

PHARMACOLOGICAL STUDY OF ANNONA SQUAMOSA

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Abstract: Plants have been one of the important sources of medicines since the beginning of human civilization. *Annona squamosa*. (Annonaceae) is a fruit tree with a long history of traditional uses. *A. squamosa* is an evergreen plant mainly located in tropical and subtropical regions. Sri kayas, the fruits of *A. squamosa*, are extensively used to prepare candies, ice creams and beverages. There is a growing demand for plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. Alternative medication and natural remedies have been used from ancient time for the treatment and wellbeing of human. Medicinal plants are considered to be effective and for most important for the above purposes. The Mother Nature has provided us with a huge count of flora and fauna. Some of the natural medicinal plants are so common that we use them in daily life without knowing their medicinal importance *Annona squamosa*. The fruit of this plant is commonly known as custard apple which is eatable. *Annona squamosa* is used as an antioxidant, antidiabetic, hepatoprotective, cytotoxic activity, genotoxicity, antitumor activity, Antilice agent.

Keyword: - *Annona squamosa*, food supplements, custard apple.

Introduction:

Annona squamosa is a small, well-branched tree or shrub of the Annonaceae family which bears edible fruit called sugar apples or candies. It tolerates a tropical lowland climate better than its relatives *Annona reticulata* and *Annona cherimoya*, making it the most widespread of these species. *Annona squamosa* is small, semi- (or late) deciduous, a much-branched shrub or small tree 3 to 8 meters (10 to 26 feet) tall similar to soursop (*Annona muricata*). 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. *A. squamosa* has been named botanically from Jamaica. Apart from the critical role of photosynthesis, plants can also be manufactured as natural products. (1) Natural products have been used to help human sustain its health since the start of medicine. Over the past century, the phytochemicals and active constituents in plants have played a pivotal role in pharmaceutical discovery. *Annona squamosa* is a tropical, endemic species of the West Indies, South and Central America, Ecuador, Peru, Brazil, India, Mexico, Bahamas, Bermuda and Egypt. In India, as reported by the Council of India of Agricultural Research (ICAR), *Annona squamosa* is widely cultivated in various states (Maharashtra, Gujarat, Madhya Pradesh, Chhattisgarh, Assam, Uttar Pradesh, Bihar, Rajasthan, Andhra Pradesh and Tamil Nadu) with a total area of 40,000 ha. *Annona squamosa* is known for its edible fruits and the tree grows as a small sapling, growing from 3 m and reaching up to 8 m, with large, randomly spreading branches with brownish or light brown bark with thin leaves.(2)

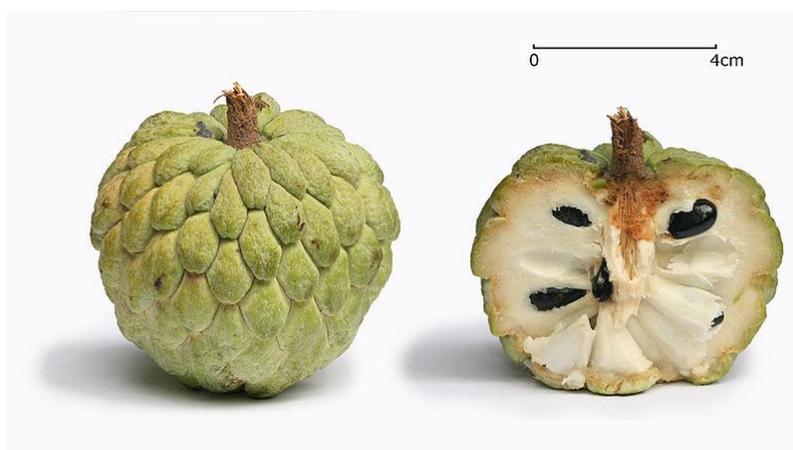


Fig no.1: *Annona Squamosa*

The fruit is spherical-conical, 5–10 centimetres (2–4 inches) in diameter and 6–10 cm long, and weighing 100–240 grams (3.5–8.5 ounces), with a thick rind composed of knobby segments. The colour is typically pale green through blue-green, with a deep pink blush in certain varieties, and typically has a bloom. It is unique among *Annona* fruits in being segmented; the segments tend to separate when ripe, exposing the interior. The flesh is fragrant and sweet, creamy white through light yellow, and resembles and tastes like custard. It is found adhering to 13-to-16-millimetre-long (1/2 to 5/8 in) seeds forming individual segments arranged in a single layer around a conical core. It is soft, slightly grainy, and slippery. The hard, shiny seeds may number 20–40 or more per fruit and have a brown to black coat, although varieties exist that are almost seedless. The seeds can be ground for use as an insecticide. *Annona squamosa* was used as a natural in medicine and in various other food applications, e.g. its pulp is used as a flavouring agent an ingredient in ice cream and 50–80% of the custard apple fruit is edible and can be crushed as juice. It contains considerable vitamin C in the range of 35–42 mg per 100 g and dietary fibre, the content of vitamin B1 (thiamine) and potassium is also remarkably high. (3)

Climate and cultivation:

Like most species of *Annona*, it requires a tropical or subtropical climate with summer temperatures from 25 °C (77 °F) to 41 °C (106 °F), and mean winter temperatures above 15 °C (59 °F). It is sensitive to cold and frost, being defoliated below 10 °C (50 °F) and killed by temperatures of a couple of degrees below freezing. It is only moderately drought-tolerant, requiring at least 700 millimetres (28 in) of annual rainfall, and will not produce fruit well during droughts. It will grow from sea level to an altitude of 2,000 metres (6,600 feet) and does well in hot dry climates, differing in its tolerance of lowland tropics from many of the other fruit bearers in the *Annona* family. It is quite a prolific bearer, and it will produce fruit in as little as two to three years. A five-year-old tree can produce as many as 50 sugar apples. Poor fruit production has been reported in Florida because there are few natural pollinators (honeybees have a difficult time penetrating the tightly closed female flowers); however, hand pollination with a natural fibre brush is effective in increasing yield (4)

Taxonomic Classification	
Kingdom	Plantae
Subkingdom	Trophobiont
Super division	Spermatophyta
Division	Magnoliophyte
Class	Magnoliopsida
Sub class	Magnoliid
Order	Magnoliales
Genus	<i>Annona</i> L
Species	<i>Annona squamosa</i>

(A)

(B)



(C)

(D)

Figure 2. *Annona squamosa* L. (A); appearance of leaves (B), fruits (C) and seeds (D)

Family: Annonaceae:

Species: 1) *Annona cherimoya*
 2) *Annona squamosa*
 3) *Annona senegdensis*

Plant part used:

Fruit, bark, seed, Root, Leaf.

Synonyms of *Annona Squamosa*

a) English	Custard apple, Sugar apple, sweet sop
b) Sanskrit	Seetaphalam, Sudha, Subha
c) Hindi	Seetaphal, Sharifa, Ata
d) Malayalam	Athachakka, Atha, Seetapazham
e) Kanda	Sitaphal
f) Telgu	Sitaapandu
g) Tamil	Sitapplam
h) Bengali	Sitapplam
i) Arabic	Ghista
j) Italian	Pomo canella
k) French	Corossolier, CA chimancanella, Pomme de cannelle, Attier
l) Portuguese	Atta, Fructa do conde
m) Malay	Nona Sri kaya, Sri kaya, Buah Nona

Table: Morphological characterization of *Annona squamosa*

Characters	Seeds	leaves	Stem	Roots	Fruits
Colour	Black	Green	Green to brown	Light brown/Dark brown	Greenish outside, whitish pulpy inside
Odour	Odourless	Characteristic odour	Characteristic odour	Odourless	Sweetish
Taste	Tasteless	Bitter	Sight bitter	Bitter	Sweetish

Morphology:

The height of *A. reticulata* is approximately 6.0 to 7.5 m. Contains numerous lateral branches. It is a small tree with a bald head branch. The stems are cylindrical with lenticels and very short coffee-coloured hairs. The leaves are oblong, lance late, membranous, acute and rounded or vulcanized at the base. Upper surface of leaves it is globes and contains few shedding hairs on the lower surface. Two up to four flowers can occur on a lateral peduncle. The fruits are edible, somewhat heart-shaped, and rough and of a yellow colour that changes to yellowish red when ripe the fruits are sweet, astringent and useful in blood problems. The seeds are smooth and blackish. (5)

❖ **Seed:**



Fig no 3: seed

A. squamosa has a variety of uses, including folk medicine and food development. The pulp is used as a juice or flavouring. The Pomegranate industrial processing unit produces large quantities of seeds, husks, or husks. Seeds are underutilized as the inedible parts of the fruit are discarded as waste. Custard apple waste (seed) contains many beneficial bioactive compounds. The seeds are therefore potentially extracted and could bring significant revenue to the food processing industry. In India, the seeds were used to make a hair lotion to combat head lice. Ground seeds soaked in water have been used as insecticides, fish poisons, potent eye irritants, and abortion inducers. A recent study demonstrated that various parts of plants, namely seeds, leaves, husks, husks and seed coats left over after the main harvest, are rich sources of photochemical and nutrients that are used in food and can be used for new product development, including use in the pharmaceutical industry. More than 400 active compounds have been isolated from *A. squamosa*. In recent years, studies related to the pharmacological and photochemical activities of *A. squamosa* seeds have confirmed that the major active chemical constituents are annonaceous acetogenins and cyclopeptides. Annonaceous acetogenins, a class of polypeptides, containing oxygenated functional groups including ketenes, epoxies, hydroxyls, tetrahydropyrans and tetrahydrofurans, essentially found in the seeds, have been shown to have strong antibacterial, anti-ovulatory, anti-inflammatory, antithyroidal and other properties. *In vivo* studies have shown that *A. squamosa* seed extract is beneficial in treating liver, prostate, cervical, and pancreatic cancers. *A. squamosa* seed, biological activities of custard apple seed *in vitro* and *in vivo*, bioactive compounds in *A. squamosa* seeds oral cancer, toxicity of custard apple seed

Fresh fruits of *A. squamosa* are commonly eaten in various parts of India, but there are no reports yet of the seed oil being used for edible purposes. Seeds of Cinnamon Apple are mainly composed of seed coat (32.4%) and seed nucleus (67.7%). Studies show a fatty crude oil content of 22.2% in the seeds, based on a dry weight of method of gas chromatography-mass spectrometry (GC/MS) was used to study the methyl esters of custard Appleseed fatty oil and determine its chemical composition. Large amounts of palmitic acid (12.1%) and stearic acid (13.6%) were present. 11-Eicosanoic acid (0.2%), Dihydrosteruic acid (0.1%), It was concluded that the presence of high levels of Ca is important for healthy teeth and bones, and Fe is essential for preventing anaemia. The mineral is also involved in maintaining pH and blood pressure levels in the human body. (6)

Toxicity of Annona Seeds:

Annona squamosa seeds have been used in traditional medicine for skin exfoliation and head lice control for as long as years [87,88]. Custard apple seeds contain bioactive substances such as polyphenols, alkaloids, acetogenin and cyclohexapeptide [89, 90]. In recent years, the pharmacological properties of certain acetogenins, including wound-healing ability, anti-lice, and anti-mosquito, anti-cancer, anti-fungal and antioxidant properties have been studied. Pomegranate seeds are toxic, mainly due to the presence of large amounts of anionic acetogenins (neurotoxins), which have been reported to irritate mucous membranes and eyes and cause vomiting (ingestion).

Use of seeds:

It was found from a number of *in vivo* experiments in animals that custard apple seed extract was effective in the treatment of leukaemia, liver cancer, prostate cancer, pancreatic cancer, cervical cancer, etc. *Annona squamosa* seed powder is utilised to abolish lice, leaf extract is used to pacify boils and treat ulcers, and the fruit acts as a sedative in cases involving heart ailments and can be used to alleviate vomiting and treat tumours (7)

❖ **Leaves:**

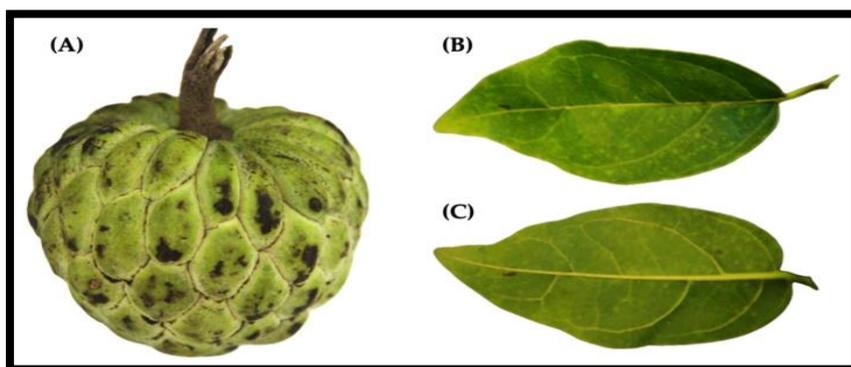


Fig no 4: Leaves

A study conducted at four different sites in Egypt showed the highest protein content in ASLs compared to seeds and fruit. ASLs from Menofia showed a protein content of 13.47 mg/g on a fresh weight (FW) basis, whereas ASLs from Mansoura demonstrated the highest protein content of 17.26 mg/g FW. ASLs from Alexandria (3.52 mg/g FW) and Giza (6.80 mg/g FW) showed the lowest protein content. Thus a higher protein content in ASL extracts can harness the nutritional value of the food for use by humans as well as animals. The leaves of the custard apple plant have been studied for health benefits attributed to a considerable variety of phytochemicals. These compounds include phenol-based compounds. B.Proanthocyanidins composed of 18 phenolic compounds, mainly alkaloids and flavonoids. Extracts of *Annona* leaf (ASL) have been studied for their biological activities, including anti-cancer, anti-diabetic, antioxidant, antibacterial, anti-obesity, lipid-lowering, and hepatoprotective functions. (8).

A literature review based on ASL's photochemical profile and health-promoting effects indicated that ASL could be used as a potential ingredient in the development of pharmaceuticals and functional foods. Although there is ample evidence from in vitro and in vivo studies, clinical studies are still needed to determine the exact effects of her ASL extracts on human health. Phytochemicals A review also highlights that numerous active compounds such as acetogenins and flavonoids found in *Annona* citrus produce the cytotoxic, malaria, diabetes and immunosuppressive effects of this plant. Extracts of ASL help maintain plasma insulin and lipid profiles and can significantly reduce blood glucose and lipid peroxidation [5]. The existing literature on *Annona* lacks a comprehensive compilation of important information on its phytochemical, dietary supplement and biological activities. Therefore, this review is an honest attempt to collect important information on the nutritional, pharmacological and biological aspects and activities of ASL. (9)

Minerals and Vitamin:

ASL contains significant amounts of various minerals such as phosphorus (P), potassium (K), iron (Fe), calcium (Ca), magnesium (Mg), sodium (Na), copper (Cu), and selenium (Se). It contains a concentration of Zinc (Zn) and vitamins namely A, C (ascorbic acid), E, B1 (thiamine), B2 (riboflavin), B3 (niacin) and B9 (folic acid). These minerals are necessary for maintaining a healthy human body as they help us perform a variety of activities such as: B. Maintaining healthy teeth and bones, muscle contraction and relaxation, blood clotting, blood pressure regulation, nerve function, immune system health, energy metabolism, and many enzymes.

Use of leaves:

Annona squamosa leaves (ASLs) possess valorisation potential owing to their extensive pharmacological properties and biological activities, such as antioxidant, antimicrobial, antidiabetic, antiviral, anticancer, and hepatoprotective activities. Sweetsop can be used for treating skin infections and diseases such as psoriasis, boils, eczema, abscesses due to its constituent of vitamin C. Leaves decoction of sweetsop can also be used to treating individuals suffering from infections such as cold, fever and dysentery. The leaves are warmed in open fire and applied to the stomach while still warm, kept in place by an abdominal binder, and renewed every 2 hours. Also used for babies.(10)

❖ **Flower:**



Fig no 5: Flower

The tree is semi-deciduous, flowering from spring to early summer, and year-round in permanently moist areas. 2 to 4 greenish-yellow flowers solitary or transversely short in tufts, about 2.5 common slender 2 cm long stems covered with hairs. 3 outer petals green, base purple, long, 1.6-2.5 cm long, 0.6-0.75 cm wide, inner petals reduced to fine scales or missing. Very numerous stamens; Dense, white, less than 1.6 cm (5/8 in) long. Ovary pale green. Compact white style on raised shaft. Each pistil forms an independent tubercle (a small rounded, wart-like ridge), most often 1/2 to 3/4 in long, 0.6 long ~ 1/4 cm (1/4 to 1/2 in) wide and ripens to whole fruit. Inflorescence is supraaxillary. The flowers are anther-like, stalked, activate, primordial female (Vithanage, 1983) (pistil matures before pollen is expelled from the anther), spirocyclic, bisexual. The flower is 2-4 cm long and contains 3 degenerate sepals and his six petals. The six petals are in two rings of each, and the inner ring petals have degenerated into small scales or disappeared completely. The pistils grow on a cone-shaped base in the centre of the flower, surrounded by rows of stamens. Pollination of flowers is carried out by beetles. Regarding the successful application of artificial pollination techniques, especially the study of pollen grain viability, special attention should be paid to aspects of floral biology. With this in mind, we determined the ban thesis (flowering time), female, male and senescent stages of *A. squamosa* L flowers under tropical climatic conditions and assessed germination and survival of pollen-exposed pollen grains. We performed two experiments aimed at Storage conditions are different. In our first experiment, we started observations and data collection when the flowers were still closed. Readings were taken every 2 h for 46 h until all flowers reached the senescence stage. (11)

❖ Bark:



Fig no 6: Bark

Photochemical investigation of the bark of *Annona squamosa* L. (Annonaceae) yields three known alkaloids namely, two aporphine (anonaine (A) and asimilobine (B)), one oxoaporphine (lysicamine (C)) together with two unknown compounds. Dried and powdered bark of *A. squamosa* (950g) were defatted with hexane at room temperature for 24h, dried and extracted with EtOH at room temperature for 72 h. The ethanol extract was separated by filtration and concentrated under reduced pressure to yield 42.3g of crude extract. Small portion of the extract was analysed chemically to determine the presence of different chemical constituents. Compound a Anonaine (Compound A) was obtained as amorphous powder; brown solid Asimilobine (compound B) was obtained as powder; white solid. Lysicamine (compound C) was obtained as amorphous powder; brown solid Compound D was obtained as powder; colourless solid. Compound E was obtained as amorphous powder; colourless solid. (12)

Use:

The bark is used for treating guinea worms and other worms, diarrhoea, gastroenteritis, snakebite, toothache and respiratory infections. Gum from the bark is used in sealing cuts and wounds. The leaves are used for treating pneumonia and as a tonic to promote general well-being. The roots are used for stomach-ache, venereal diseases, chest colds and dizziness. Various plant parts are combined for treating dermatological diseases and ophthalmic disorders. (13)

PHYTOCHEMICALS AND BIOACTIVITIES OF *A. SQUAMOSA*:

Anticancer activity:

The ability to evade apoptosis is a unique property of human cancers that leads to effective cancer progression and tumorigenesis. The high resistance of cancer cells to apoptosis to relevant stimuli is an important rationale underlying treatment failure. Therefore, many cancer treatment strategies, including radiotherapy and chemotherapy, are primarily based on cancer cell apoptosis. Numerous studies on extracts of various parts and ACG isolated from this plant showed significant ant proliferative activity against various cancer cell lines. However, few studies have described the mechanisms underlying their anticancer effects. A recent metabolic study was performed by our team in vivo to determine the mechanism of seeded total ACG on hematoma (H22) cells. This moiety was able to induce apoptosis via a mitochondrial-mediated pathway. In addition, in vitro studies were performed to explain the mechanism of anticancer effects of the isolated ACG. Results showed that different ACG types exhibited different inhibitory activities against different cancer cells. Recently, a study on various extracts from *A. squamosa* on mice bearing S180 tumours

concluded that the most important anti-tumour and toxic compounds may be present in seeds (Deng et al.2012). An in vivo study was performed using aqueous and organic seed extracts against a rat histolytic tumour cell line, AK-5. The results showed that both extracts caused significant apoptosis of tumour cells due to increased caspase-3 activity and caused down regulation of the anti-apoptotic genes Bcl-2 and BclXL, thus reducing intracellular reactive oxygen species (ROS) is enhanced.(14)

Antidiabetic Activity:

Since ancient times, diabetes has been treated orally with several medicinal plants or their extracts. These herbal remedies are minimally effective, have no side effects, and are more economical than other synthetic oral hypoglycaemic agents. The chronic disease of diabetes mellitus affects many people around the world. According to International Diabetes Federation (IDF), the prevalence of diabetes mellitus (DM) is escalating worldwide. In 2016, 415 million people had diabetes, and by 2040, 642 million people are expected to have diabetes. Effective traditional plant-based therapies are therefore highly beneficial in reducing the prevalence of diabetic complications and improving patient quality of life. Several studies have been conducted due to the traditional use of *A. squamosa* for diabetes. Based on the traditional use of *A. squamosa* against diabetes, other similar studies were conducted to examine aqueous extracts of *A. squamosa* leaves against STZ-induced diabetes in rats, reporting the same prospective antidiabetic activity.

Antioxidant Activity:

Antioxidants are compounds that play a role in protecting the body from damage caused by abnormal generation of reactive oxygen species associated with lipid per oxidation, protein damage, DNA strand breaks, etc. In the process of metabolic reactions, cells are a by-product of free radicals. High concentrations of free radicals induce oxidative stress in cells and contribute to disruption of cell function. Several recent studies have shown that the harmful free radical causes various degenerative diseases such as diabetes, cancer, and neurodegeneration. Several Studies Demonstrate the Importance of Antioxidant Compounds from ASL in Mitigating the Harmful Effects of Free Radicals. polar extracts were found to be better free radical scavengers compared with those less polar. The leaves extracts of the two parts showed high flavonoid content. The authors also showed that ASL extract has better antioxidant properties than bark extract. In summary, many interesting results point to the potential of his ASL extracts as antioxidants, but few studies have been conducted on the application of these extracts.(15)

Anti-tumour activity:

Twelve different acrogenins with different stereo chemical structures and configurations with squamostatin-A19, deoxyannoreticuin₂₀ and cis-4-deoxyannoreticuin₂₀ were used to stimulate the proliferation of cancer cell lines using the MTT method. The ability to inhibit was investigated. A likely essential factor for is the strong activity of the compounds tested, independent of bicontiguous THF-ACG or non-contiguous is-THF-ACG. ACG with the S configuration at C-24 had more selective cytotoxicity than ACG with the R configuration at C-ACG showed significant inhibitory activity against the proliferation of various tumour cell lines and multidrug resistant (MDR) tumour cell lines. Therefore, ACG can be considered as a promising anti-tumour candidate for future clinical application 20. The plant *Annona squamosa* Linn traditionally known as Custard apple possesses potent bioactive principals in all its parts. *Annona squamosa* seed extract has shown, in previous studies, significant anti-tumour activities against human hematoma cells in vitro and in vivo, indicating potential for developing the extract as a novel anti-liver cancer drug. Aqueous extracts of *Annona squamosa* seeds possess significant antitumor activity in vivo against AD-5tumour.

Antimicrobial Activity:

The leaves of *Annona squamosa* Linn have reported to have antibacterial properties. Studies have shown the high potency of antibacterial action of the plant. Plant-based antimicrobials have substantial prophylactic properties and are considered to be efficient, safe, and cost-effective alternatives for synthetic antimicrobials that possess more notable side effects. Despite being a commercial fruit plant because of its creamy succulent flesh, *Annona squamosa* is reported to have enormous pharmacological properties, including antimicrobial activity, owing to the presence of different secondary metabolites, such as glycosides, phytosterols, alkaloids, oils, saponins, phenols, and flavonoids in several research studies, the leaf extracts of *Annona squamosa* were identified to have remarkable antibacterial activity and antifungal activities. Significant antimicrobial activities were exhibited by an active acetogenin compound known as annotemoyin isolated from chloroform leaf extract and by certain flavonoid compounds purified from aqueous leaf extractor the plant.

Antiulcer activity:

Peptic ulcer is a disease that affects large population throughout the world and it is caused mainly due to the development of gastric lesions, when there is a delicate balance between some of the gastro protective and aggressive factors is being lost. Increase secretion of the gastric acid is found to be a pathological condition, which occurs mainly due to the uncontrolled secretion of hydrochloric acid through the proton pumping H⁺ K⁺-AT Pase. Anti-ulcer activity of the plant extract was evaluated against the cold restraint (CRU), pyloric ligation (PL), aspirin (ASP), alcohol (AL) induced gastric ulcer and the histamine (HA) induced duodenal ulcer models and then further confirmed through in vitro assay of H⁺ K⁺-ATPase activity and the plasma gastrin level. (16)

Antibacterial activity:

The antibacterial screening by agar cup method indicates that highest zone of inhibition was shown by the methanol extract followed by petroleum ether and aqueous extracts for *Annona squamosa* leaf. Extracts of *Annona squamosa* inhibited the growth of all test

strains except *Salmonella typhimurium*. Aqueous extracts showed less activity than methanol extracts possibly because i) the same active substances were present in water extracts, but in low concentrations ii) active substances were soluble in organic solvents and therefore, not present in water extracts. The antibacterial action of the extracts is more pronounced on Gram-positive than on Gram-negative bacteria, and these findings correlate to the observations of previous screenings of medicinal plants for antibacterial activity. *Bacillus subtilis*, *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Vibrio alginolyticus* were the most sensitive bacterial strains in the present experiments. *Annona squamosa* had strong antibacterial activity against these bacterial strains (17).

Cytotoxic Activity:

Annonaceous acetogenins are a new class of compounds that have been reported to have potent pesticidal, parasitical, antimicrobial, cell growth inhibitory activities. In this study, organic and aqueous extracts from the defatted seeds of *Annona squamosa* (custard apple) were tested on different human tumour cell lines for antitumour activity. While organic and aqueous extracts induced apoptosis in MCF-7 and K-562 cells they fail to do so in COLO-205 cells. Treatment of MCF-7 and K-562 cells with organic and aqueous extracts resulted in nuclear condensation, DNA fragmentation, induction of reactive oxygen species (ROS) generation and reduced intracellular glutathione levels. In addition down regulation of Bcl-2 and PS externalization by Annexin-V staining suggested induction of apoptosis in MCF-7 and K-562 cells by both the extracts through oxidative stress. On the contrary, COLO-205 cells showed only PS externalization but no change in ROS and glutathione levels. These observations suggest that the induction of apoptosis by *A. squamosa* extracts can be selective for certain types of cancerous cells. (18).

Insecticidal Activity:

The present study investigated insecticidal activity of ethanolic extract of *Annona squamosa*. The preliminary phytochemical investigation was carried out to identify the various constituents present in the extract. It was found that the *Annona squamosa* contain alkaloids, protein, amino acid, carbohydrate, glycosides, phytosterols, tannins and phenolic compounds. The ethanolic extract of *Annona squamosa* produced significant knockdown (KD 50) in the concentration 1% w/v and 5% w/v tested 23.1 min and 11.4 min for respectively. The mortality (100%) was achieved at 39.6±1.4 and 14.5±1.1 min for 1% w/v and 5% w/v concentration respectively. No mortality of the insects was found in any of the controls up to 100 hours. The ethanolic *Annona squamosa* extract showed potent activity against *Sitophilus orate* pest. The finding of new insecticidal activity is of great economic importance both from the agronomic and preventive medicine point of view. (19)

Health benefits:

- Relaxing muscles and protecting heart against diseases
- useful in ulcer, abscesses and boils
- Helps to grow weight
- Replenish energy levels
- For a better brain health
- For a better immune system
- Resistant to infectious diseases
- Natural anti-cancerous properties
- For a strong dental system
- For a better vision
- Lower the risk of Arthritis
- For a better cardiovascular health
- Good for foetal skin and hair
- Prevents premature labour
- Good for better foetal brain development
- Natural antidote for morning sickness
- Good for skin rejuvenation
- Naturally heals the skin infections
- Delays ageing and keeps the skin youthful
- Keeps skin cancer away
- Good for pimple prone skin
- Natural detoxifying agent
- Helps to eliminate lice
- For better collagen levels
- For a luxurious moisturised hair
- Prevents premature greying
- Natural antidote for scalp infections
- For better hair growth
- Lowers pigmentation problems
- Decoction from leaves promote healthy blood flow during M.C. in women
- To relieve dysentery, cold flu
- Juice of unripe fruit –insect bites
- Paste of leaves help in wound healing
- Decoction of leaves alleviate rheumatic pains
- Leaves are quite useful in Diabetes

- Seeds –insecticidal, abortifacient properties
- Expectorant stimulant, coolant
- Useful in anaemia (20)

❖ Conclusion:

A. squamosa is a tropical fruit tree on which extensive photochemical and bioactive investigations have been implemented. Except for being an important part of the food industry, *A. squamosa* has been proven to possess a series of bioactivities. From the detailed literature survey above, the most promising are considered as anticancer, antiphlastic, and pesticide activities. Because most previous investigations only focused on the bioactivities of different extracts of plant, further studies on the bioactive compounds and their exhaustive underlying mechanism are a crucial pivot for exploiting it in pharmaceutical and agricultural productions. In addition, the current clinical tests investigate the huge pharmacological potential of *A. squamosa* and neglect its neurodegenerative effects. Further investigations are necessary to distinguish all the constituents that contributed to the neurodegenerative effect and to ascertain the threshold of these constituent sat which the mentioned effect is caused.

References:

- (1) Orwa C, Mutua A, Kindt R et al, Simons A. 2009. Agroforestry Database: a tree reference and selection guide version 4.0. World Agroforestry Centre, Kenya. <https://www.worldagroforestry.org/output/agroforestry-database> accessed on 08-11-2022.
- (2) Dina M. El-Baz, Z. El-Khayat et al. Hssan Effects of Egyptian *Annona squamosa* leaves extracts against alloxan induced hyperglycaemia in rats. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2019 Volume 8, Issue 3, 145-163.
- (3) Chengyao Ma, Yayun Chen, Jianwei Chen et al, A Review on *Annona squamosa* L.: Phytochemicals and Biological Activities. *The American Journal of Chinese Medicine*, Vol. 45, No. 5, 1–32.
- (4) Anshuman Bhattacharya and Raja Chakravarty, The pharmacological properties of *Annonasquamosa* Linn: A Review. *International Journal of Pharmacy and Engineering* 4(2) pp 692-699 June-2016.
- (5) Prasad G. Jamkhande, Amruta S. Wattamwar .*Annona reticulata* Linn. (Bullock's heart): Plant profile, phytochemistry and pharmacological properties. *Journal of Traditional and Complementary Medicine* 5 (2015) 144e152.
- (6) Kumari N, Prakash S, Kumar M et al. Seed Waste from Custard Apple (*Annona squamosa* L.): A Comprehensive Insight on Bioactive Compounds, Health Promoting Activity and Safety Profile. *Processes*. 2022; 10(10):2119.
- (7) Kumar, M.; Dahuja, A.; Sachdev, A et al. Evaluation of enzyme and microwave-assisted conditions on extraction of anthocyanins and total phenolics from black soybean (*Glycine max* L.) seed coat. *Int. J. Biol. Macromol.* 2019, 135, 1070–1081.
- (8) Kumar M, Changan S, Tomar M et al. Custard Apple (*Annona squamosa* L.) Leaves: Nutritional Composition, Photochemical Profile, and Health-Promoting Biological Activities. *Biomolecules*. 2021 Apr 21; 11(5):614.
- (9) Gavamukulya, Y. Abou-Elella, F. Wamunyokoli, F. et al. Phytochemical Screening, Anti-Oxidant Activity and in Vitro Anticancer Potential of Ethanolic and Water Leaves Extracts of *Annona muricata* (Graviola). *Asian Pac. J. Trop. Med.* 2014, 7, S355–S363.
- (10) Pinto, A.D.Q. Cordeiro, M.C.R. de Andrade, S.R.M. et al. *Annona* Species; International Centre for Underutilised Crops: Southampton, UK, 2005.
- (11) Mohamed Saleem TS, Hepatoprotective activity of *Annona squamosa* Linn. On experimental animal model, *International Journal of Applied Research in Natural Products*, Vol. 1(3), pp. 1-7, Sep/Oct 2008.
- (12) H.-J. Yang et al, Two new cytotoxic acetogenins from *Annona squamosa*, *Journal of Asian Natural Products Research*, Vol. 11, No. 3, March 2009, 250–256 .
- (13) Ngbolua KN, Moke EL, Baya JL et al , A mini-review on the pharmacognosy and phytochemistry of a tropical medicinal plant: *Annona senegalensis* Pers. (*Annonaceae*). *Tropical Plant Research* 4(1): 168–175 .
- (14) Singh SK, Rai PK, Jaiswal D, Watal G. Evidence-based Critical Evaluation of Glycemic Potential of *Cynodon dactylon*. *Evid Based Complement Alternat Med.* 2008 Dec;5(4):415-20.
- (15) Kothari, V. and Seshadri, S. (2010), "Antioxidant activity of seed extracts of *Annona squamosa* and *Carica papaya*", *Nutrition & Food Science*, Vol. 40 No. 4, pp. 403-408.
- (16) Anshuman Bhattacharya and Raja Chakravarty. The pharmacological properties of *Annona squamosa* Linn: A Review. A. Bhattacharja. et. al. / 4(2) pp 692-699 June-2016.
- (17) Padhi, L.P, Panda, S.K. , Satapathy, S.N. et.al ,In vitro evolution of antibacterial potential of *Annona squamosa* Linn. And *Annona reticulata* L. from Similipal Biosphere Reserve, Orissa, India". *Journal of agricultural Technology*; 2011, 7 (1), pp 133-142.
- (18) Khar Ashok , Pardhasaradhi B V V, Reddy Madhurima, et.al. "Differential cytotoxic effects of *Annona squamosa* seed extracts on human tumour cell lines: Role of reactive oxygen species and glutathione". *J. Biosci*; 2005,30(2), pp 237-244.
- (19) Neha Pandey, Dushyant Barve. Phytochemical and Pharmacological Review on *Annona squamosa* Linn .*International Journal of Research in Pharmaceutical and Biomedical Sciences* Vol. 2(4) Oct - Dec 2011, pp1404-1412.
- (20) Muhammad Ajaib, Iqra Nasir , Muhammad Ishtiaq et al . Exploration of Traditional Knowledge of wild plants of Sarsala and its adjoining areas, District Bhimber, Azad Jammu and Kashmir, Pakistan. *Bioscience Research*, 2020 volume 17(4): 2739-2749.