs since the start of human progress. *Annona squamosa* is widely used in traditional medicine. It possesses effective bioactive principals in all its parts (Ranjan and Sahai 2009). The distinctive pieces of Annona squamosa, for example, fruits, seeds, leaves and barks have been utilized to treat diverse aliments. The pharmacological potential of Custard apple has many uses in medicine. Furthermore custard apple has number of uses in food and it is a source of industrial products. Recently, extensive research were done on the pharmacological properties of various pieces of *Annona squamosa* and has effectively disengaged and distinguished dynamic constituents in charge of therapeutic potential. Uses of various pieces of *Annona squamosa* plant are given in Table 12.1.

12.6 Food Uses

Custard apple is a multipurpose tree with edible fruits. Its chemical constituents have shown the potentially useful source of nutraceutical and flavoring agents. This fruit is soft and juicy and has a sweet taste. Furthermore, Custard Apple is widely used at homes, hotels and restaurants to make salads. Spray dried apple powder is extensively used to make juice, mango flavored, yoghurt and in many other applications (Zahid et al. 2018). It's also used in making of ice creams and milk beverages (Pandey and Barve 2011), or eaten fresh (Vanitha et al. 2010). It is a mixture of cooked rice and sitaphal in specific proportions with added flavor with cardamom (Kaur et al. 2015). It is also used to make wine (Leal 1990). The higher quality oil can be extracted from the seeds (Mariod et al. 2012). Delicious products such as jam and squash can also be made from the fruit pulp (Haq and Hughes 2002).

Table 12.1 Uses of different parts of *Annona squamosa* plant

Pharmacologyical action	Plant part	Active ingredients	Reference
Anti-head lice effect	Seed	Oleic acid and triglyceride	Kumar et al. (2010)
	Leaf	Linalool, Borneol, Eugenol, Farnesol, Geraniol and Flavonoids	Padhi et al. (2011)
	Leaf	Flavonoids	(Patel and Kumar (2008)
Antimicrobial activity	Seeds	Ent-kauranes, Acetogenins, essential oils and Benzylisoquinolines alkaloids and diterpene	Kumar et al. (2010)
		Annotemoyin-1, Annotemoyin-2, squamocin and cholesteryl glucopyranoside	Rahman et al. (2005)
		16-hentriacontanone (palmitone) and 10- hydroxy-16-henriacontanone while squamocin A and G, and squamostatin A	Dang et al. (2011)
Antimicrobial activity	Seeds	2,2-azinobis- (3-ethylbenzothiazoline-6-sulphonate) (ABTS) 1,1-diphenyl, 2-picryl hydrazyl (DPPH)	Shirwaikar et al. (2004); Baskar et al. (2007)
	Seeds	1, 1- diphenyl-2-picrylhydrazyl, nitric oxide, and hydrogen peroxide	Kalidindi et al. (2015) and El-Chaghaby et al. (2014); Chandrashekar and Kulkarni (2011)
	Leaves	Quercetin-3-O glycoside	Panda et al. (2007)
	Leaves	5,7,4′ trihydroxy-6,3′ dimethoxyflavone 5-O-α-I-rhamnopyranoside (THDMF-Rha)	Panda et al. (2015)
Antimicrobial activity	Leaves	Ascorbic acid	Kothari and Seshadri (2010)
Antimicrobial activity	Leaves	Tocopherol	Luzia and Jorge (2012)
Antimicrobial activity	Seeds	O-methylarmepavine and C37 trihydroxy adjacent bistetrahydrofuran acetogenins	Vila-Nova et al. (2011)
Anti-fungal activity	Seeds	Annonaceous acetogenins and alkaloids asimicin and bullatacin	Nandagaon and Kulkarni (2012)
Antioxidant – activity	Leaf	Squadiolins A and B and squafosacin B	Liaw et al. (2008)
Antioxidant – activity	Fruit	Annosquamosin A, B and C	Sun et al. (2012)
Antioxidant – activity	Seed	Acetogenin squamotacin	Hopp et al. (1996)

(continued)

Table 12.1 (continued)

Pharmacologyical action	Plant part	Active ingredients	Reference
Antioxidant – activity	Bark	12,15-cissquamostatin-A and bullatacin	Chen et al. (2012)
	Bark	Squamoxinone-D	Miao et al. (2016)
	Seed	Annosquacin A, B and C, annosquatin A and B, and squamostanin A, B and D, squamostolide, bullatacin and uvarigrandin A	Chen et al. (2011, 2012); Yang et al. (2009)
	Pericarp oil	Two entkaurane diterpenoids, ent-kauran-16-en-19-oic acid and ent-kauran-15-en-10-oic acid	Chen et al. (2017)
	Bark	Mosin A, B and C, annoreticuin-9-one, squamotacin, bullacin B, tetrahydrosquamone and bullatacinone	Hopp et al. (1998)
Antioxidant – activity	Leaf seeds	Lanuginosine	Nakano et al. (2013)
Antitumour activity	Leaf, pericarp	*Squamocin P* and *annosquatin III*	Ma et al. (2017)
		asimicin and *bullatacin*	Nandagaon and Kulkarni (2012)
Renoprotective activity	Leaf, pericarp	5,7,4′ trihydroxy-6,3′ dimethoxy-flavone 5-O-α- Irhamnopyranoside (THDMF-Rha), acetogenins	Panda and Kar (2015); Singh and Singh (2001)
Mosquitocidal activity	Seeds stem	The ent-kaurane diterpenoids ‘ent-Kaur-16-en-19-oic acid’ and ‘16alpha-hydro- 19-al-ent-kauran-17-oic acid’ 18-acetoxy-ent-kaur-16-ene	Chavan et al. (2011)
Molluscicidal activity	Bark	18-acetoxy-ent-kaur-16-ene	Chavan et al. (2011)
	Leaf	A kaurane diterpenoid 16β, 17-dihydroxy-entkauran- 19-oic acid	Wu et al. (1996)
	Seed	(+)-O-methylarmepavine, Nmethylcorydaldine and isocorydine	Yadav et al. (2012)
	Leaves, bark	Glycosaminoglycan	Ponrasu and Suguna (2014)
	Fruit	Glycosaminoglycan	Ponrasu and Suguna (2014)
	Fruit	A cyclic octapeptide, cyclosquamosin B	Iizuka et al. (2006); Morita et al. (2006)
	Seeds	The ent-kaurane diterpenoids ‘ent-Kaur-16-en-19-oic acid’ and ‘16alpha-hydro- 19-al-ent-kauran-17-oic acid’	Yang et al. (2002)
Vasorelaxant activity	Stem	Carophyllene oxide	Chavan et al. (2010)
Anti-platelet activity	Bark	18-acetoxy-ent-kaur-16-ene	Chavan et al. (2011)
Analgesic & Anti-inflammatory	Bark	A kaurane diterpenoid 16β, 17-dihydroxy-entkauran-19-oic acid	Wu et al. (1996)

(continued)

Table 12.1 (continued)

Pharmacologyical action	Plant part	Active ingredients	Reference
Analgesic & anti-inflammatory Antiviral activity	Fruit	Acidic heteropolysaccharide known as GASP3–3-I isolated	Ren et al. (2017)
	Fruit	Quercetin-3-O-glucoside	Panda et al. (2007)
Antidiabetic	Leaf	L-lysine and L-proline,	Singh et al. (2010)
		1-(4-β-D glucopyranosyloxyphenyl) – 2 – (β – D -glucopyranosyloxy)-ethane	Yadav et al. (2011)
	Twigs	(+)-O-methylarmepavine, Nmethylcorydaldine and isocorydine	Yadav et al. (2012)
Antiulcer	Twigs	Glycosaminoglycan	Ponrasu and Suguna (2012, 2014)
	Leaves	EtOAc fractions	Rahman et al. (2005)
Wound healing activity	Leaf	N-Nitrosoxylopine, roemerolidine and Duguevalline	Ponrasu and Suguna (2012)

12.7 Other Uses

Annona squamosa leaves yield an excellent oil rich in terpenes and sesquiterpenes, mainly B-caryophyllene, which finds limited use in perfumes (Bhattacharya and Chakraverty 2016). The leaves also provide ingredients used to make dyes, stains, inks, tattoos and mordants (Singh 2011). The strongest bark of the plant is used for carrying burdens in the Amazon Rainforest (Raj et al. 2009), and for wooden implements, such as tool handles and pegs. The wood is valued as firewood. Furthermore it is used as ornamental plant and it is cultivated along with banana plantation (Oliveira et al. 2010). A. squamosa seed oil was reported to be use in the soap and plasticizer industry as well as in alkyd manufacturing, the seeds are acrid and poisonous (Morton 1987).

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