REVIEW ARTICLE

Exploring the Multifaceted Potential of *Annona squamosa*: A Natural Treasure for Health and Wellness

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ABSTRACT

This article gives an in-depth look at the tropical fruit *Annona squamosa* L., which has a long history of traditional medicinal usage and is discussed in this review for its phytochemical and pharmacological qualities. The botanical specimen showcases an extensive assortment of bioactive constituents, encompassing glycosides, proteins, carbohydrates, saponins, alkaloids, flavonoids, and phenolics, which have significant antioxidant, antibacterial, antiviral, anticancer, antidiabetic, anti-inflammatory, anti-ulcer, and skin-protective properties. The leaves contain high protein content and essential oils amusing in terpenes and sesquiterpenes, which have shown potential in treating health conditions.

Keywords: Traditional Medicine, Phytoconstituents, Antidiabetic, Antioxidant.

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INTRODUCTION

Annona squamosa L., is a commonsultry fruit grown all over the world. It is from the Annonaceae family.[1] The pomace, seeds, husk, coat, branpeel, and leaves of fruits also vegetables, as well as other plant byproducts, have all been shown in recent papers to be rich in phytochemicals and to have potential as novel culinary ingredients. Traditional pharmaceutical applications in several nations have made use of *A. squamosa* plant extracts derived from its bark, leaves, roots, stem, peel, fruit, and seeds to treat aextensive range of ailments[2]. There is a paucity of comprehensive collection of key information on the phytochemical, nutraceutical, and formulation properties of *A. squamosa* in the extant literature.

Pharmacognosy of Plant

The little tree *A. squamosa*, which is grown for its edible fruits, reaches heights of 3 to 8 metres, has broad, irregularly spaced branches covered in brown or light brown bark, and has thin leaves[3]. The leaves are alternately arranged, either lanceolate or oblong-lanceolate in shape, measuring 6 to 17 centimeters in length. They can be pointed or rounded at tip and have a rounded or broadly wedge-shaped base. Each of the two to four flowers that make up a cluster is around 2.5 cm in length. The lower outer petals are green and the upper ones are purple. The inner petals wither away to tiny scales or disappear altogether. The full fruit has a greenish-yellow color, is plump, ellipsoid, heart-shaped, or tapering in shape, and has many spherical protuberances that are covered in white powdery bloom. The edible white pulp has a pleasant, floral flavor. Each carpel bears a single, smooth, 1.3 to 1.6 cm long, lustrous, blackish seed[4-5].

Phytoconstituents

The tropical lowland shrub *A. squamosa* shows promise in the treatment of cardiovascular disease, thyroid disease, diabetes, and cancer. Proteins, saponins, phenolics, carbohydrates, alkaloids, flavonoids, and glycosides are only some of the many phytochemicals discovered in leaves extracts by phytochemical research[6]. When compared to seeds and fruit, leaves were shown to have the maximum protein content. There were abundant proteins and amino acids in both the methanolic and aqueous extracts. However, there is a lack of studies quantifying protein and amino acids in leaf extract, thus extra studies are required to investigate the protein and amino acid profiles of these foods.[7]

High concentrations of amino acids were found in both the methanolic and aqueous extracts. Numerous studies have looked into the ingredients of essential oil from leaves, and scientists have identified 43 of them in shade-dried leaves from the lower Himalayas. About 59 different chemical compounds may be extracted from leaves, the majority of which are terpenes and sesquiterpenes (Figure 1), the most abundant of which are δ-cadinene (6.7%) and β-caryophyllene (31.1%). A total of 0.12% essential oil was extracted from fresh *A. squamosa* leaves, with 18 components accounting for 86% of the total. Bioactive phytochemicals found in leaf products may help fight diabetes, the common cold, cancer, bacterial

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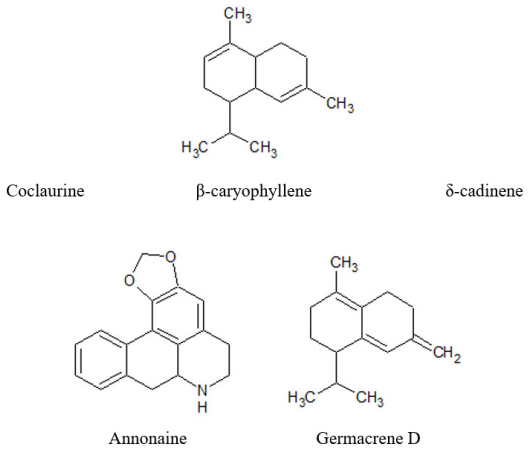

Figure 1: Active chemical constituents of *A. squamosa*

infections, viruses, obesity, and diarrhea[8-10]. To identify the volatile components of *A. squamosa*, essential oil was distilled using steam and analyzed using GC/MS. Bark, or Linn. Many of the effects are due to the alkaloid annonaine, which can be found in the bark. Six chief constituents were isolated: germacreneD, bisabolene, caryophyllene oxide, 1H-cycloprop (e), azulenebisabolene epoxide, and kaur-16-ene. Oil was tested aimed at its antibacterial properties, and it showed promising results against *Bacillus subtills* and *Staphylococcus aureas*. Around 30 acetogenins (including Squamocins B–N and Coumarinoligins) were isolated from *A. squamosa* Linn seed.[11,12]

A. squamosa Linn produce the active ingredients annotemoyin-2, annotemoyin-1, squamocin, and cholesteryl, glucopyranoside. Antibacterial and cytotoxic properties of these compounds are particularly noteworthy. The essential oils caryophyllene, pinene, humulene, and gurjunene make up the 0.15% found in the roots. Annotemoyin is one of the active ingredients in the chloroform extract of the *A. squamosa* Linn plant. Antimicrobial activity of flavonoids extracted from *A. squamosa* Linn. aqueous extract. The chemical bullatacin, for example, showed antitumoral and pesticidal action *in-vitro*. There is evidence that an ethanolic extract of the leaves and stem can inhibit cancer growth.[13.14]

Pharmacology of *A. Squamosa*

Antioxidant and antibacterial

Seed, peel, and pulp from *Annona* b. and h. have been revealed to have antibacterial, antioxidant, and *in-vitro* anticancer effects. Antibacterial activity is higher in peel extracts, while antioxidant activity is highest in annona h. seed extract. Cancer cell lines demonstrate considerable downregulation of Bcl-2 mRNA and upregulation of p53 by seed extracts. Characterizing the bioactive chemicals and understanding their anticancer mechanism need more research.[15]

The *A. squamosa* seed extract is used to make nanoparticles of plant-mediated copper oxide that can kill bacteria and help find hydrogen peroxide (H_2O_2) in farming settings. Various methods showed that the NPs treat *Xanthomonas oryzae* caused rice bacterial blight. Their excellent electrochemical sensitivity to H_2O_2 and low detection limit make them a promising electrochemical sensing platform[16]. Chemical composition of *A. squamosa* L. pulp and seed extracts is examined for antioxidant and acetylcholinesterase inhibition. Qualitative assays measured total phenols, flavonoids, vitamin C, and carotenoids. Liquid chromatography-mass spectrometry (LC-MS) identified compounds. Seed extract contained more total phenols and flavonoids, while pulp had more AChE inhibitory action. *A. squamosa* may help neurological illnesses and is nutritious, according to the study.[17] Four extracts of *A. squamosa* seeds were tested for their ability to get rid of free radicals. These extracts are chloroform, ethyl acetate, petroleum ether, and methanol. Results show that the extracts have a lot of reducing power, along with antioxidant and overall phenolic content. Strong antioxidants were found in the samples, which could prime to creation of strong antioxidants from seeds. Extracts had stronger antioxidant qualities than gallic acid, and the antioxidant activity went up as the concentration of the extracts went up.[18] The research looked at how well chloroform, methanol, and water-based extracts of leaves killed five types of fungi and how well they protected against free radicals. Inhibition of all studied fungi strains was seen in both organic and aqueous extracts, and it depended on the dose. The methanol extract has the highest antioxidant activity, followed by the chloroform and then the water extracts. Phytochemical testing showed that glycosides, saponins, tannins, flavonoids, and phenols were present.[19]

Anticancer

Developed nano-*A. squamosa* leaves extract, a nanoparticle loaded with chitosan from *A. squamosa* leaf, to combat human colon cancer cells. The nano-*A. squamosa* leaves extract was prepared using ionic gelation and tested on WiDr cells. The results showed strong cell death, higher levels of caspase-3, cell cycle halt, and apoptosis. More exploration is desirable to invention out how well drug is loaded and how much of it is present.[20] *A. squamosa* leaf extract to bio-reduce and stabilise silver nanoparticles. The nanoparticles inhibited five wound/burn infection-causing skin isolates and synergistically interacted with antibiotics. They targeted and killed alien cells selectively, making them biocompatible with mammalian cells. Nano-green synthesis may be an effective cancer treatment and antibiotic potentiator.[21] Nano-ASLE-induced *A. squamosa* leaf extract to treat HeLa cells for malignancy. Nano-ASLE inhibits HeLa cell multiplication and increases caspase-3 activity, causing mitochondrial cell death. Further research is needed to establish loading efficiency, drug concentration release, and *in-vivo* study.[22] It was possible to separate two benzylisoquinoline compounds from *A. squamosa*. Natural sources were used to get an alkaloid. *A. squamosa* L., on the other hand, was already known to have coclaurine. Also, the split alkaloids were tested on three categories of cancer cells to see if they could kill the cells.[23] Extracts of pulp and seed were intentional for their chemical composition and biological activity including antioxidant and acetylcholinesterase

inhibition. Extracts showed maximum cytotoxic activity against six cell lines, with no significant toxicity towards normal lymphocytes. *A. squamosa* is traditionally used for treating cardiac problems, antibacterial infections, and antitumor properties. The study suggests that *A. squamosa* seed extract contains compounds with anticancer activity, suggesting potential for further development.[24] Both *in-vitro* and *in-vivo* investigation showed that plant products had strong effects on stopping cell lines from multiplying and killing them. *In-vivo* studies showed that the extracts had a big effect on the size of the tumors and the levels of proliferative and death markers. This suggests that it might be a good idea to use this as a new drug to treat breast cancer.[25] Anticancer and biomarker effects of *A. squamosa* leaves extract and its noisome-loaded extract were looked into in this work. It was discovered that the extract could help treat Ehrlich ascites cancer, and the loaded extract worked even better. The groups that were treated had smaller tumors, better liver and kidney functioning, lower levels of inflammatory markers, and better oxidative stress in the liver, kidneys, and tumors. The leaves of *A. squamosa* have powerful chemicals that fight cancer.[26]

Antiviral

Vero cells were diseased with dengue virus type 2 (DENV-2) and tested for antiviral efficacy using *A. squamosa* leaf extract (ASLE). Anti-DENV-2 action of ASLE has never been reported before, highlighting the compound's novel therapeutic potential[27].

Skin protection

This research looks into whether or whether a niosomal-entrapped version leaf extract is beneficial in preventing UVA-induced skin damage. When compared to the native plant leaf extract, niosomal-entrapped A.SLE was found to be superior in its ability to prevent UVA-induced skin damage. Research indicates that niosomal-encapsulated A.SLE can shield skin from UVA radiation, serving as a photoprotector[28].

Antidiabetic

This research investigates the potential antioxidant impact of administering *A. squamosa* leaf extract orally on plasma insulin, lipids, blood glucose, hemoglobin, and lipid peroxidation in rats with diabetes induced by streptozotocin. Results show that extract significantly reduced blood glucose levels, lipids, and lipid peroxidation while increasing plasma insulin and antioxidant enzyme activities. This suggests that the extract could be beneficial for diabetes prevention or early treatment[29]. Rabbits with diabetes were orally administered an ethanolic extract of leaves. Among animals with STZ-induced diabetes, FBG decreased by 13.0% and glucose tolerance improved. Additionally, the extract amplified levels of HDL and diminished levels of LDL and triglycerides, while decreasing total cholesterol by 49.3%.[30] The study discovered that quercetin-3-O-glucoside, which was extracted from the leaves of *A. squamosa*, could control lipid peroxidation and alloxan-induced hyperglycemia in rodents. It decreased hepatic and renal LPO, inhibited hepatic glucose-6-phosphatase activity, and reversed the effects of alloxan treatment. It also increased antioxidative enzyme activities and glutathione content, suggesting its potential in diabetes amelioration and tissue lipid peroxidation[31].

Anti-inflammatory

Undiluted petroleum ether extract of the bark of *A. squamosa* was utilized to isolate caryophyllene oxide. Following this, its capacity to alleviate pain and decrease inflammation was evaluated. Caryophyllene oxide exhibited potent analgesic and anti-inflammatory belongings in both brain and body at concentrations of 12.5 and 25 mg/kg body weight, at 50 mg/kg,unsaponified petroleum ether extract had a similar impact. These effects of caryophyllene oxide were about same as those of the usual drug used in the tests.[32]

Anti-ulcer

The study reveals twelve known compounds from *A. squamosa* twigs, including a synthetically known ethane. The H+ K+-ATPase activity of these compounds was assessed, and they exhibited encouraging anti-secretory activity that was on par with that of the standard drug omeprazole. Additional results from the research indicate that *A. squamosa* (AS) exhibits a noteworthy inhibitory impact on a range of ulcer models, such as those induced by alcohol, cold restraint, pyloric ligation, aspirin, and duodenal ulcers induced by histamine. AS and its active constituents attenuated ulcer formation and displayed anti-secretory activity.[33]

ADR of A. squamosa

Rarely used orally in traditional medicine, *A. squamosa* seeds are notoriously toxic. In India, aqueous preparations are used as an abortive. It has been said that they are irritating to the mucosa and the eyes. When taken orally, the ACG causes nausea and vomiting. Both the American Food and Drug Administration's (FDA) and the Animal and Plant Safety Assessment System's (AFSSA) databases list this plant as poisonous[34].

CONCLUSION

The tropical fruit *A. squamosa* L. has many phytochemical and pharmaceutical qualities. Its fruit, seeds, foliage, and bark have all been utilized in modern research and traditional medicine to promote health. Researchers have found that the plant's extracts can fight cancer, diabetes, free radicals, germs, viruses, inflammation, and sores, and protect the skin.

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