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A Review: An Analysis of the Nutritional Value, Phytochemical Traits, Pharmacological Characteristics, and Toxicity of Annona Squamosa-A Brief Rewiew

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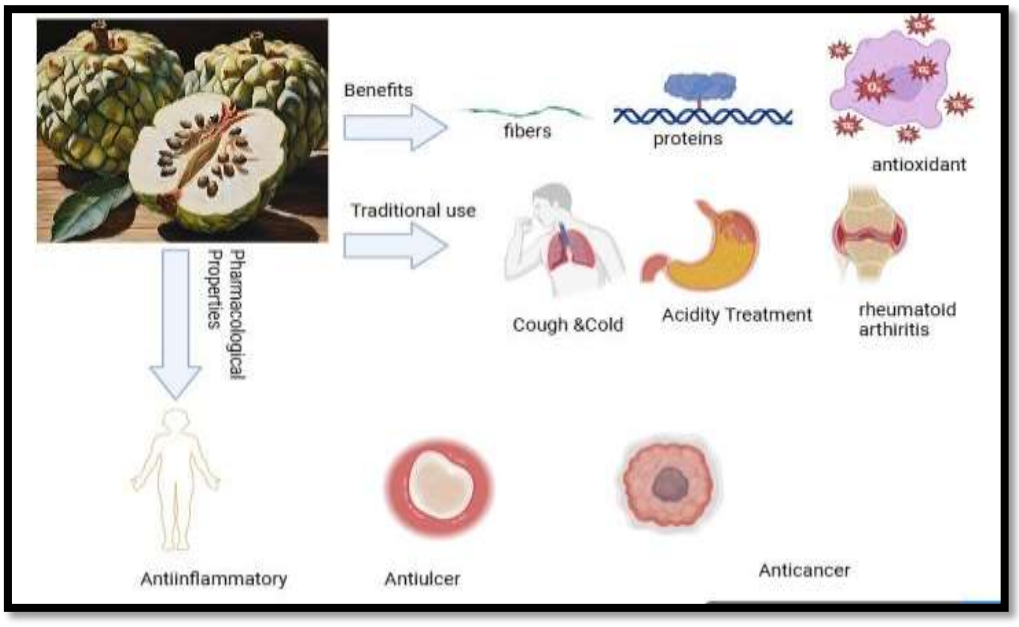
ABSTRACTS:
The tropical fruit-bearing tree known as the custard apple or sugar apple, sweetsop, or Sita phal in India, is a member of the Annonaceae family. Originally from the West Indies and Central America, it is currently widely grown in tropical and subtropical climates across the world, such as Egypt, Brazil, Mexico, and India. The fruit is prized for its sweet, creamy pulp, rich in vitamins notably vitamin C and B1, minerals, and dietary fiber. In addition to its nutritional benefits, custard apples have a number of therapeutic uses. It has long been used to support cardiovascular health, aid digestion, and strengthen the immune system. Bioactive substances such acetogenins, alkaloids, and flavonoids have been found by phytochemical investigations, and they contribute to the plant's anti-inflammatory, antidiabetic, and antioxidant properties. The plant's phylogeny and evolution have been better understood thanks to recent genetic studies, which may also help with its cultivation and therapeutic uses. Despite its advantages, the fruit's extreme perishability makes storage and transportation difficult, which has led to research into value-added goods and post-harvest processing. All things considered, Annona squamosa is a fruit with substantial nutritional and therapeutic value that merits more study to maximize its production, use, and preservation.

Keywords: Custard apple, Nutritional content, Pharmacological properties**,** Proteins, Sitaphal.

Graphical abstract:



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I. INTRODUCTION:

The custard apple's scientific name is Annona squamosa. Another name for custard apples is sugar apples or sweetsop. Native to the Americas, specifically the Caribbean, Central America, and portions of South America, it is a tropical fruit. This flowering plant is a member of the Annonaceae family, which also includes other well-known species such as Annona reticulata (atemoya) and Annona cherimola (cherimoya) [1]. These days, custard apples are grown extensively throughout tropical and subtropical regions of the world, such as Asia, Africa, and the Pacific Islands. India alone accounts for a sizable amount of global output, with sother nations including Thailand, the Philippines, Vietnam, Egypt, and India becoming as key producers. The fruit is good for digestion, the immune system, and the heart since it is high in vitamins, including vitamin C, minerals, such as potassium and magnesium, and dietary fiber. 73.30% moisture, 1.60% protein, 0.30% fat, 0.70% mineral matter, 23.90% carbohydrates, 0.20% calcium, 0.40% phosphorous, 1.00% iron, 12.4-18.15% sugar, 0.26-0.65% acidity, and 12.4-18.15% sugar make up the approximately 28–55 percent edible portion of a custard apple, which has a calorific value of 105 Kcal/100g. Fruits are processed to make ice cream, milk shakes, fermented liquor, pulp, and beverages. Flavonoids, glycosides, tannins, phenolic compounds, and other substances are said to be present in the leaves and bark of the Custard apple plant. Similarly, alkaloids, flavonoids, and acetogenins that have lipid peroxidation, antidiabetic, antioxidative activity against different ROS, and hypoglycemic properties were found in the fruits, seeds, and other sections of custard apples when they were phytochemically characterized [2]. In tropical nations like Vietnam, the custard apple (Annona squamosa L.) is well-liked. It is an edible fruit that is sold commercially. It has a delicious, white flesh and a thin coating of peel. The majority of custard apple peels are thrown away as organic trash, which can harm the ecosystem. Alkaloids, tannins, flavonoids, and saponins, which have antioxidant capabilities and can scavenge free radicals, are among the biological phenolic chemicals found in Custard apple peel. Antioxidants from the fruit's byproducts may therefore be beneficial to human health. [3]. The most powerful inhibitor of mitochondrial complex I is acetogenin, which is effective at concentrations as high as nanomolar. Research has shown that the aqueous extracts and organic extract solvent from the roots, leaves, fruits, and seeds of custard apples have good antibacterial and antimicrobial properties. These extracts have also been found to be an insecticide, inhibiting the activity of insect feeding (antifeedant) and repelling some important agricultural and storage pests. For these reasons, it is necessary to determine the effectiveness of five bioactive components and compare the activity of a fraction consisting of all components (crude) on dandruff-causing microorganisms and a control[4]. Annona Squamosa plant parts and its morphological features are:[19]

Table no.1: Morphology features of Annona squamosa

Sr. No.	Parts of Plants	Morphological Features
1.	**Leaf**	rectangular, deciduous, and slender-lanceolate
2.	**Fruit**	Compound, irregular, heart-shaped, and when torn, yellow or brown
3.	**Seed**	Smooth, oblong, glossy, dark brown or black in colour.
4.	**Flower**	Drooping clusters of fragrant, thin, greenish yellow flowers are shown

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II. CUSTARD APPLE'S NUTRITIONAL VALUE:

Figure no.1: Annona squamosa

Nutrient-dense custard apples have a major positive impact on our health. An amazing variety of vitamins and minerals necessary for our bodies to perform at their best are included in each serving. **Vitamins:** Vitamin B6 found in custard apples is essential for the production of neurotransmitters that aid in mood regulation, and vitamin C, which is abundant in custard apples, helps strengthen immunity.

Antioxidants: Vitamin C, phenolic chemicals, flavonoids, and kaurenoic acid are all abundant in custard apples. Free radicals, which are frequently linked to both chronic illnesses and more serious ailments including cancer and heart disease, are eliminated by these antioxidants. In addition to helping to prevent cataracts, age-related macular degeneration, and vision loss, antioxidants are crucial for shielding the eyes from oxidative damage. Because flavonoids and kaurenoic acid have anti-inflammatory qualities, these antioxidants also lower the risk of a number of inflammatory diseases. According to this study, sugar apples have very high antioxidant activity, with >70 mol/100 g of edible component. Annona squamosa, Annona cherimola, and Annona muricata extracts have been shown to have strong antioxidant activity in numerous investigations, including those carried out in India[5].

Minerals: Custard apples include potassium and magnesium, which help control blood pressure. minerals that are necessary for preserving general health and wellbeing, like potassium and magnesium. The body uses these nutrients for a number of purposes, including as energy metabolism, bone health, and immunological function. As part of a balanced diet, eating Annona reticulata fruits can help meet daily nutritional needs and promote good health[6].

Fibers: Custard apples, which are high in dietary fiber, support a healthy digestive system. The high fiber content of custard apples aids in better digestion and supports the beneficial bacteria in your stomach.

Protein: Lowland tropical shrub Annona squamosa has great medicinal potential for the treatment of cancer, diabetes, thyroid issues, and heart problems. Numerous phytochemicals, including proteins, carbohydrates, saponins, alkaloids, flavonoids, phenolics, and glycosides, were found in ASL extracts after phytochemical investigation. ASLs had the highest protein content when compared to seeds and fruit, according to a study done at four distinct locations in Egypt. The highest protein concentration, 17.26 mg/g FW, was found in ASLs from Mansoura, while the protein level of ASLs from Menofia was 13.47 mg/g FW. The lowest protein concentration was found in ASLs from Giza (6.80 mg/g FW) and Alexandria (3.52 mg/g FW).Therefore, a higher protein concentration in ASL extracts can maximize the food's nutritional value for both human and animal consumption. The methanolic and aqueous extracts of ASLs also contained significant amounts of proteins and amino acids. While Millon's test verified the presence of proteins and amino acids in methanolic ASL extracts, the biuret test verified their presence in aqueous ASL extracts. More research is required to examine the protein and amino acid profiles of ASLs because there has been little study done on the measurement of protein and amino acids in these organisms[1].

Table no.2: Nutritional Value of Annona squamosa

Nutrients	Amount	% Daily Value
Calories	101kcal	5%
Carbohydrates	25.2g	8%
Total fat	0.6g	1%
Protein	1.7g	3%
Sodium	4mg	0%
Potassium	382mg	8%
Calcium	30mg	2%
Iron	0.71mg	4%
Vitamin C	19.2mg	32%
Vitamin A	33IU	1%

III. ADVANTAGES OF ANNONA SQUAMOSA:

In addition to being delicious, custard apples are a great source of vital nutrients. Let's

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explore the amazing health advantages of custard apples and discover why they ought to be a regular part of your diet.Custard apples' high carbohydrate content makes them a great source of energy. This fruit is a great snack for athletes or others who need a quick pick-me-up during the day because it can provide you an instant energy boost. Custard apples' natural sugars provide a steady stream of energy, which keeps you awake and energetic. It manages diabetes. People with diabetes may benefit from custard apples despite their sweetness. It can avoid abrupt rises in blood sugar levels because it has a low glycemic index and delivers carbohydrates into the bloodstream gradually. Additionally, the fibres content helps in regulating blood sugar by slowing down the absorption of glucose[7]. Using Jurkat and HL60 cell lines, A. squamosa leaves showed encouraging cytotoxicity, with CI50 values of 4.2 and 6.4 g/ml, respectively. At higher doses (IC90), A. squamosa leaves reduced clonogenic endurance and hindered VERO cell development in the MCF-7 and HCT-116 lineages. The alkaloids asimilobine, nornuciferine, liriodenine, anonaine, corypalmine, and reticuline were identified in the extracts by UPLC-ESI-MS/MS analysis. Consequently, A. squamosa leaves exhibit antitumor qualities [8]. Vitamin C is a natural antioxidant that is abundant in custard apples. This vitamin is also well-known for its antiinflammatory and immune-boosting properties. To strengthen your immune system's defenses against infectious invaders, including one serving of this delicious fruit in your regular diet. By scavenging harmful free radicals in the body, it stops the onset of several diseases and ailments. Boils, abscesses, and ulcers can all be treated with custard apple paste. Vitamin C, which is found in custard apples, promotes the growth of cartilage, tendons, and ligaments as well as wound healing. Regularly consuming custard apple juice encourages the skin's layers to produce new cells. Additionally, it aids in the recovery of cuts and abrasions. Skin conditions like psoriasis, eczema, and inflammation can be treated by applying the custard apple tree's latex topically [5]. The plant's custard apple leaves, which have antibacterial and wound-healing properties, were thoroughly extracted using a Soxhlet apparatus using a variety of solvents, including petroleum ether, solvent ether, chloroform, alcohol, and chloroform water, in ascending order of polarity. The cup plate method was used to screen each of the five extracts for microorganisms. The highest zone of inhibition was displayed by the petroleum ether, alcoholic, and chloroform water extracts. Thus, these extracts were used to promote wound healing. All models that used Annona squamosa leaf petroleum ether extracts produced noteworthy outcomes. When compared to the control group, all of the results were significant for various wound healing activity criteria [9]. Because of its nutritious content and mouthwatering flavor, custard apples are typically utilized as dessert fruits. The fruit has 70.5% moisture, 23.5% carbs, 1.6% proteins, and 104 Kcal/100g of the edible component, along with fat (0.4%), mineral matter (0.9%), iron (1.0%), calcium (0.2%), and phosphorus (0.04%). The fruit of the custard apple has a pH of 5.5, a TSS of 26.40B, and 0.5% tannin.The fruit's seeds make from 23–40% of its weight, while the edible component ranges from 28–37%. examined the chemical makeup of seven distinct species of custard apple pulp and found that they were all low in protein, pectin, and vitamin C [10]. It is thought to strengthen the immune system, which benefits general health. It is thought that Annona reticulata has immunomodulatory properties, which means that it can support and fortify the immune system. Frequent ingestion of Annona reticulata may improve the body's defenses against illnesses and infections. Dietary fiber from Annona reticulata helps with digestion and keeps constipation at bay. Dietary fiber, which is abundant in Annona reticulata, facilitates regular bowel motions and keeps constipation at bay. By encouraging the development of advantageous gut bacteria, the fiber also contributes to the maintenance of a healthy digestive system.The high levels of B vitamins in custard apple, particularly vitamin B6, play a crucial role in brain health. Vitamin B6 helps in the production of neurotransmitters like serotonin and dopamine, which regulate mood and cognitive function. Consuming custard apple can enhance brain activity, improve mood, and reduce the risk of neurological disorders [11]. Because of its extensive distribution, Annonaceae species are wellknown and historically utilized in tropical climates. The species' leaves, seeds, bark, fruit, stem, roots, and twigs are among the parts that are traditionally used. Numerous preparation techniques, including infusions, pastes, and decoctions, have been documented . In Brazil, for example, fresh Annona dioica fruit is used to treat wounds. In certain regions of Indonesia, dried Annona muricata leaves are taken orally for their analgesic properties. While the leaves of Annona muricata are used to treat both fever and dysentery,

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the bark and roots are used to treat both in Burkina Faso and as an anthelmintic [12].

IV. TRADITIONAL USE OF ANNONA SQUAMOSA:

Some species' roots, bark, and leaves are utilized in traditional treatments. In the Amazon Rainforest, the robust bark is utilized for hauling loads and for making wooden objects like pegs and tool handles. The wood is prized for its brown and yellow colors and fuel. According to a recent study, the alcoholic seed extract of Annona glabra may contain anti-cancer chemicals. An anti-nociceptive action was observed in the leaf extract of Annona diversitolia. It was discovered that roots had anticonvulsant properties. Annona purpurea juice is used to treat fever and chills in Mexico. The pulp of Annona craciljlora was discovered to possess mutagenic qualities. The leaves of Annona squamosa are used to cure fainting spells and hysteria. Colds, coughs, intestinal infections, and acidity disorders are all treated with leaf decoction. Diarrhea is treated with bark decoction. In cases of dysentery, roots are employed. Milk beverages and ice creams are made using fruit[13]. Many traditional medicines from around the world have been based on natural materials. Furthermore, the development of treatments for a wide range of inflammatory diseases has been greatly aided by these medical approaches. Because the Annonaceae family is widely used in traditional medicine, it is highly well-known in tropical locations. In Brazil, for example, the juice of the macerated leaves of Annona muricata is used to treat neuralgia, rheumatism, and arthritis. Africa Due to their affordability and ease of use, 80% of the population still relies on traditional treatments. Strong immunomodulatory action has been documented for a number of native species, including Enantiachlorantha. The bark powder is combined with lemon juice, and the resulting paste is applied as an arthritic treatment. In contrast, Xylopiaaethiopica's whole fruit and ethanolic root extract are used in Sudan as a treatment for colic pain, headaches, and neuralgia. In central Africa, Xylopiaparvifolia root decoction is used as a natural pain reliever, and the roots are chewed and then consumed to treat inflammations and stomach ulcers [14]. The application of custard apple to the scalp can help manage hair loss. Because custard apples have vata-balancing properties and if used consistently, they can be utilized to control hair loss. It may aid in giving the hair nourishment [15]. The leaves and twigs of Duguetiachrysocarpa are pulverized and their extract used as a treatment for bowel disorders and gastrointestinal ulcers in the northwest region of Brazil. In Cameroon, wounds and fever are treated using an oral infusion of the stem bark of Annickiachlorantha [12].

1.Phytochemical Characteristics of Annona squamosa:

Besides its leaves, stem, and roots, which are equally significant due to its nutraceutical and medicinal significance, Annona squamosa has been extensively cultivated in India for its fruits. Additionally, the essential oil that is derived from ASLs exhibits strong antimalarial and antiparasitic properties [1]. Phytochemicals are bioactive substances that are non-nutrient plant chemical compounds that shield plants from pest invasion and microbiological diseases. On the other hand, phytochemistry is the study of natural products. Although it is commonly known that plants create phytochemicals to defend themselves, several studies have revealed that many phytochemicals can also shield people from illness. Different plant sections contain phytochemicals [16]. Despite being hazardous, custard apple seeds are used to cure head lice because of their insecticidal qualities (the production of these seeds can induce blindness and eye irritation). Annona seeds contain insecticidal qualities as well. Chemical pesticides are no longer the preferred method of protecting crops from insect invasion. Custard apple seeds can be utilized as biopesticides, which are good substitutes for conventional pest management methods. There is a lot of oil in the seeds, which can be used to create soap or as cooking oil if the harmful alkaloids are removed. Previous research has examined compounds derived from seeds and leaves [17]. Numerous primary and secondary metabolites are known to be present in Annona reticulata L. Primary metabolites play a direct role in the growth and development of plants, while secondary metabolites aid indirectly by offering defense mechanisms against herbivory, insect, and pathogen attacks as well as aiding in the tolerance of harsh, stressful weather conditions. The following phytochemicals have been identified in plant leaf extract: proteins, steroids, triterpenoids, tannins, starch, saponins, anthraquinones, amino acids, flavonoids, glycosides, phenolic compounds, alkaloids, and aleurone grains. One kind of secondary metabolite that is unique to the Annonaceae family is acetogenin. They are distinguished by having a terminal γlactone and a C32 or C34 fatty acid chain. Certain

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pharmacological properties of acetogenins include antifeedant, antibacterial, antiparasitic, anticancer, immunosuppressive, and pesticidal effects. A bioactive acetogenin called reticulatacin was extracted from Annona reticulata L. and exhibits strong anti-tumo r and anti-cancer properties. Annonaretin A, kaurenoic acid, taraxerol, βsitosterol, 16α-hydro-19-al-ent-kauran-17-oic acid, 6βhydroxystigmast-4-en-3-one, 17-acetoxy16β-ent-kauran-19-oic acid, 16α-hydro-ent-kauran-17,19-dioic acid, and (2S)-diOmethylquiritigenin were among the compounds that were extracted from Annona reticulata L. leaf extracts and the following chemicals were found by GC-MS analysis: Benzene, 1-methyl butyl, palmitic acid, mitoflaxone, oleic acid, piperidine, 2-propyl-, piracetam, and (1,1′bicylopropyl)Cholesta-7,14-diene, 4-H-1-Benzopyran-4-one, 2-(3,4-dimethoxyphenyl)-5hydroxy-3,6,7-trimethoxy, 4-(4-nitrophenylazo)-benzoicacid, methoxycarbonylmethyl ester, 2,6,10,14-Hexadecatrienoic acid, 3,4-dihydroxy-1,6-bis (3-methoxy-phenyl)-hexa-2,4-diene-1,6dione, Cholesta-7,14-diene, and N-(4-Hydroxyphenyl)acetamide[18].Fruits: Vitamin C, iron, calcium, thiamine, potassium, carotene, riboflavin, niacin, ascorbic acid, magnesium, dietary fibers, and sugar (up to 28%).Atrophine, Roemerine, Dopamine alkaloid, Salsolnol, Coclaurine, Carvone, Eugenol, Farnesol, Geraniol, Limonene, Linalool, Menthone, Isoquinoline alkaloids, Acetogenine (annoreticulin and isoannoreticuin), and sugars such as rhamnoside and quercetin-3glycoside are all found in leaves. A total of 59 chemical substances were found in leaf oil.Liriodenine, Oxoanalobine, Borneol, Camphene, Camphor, Car-3-ene, β-Caryphyllene, Eugenol, Farnesol, Geraniol, 16-Hetriacontanone, Hexacontanol, Higemamine, Isocorydine, and Limonine are found in the roots and stem.Bark: Squamone, Duguevalline, Roemerolidine, Nnitrosoxylopine, Bullatacin, and Mosinones A, B, and C.Acetogenin, Solamin, Squamocin, Annotemoyin-1, Annotemoyin-2, triterpenoids (stigmasterol and sitosterol), cholesterol, and glucopyranoside are seeds[19]. Additionally, flavonoids, phenolic chemicals, sulfated polysaccharides, tannins, and triterpenoids are found in the custard apple's seeds[20].

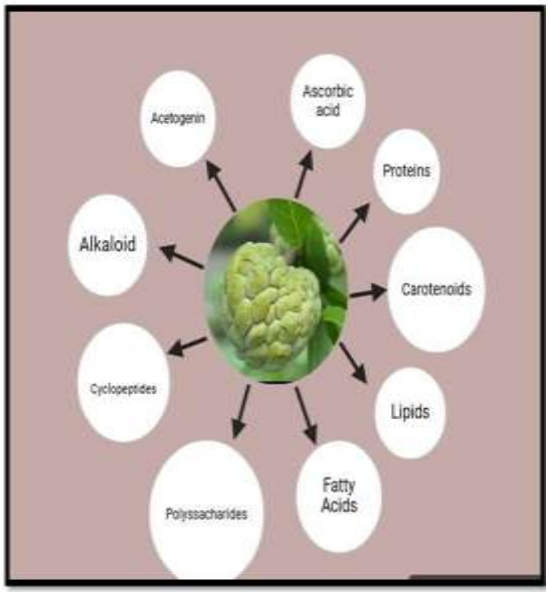

Figure no 2: Phytochemical Characteristics of Annona squamosa

1. Custard apple seeds have gained attention as a possible component for the creation of supplemental foods due to their noteworthy phytochemical and nutraceutical makeup. By combining the bioactive substances from the custard apple seeds, by-products can be created that have unique **pharmacological characteristics, Numerous** studies have been conducted on:

- Anticancer/Antitumor
- Antimalarial
- Antidiabetic
- Antioxidant
- Antiulcer
- Antimicrobial
- Anti-inflammatory effects of A. squamosa.

Anticancer/Antitumor:

A. squamosal contains anconaeusacetogenins, which have potent antitumor and anti-cancer properties. Researchers from many nations have studied mitochondrial interference energy metabolism in great detail because of its distinct structure and function. It can generate cytotoxicity to lung, breast, colon, prostate, pancreatic, and other malignancies selectively, and its anti-tumour activity was 40–300 times that of paclitaxel. It has active chemicals that fight cancer and have a lot of room to grow [21]. Annona reticulata contains compounds that have demonstrated promise in combating cancer cells. According to some research, acetogenins and

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flavonoids, two bioactive substances present in Annona reticulata, may have anti-cancer effects. In lab experiments, these substances have demonstrated encouraging outcomes in preventing the proliferation of cancer cells [11]. The anticancer activity of Annona squamosa seeds that had been defatted was assessed. Both organic and aqueous solvents are employed in the extraction procedure. Assessments of intracellular ROS, estimation of intracellular GSH, DNA fragment analysis, and quantification of apoptosis were the criteria that were looked at in order to stop the activity. Rat histolytic tumor cells that line AK-5 were used in the investigation. Significant apoptotic tumor cell death was documented in the study along with increased caspase3 activity, downregulation of the antiapoptotic genes Bcl-2 and Bcl, and an increase in intracellular ROS production that was connected with decreased intracellular GSH levels. Similarly, annexinV staining and DNA fragmentation verified that the extracts caused oxidative stress, which in turn caused tumor cells to undergo apoptosis. Custard apple seeds aqueous extracts exhibit strong anticancer efficacy against AK-5 tumors in vivo [22]. A. muricata's anticancer properties have been documented in a limited number of clinical investigations. After taking an aqueous extract of A. muricata leaves for over five years, a patient with breast cancer has maintained constant disease activity with no known negative effects. After beginning to take a supplemental treatment that contained A. muricata as a pill, another patient with metastatic ovarian cancer reported illness stability. Lastly, in a randomized controlled trial, the supplemented group with colorectal cancer showed more cytotoxicity from the extract of A. muricata leaves than the placebo group [12]. We investigated the possibility that extracts from Annona reticulata's pulp and peel may inhibit MCF7 proliferation. The MTT test and morphological analyses were used to investigate the anticancer potential of Annona reticulata pulp and peel extracts [34].

Antimalarial Activity:

According to a recent study, the alkaloid apomorphine, which was isolated from Annona squamosa bark, has antimalarial properties. It is composed of rotemerolidine, Nnitrolopine, and duguevalline. All of the compounds present in Annona squamosa exhibited moderate antiplasmodial efficacy against the D10 and Dd2 chloroquine-sensitive and resistant strains. As most famously demonstrated by the antimalarial agents quinine and artemisinin, which were first isolated from chinchona species, plants are a significant source of novel antimalarial compounds. [23] The mosquitocidal action of Annona squamosa leaf methanolic extract against C. quinquefasciatus was studied. The findings imply that A. squamosa may have a mosquitocidal effect on C. quinquefasciatus[24].

Antidiabetic activity:

The antidiabetic effect of male albino Wistar rats is assessed. Male albino Wistar rats are given streptozotocin. When given orally to diabetic rats for 30 days, Annona squamosa aqueous extract decreased blood glucose, urea, uric acid, and creatinine while increasing C-peptide, insulin albumin, albumin/globulin ratio, and all marker an enzyme level [22]. One of the prevalent endocrine diseases, diabetes is typified by changes in the metabolism of proteins, carbohydrates, and insulin as a result of pancreatic insulin dysfunction or insufficiency. The World Health Organization (WHO) says that 80–90% of those over 40 are at an increased risk of developing non-insulin-dependent diabetes mellitus.[20] The antidiabetic or antihyperglycaemic effects of ASLs and their constituents have been studied in animal models. Panda and Kar isolated quercetin-3-O-glucoside (Q3G) from ASL, evaluated its antidiabetic potential in alloxan-induced diabetic rats, and observed that Q3G significantly improved insulin secretion and reduced the level of glucose in the blood. [1] Anona squamosa root aqueous extract was tested for its antihyperglycemic effects at doses of 250 and 500 mg/kg body weight. Six hours following oral therapy, the study showed a dose-dependent decrease in blood glucose levels [24].

Antioxidant activity:

As radical scavengers, antioxidants are crucial for the body's defense against free radical diseases. Simple phenols and polyphenols are both members of the class of chemical substances known as phenols. Polyphenols can lessen and stop the harm that free radicals cause to the human body. Flavonoids have the ability to create substances that may prevent malignant cells from invading and killing them. The purpose of this study was to assess the antioxidant activity, total polyphenol, flavonoid content, and phytochemical screening of the extract of A. squamosa on 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2,2'-and-bis-3ethylbenzthiazoline-6-sulphonic acid (ABTS)[25]. With an antioxidant activity of 69.28

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µg/mL, infused dried custard apple leaves are categorized as having strong antioxidant activity. This means that the phenolic and flavonoid components in the infused dried custard apple leaf extract allow the leaves to oxidize DPPH free radicals. The antioxidant activity of the sample is influenced by the amounts of flavonoid and phenolic chemicals present. The antioxidant activity increases with the concentration of phenolic and flavonoid chemicals. Additionally, several antioxidant molecules have anti-inflammatory qualities. Additionally, antioxidants can inhibit the production of leukotrienes, which can inactivate leukocytes and cause inflammation, by lowering the activity of lipoxygenase enzymes. Inhibiting the activity of the enzymes lipoxygenase and cyclooxygenase is one of the ways that terpenoid chemicals are known to reduce inflammation[26].

Antiulcer activity:

A. squamosa has active phytoconstituents that may be used to treat ulcerative colitis, especially methylarmepavine and isocorydine. These substances block important enzymes and pumps involved in acid secretion and lower pepsin and stomach acid levels. According to studies, they can reduce the development of stomach ulcers by blocking the ATPase, potassium, and hydrogen pumps, which lowers the release of hydrochloric acid.

Additionally, they alter pepsin activity, protecting tissue and maintaining the stomach mucosal barrier. Isocorydine and methylarmepavine are intriguing treatment options for ulceritis because of their diverse mechanisms of action. To fully comprehend their mechanisms and maximize their application in the treatment of gastrointestinal illnesses, more research is required[27].

Antimicrobial activity:

It was discovered that the leaf extract worked well against a variety of fungal species, including Aspergillus niger, Fusarium solani, Alternaria alternate, Candida albicans, and Microsporumcanis.Both gram-positive and gram-negative bacteria have been shown to be susceptible to the antibacterial properties of A. squamosa leaf extract. It possesses bacteriostatic activity against numerous species, including Enterococcus faecalis and Klebsiella pneumoniae, as well as bactericidal activity against Staphylococcus aureus. Saliva samples were used to assess the fruit extract's antibacterial properties. According to the study, the antibacterial activity of A. squamosa extract was on par with that of chlorhexidine. Additionally, certain grampositive (Bacillus subtilis, Staphylococcus aureus) and gram-negative (Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) bacteria were shown to be strongly inhibited by the methanolic seed extract. Another study found that fruit peel alcoholic extract had antibacterial properties against Pseudomonas aeruginosa and Staphylococcus aureus[28]. Numerous dangerous bacterial and fungal species are typically linked to microbial illnesses and disorders. A. reticulata is a significant source of new medicines, especially those with antibacterial qualities. Despite being only moderately active against all bacterial strains, B. cereus exhibited the biggest zone of inhibition. Candida albicans and Tricoderma viride in particular showed slower development. The extract shows promise as a possible source for novel antibacterial drugs, according to the research.

Anti inflammatory activity:

Annona reticulata is considered a medicinal plant. The bark of the plant has a potent astringent effect and is used as a tonic. The herb has been utilized for its antiinflammatory, anti-wound-healing, anti-anxiety, anti-stress, anti-mutagenic, and spasmolytic qualities. Extracts from leaves and stems exhibit spasmolytic, inotropic, and positive chronotropic qualities. The anti-inflammatory effects of A. reticulata leaf extracts are preventing or lessening the rat paw edoema caused by carrageenan.The results also demonstrated that the aqueous extract had a stronger effect than the hexanolic extract. A. reticulata leaves may exhibit stronger polar anti-inflammatory qualities, which would justify the use of this plant species' aqueous extract by traditional healers to lessen inflammation[29]. The most frequent unintentional injuries are burns. Burn injuries can have serious effects on bodily function in addition to deforming the skin. There won't be much scarring after these burn injuries heal fully. An orderly series of events is involved in the dynamic and complex process of wound healing, which aims to repair injured tissue. Several overlapping phases and processes, such as hemostasis, inflammation, proliferation, tissue remodeling, and the development of granulation tissue with angiogenesis, are involved in the burn healing process[30]. The protein denaturation assay evaluated the anti-inflammatory effects of Annona reticulata pulp and peel extracts[31].

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V. TOXICITY:

The wealth and diversity of toxicity studies on both species in our study indicate that acetogenin molecules are linked to their toxicities.According to Pinto and associates, the most significant acetogenin compounds in 2005 were annonacins, also known as annocins, which include squamocin, asimicin, annonastatin, bullatacin, and bullatacinone . The insecticidal action of extracts from six plants—Maesa lanceolata, Solanum syzymbrifolium, Annona squamosa, Cymbopogon citratus, Ocimum basilicum, and Ocimum gratissimum—against Sitophilus has been assessed by other researchers. They demonstrated that one of the poisonous plants was A. squamosa. After 24, 48, and 72 hours of exposure, the mortality rates for the dose of 0.002 g/mL are 46, 63, and 70%, respectively. The death rates for 24, 48, and 72 hours at a dose of 0.02 g/mL are 59, 71, and 86%, respectively. The death rate for the dose of 0.2 g/mL increases from 96% after 24 hours to 100% after 48 and 72 hours. We can state that our extracts have proven effective in comparison to the synthetic insecticide Malathion. After just 24 hours of exposure, Syzymbrifolium and Annona squamosa demonstrated greater mortality than Malathion, although M. Lanceolata displayed a mortality rate comparable to Malathion after 48 hours.[32]. A. atemoya had a less impact on cell viability than A. squamosa when compared to the fruit pulp extract of other Annona species in the research; yet, it produced a comparable rise in LDH, suggesting a comparable effect on cell death. This is true even though A. atemoya has almost 100 times more squamocin and a comparable quantity of annonacin (3.8 of 2.2 µg/g dry weight) than A. squamosal[33]. One investigation found that the ethanolic fraction has an LD50 value of more than 1500 mg/kg body weight[27]. Acute toxicity is typically defined as an unfavorable impact that occurs immediately or a few days after a single or brief exposure to a drug. Acute oral toxicity is determined using a lethal dose, which is the amount of substance that kills 50% of test animals. Male albino rats were tested for acute oral toxicity using a methanolic leaf extract of A. squamosa. Genotoxicity refers to the potential of an agent or substances to harm a cell's genetic information at sub-lethal concentrations, resulting in long-term detrimental consequences such as cancer and reproductive diseases. An comprehensive examination was conducted to confirm the reaction of A. squamosa in this regard. A. squamosa is unique in this regard, since it has been shown to have both genotoxic and genoprotective properties in animal models. To assess the safety profile of the biopesticide derived from A. squamosa, toxicological investigations such as genotoxicity and biochemical analysis were performed. Isosquamocin, a major component responsible for insecticidal action, was mostly extracted from defatted seed using methanol/dichloromethane solvents (1:1 v/v). Male Albino New Zealand rabbits were used in the toxicological investigation to test the ocular toxicity of petroleum ether, ether, chloroform, and ethanol extract of A. squamosa seeds and leaves. Each rabbit's eye received 50 µL of extracts and propylene glycol in the test. At five minutes, an hour, twenty-four, forty-eight, and seventy-two hours, the results were noted. The study found that the ethanolic leaves and seed extract had the least amount of toxicity on rabbit eyes, whereas the first three extracts were more toxic, resulting in conjunctival redness, edema, corneal abrasion, chemosis, and cutaneous erythema[35].

Formulations of Annona squamosa:

1.Ingredients for Foam-Mat Dried Custard Apple Powder:

Apple pulp custard are agents that cause foaming, such as egg albumen

Approach:

In order to produce a stable foam, whip the pulp with foaming agents.
Create a thin layer of foam.
The foam mat should be dried at regulated temperatures.
For use and storage, powder the dry foam.[36]

2. Ingredients for Custard Apple Squash:

Apple pulp custard
Sugar syrup
Preservatives and acidulants

Approach:

Prepare the sugar syrup and combine it with the apple pulp custard.
Add the proper preservatives and acidulants.
Pasteurize the squash in bottles.[37]

3.Whey-Based Custard Apple Drink

Ingredients: Pulp of custard apple: 12%
Whey: 88 percent
Sugar: Modified according to preference
Procedure:

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Mix custard apple pulp with whey. Add sugar to reach the desired sweetness. Pasteurize the mixture. Bottle and store under refrigerated.[38]

1.Ingredients for Custard Apple-Banana Nectar:
Apple pulp custard: 5%, 15% is banana pulp.
Adjusted sugar to 15°Brix
0.3% citric acid
Water: To maintain volume balance.

Approach:
Blend the banana and apple pulps to make a custard.
To reach 15°Brix and 0.3% acidity, add water, sugar, and citric acid and stir. Pasteurize for 30 minutes at 96±1°C.The nectar should be aseptically bottled.[39]

2.Ingredients for Custard Apple Ice Cream:
Apple pulp custard: 15%
70% buffalo milk
15% sugar
0.15% stabilizer
Approach:
Mix buffalo milk with custard apple pulp.
Mix well after adding the stabilizer and sugar.
For five minutes, pasteurize the mixture at 85°C.
Cool to 5°C after homogenizing.
To get the consistency of ice cream, freeze the ingredients.[40]

1. **Applications in Medicine and Nutrition:**
Vitamins, minerals, and antioxidants abound in custard apples. Among the formulas are:
Apple Herbal Custard Tea (fruit powder and dried leaves)
Apple Custard Energy Bar (with honey and almonds)
Custard Apple Syrup (a beverage-grade concentrated extract)[41]
2. **Apple jam custard ingredients:**
Apple pulp custard: 40%, 55% sugar, 0.5% pectin, 0.3% citric acid, Water: 4% **Procedure:**
Custard apple pulp should be extracted and filtered.
Stir in pectin and sugar.
Raise the temperature until the total soluble solids (TSS) reach 65%.
Before packaging, add the citric acid and let it cool.[42]
3. **Anti-aging Cream**: Custard apple extract is included for skin-rejuvenating and antioxidant properties. Formulation: 2–5% extract added to an aqueous cream base [43]
4. Custard Apple Seed Oil Ointment: This anti-lice and wound-healing ointment base contains custard apple seed oil.[44]
5. **Antidiabetic Herbal Tablets in Pharmaceutical and Nutraceutical Formulations** Ingredients: excipients and custard apple leaf extract.

Use: In diabetic models, exhibits hypoglycaemic action.[45]

VI. CONCLUSION:

The most well-known species, Annona squamosa, is a semi-deciduous shrub with spreading branches that is not particularly tall. that are often grown worldwide, primarily in tropical areas. This plant is called a custard apple because of its extremely sweet and delicious fruit. In addition to its culinary uses, this plant has therapeutic applications. Custard apple is a nutrient rich fruit that gives a various health benefit to us. It includes the high number of dietary fibres, Vitamins, and antioxidants. These nutrients contribute to improved digestion, enhanced immune function, and better overall health. Studies shows that custard apples, which are high in nutrients and antioxidants, provide a number of health advantages, such as enhanced immunity, better digestion, and possible advantages for skin and heart health. As such, they are a great complement to a well-balanced diet.

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