An Investigation of The Anti -Depressant Activity of Annona Squamosa Leaves

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***Abstract*—Every portion of Annona Squamosa hastherapeutic properties and has piqued the interest of organic chemists and biochemists due to its unusual structure and diverse bioactivity. The primary goal of the research was to get phytochemical estimates of chemical constituents in Annona squamosa leaves. The study includes a preliminary phytochemical investigation of an ethanolic extract of Annona Squamosa, which was tested for the presence of several phytoconstituents using conventional procedures. Thephytochemistry indicated the presence of various phytochemicals, including alkaloids, flavonoids, tannins, phenols, and triterpenoids, with rutin (a flavonoid component) being discovered to be responsible for Annona Squamosa's analgesic effect.**

***Index Terms*—Anti-Depressant, Annona Squamosa pharmaceutical activities phenols and triterpenoids, Preliminary phytochemical.**

I. INTRODUCTION

Depression is a multifaceted disorder that influences a person's emotions, physical health, and behavior. Patients with severe depression have symptoms associated with changes in brain neurotransmitters, including nor epinephrine (NE), serotonin, and dopamine. Depression is projected to impact a large proportion of the general population. Depressive episodes are anticipated to impact 5.8% of men and 9.5% of women over their lifetime. Suicidal thoughts are a common side effect of depression, which accounts for 60% of all deaths (SM, 1998) (Rechelson, 1990) (E, 2001) (KD).Despite the emergence of innovative medications for the treatment of depression, it is unfortunate that this condition remains undiagnosed and untreated. Even yet, the patient's clinical symptoms have improved to some extent with the present medications (Goodman, 2001) (Shalam MD).Medicinal herbs, on the other hand, are extremely valuable in the field of disease treatment and cure because to their low risk and side-effect profiles. Practical experiences and various recent research studies have clearly proved that it is superior to synthetic chemicals in terms of safety, as well as the synergetic impact of its active ingredient and the presence of specific minerals and salts. Ayurveda, the ancient traditional school of medicine, mentions a variety of single and compound medication compositions of plant origin that are used for the treatment of mental illnesses (Kojima).We provide an overview of Annona squamosa Linn's phytochemicals, traditional and culinary applications, and pharmacological properties in this paper

Figure 1. a) Whole plant of Annona Squamosa b) Leaves &Fruit c) Flower

Need for the study:

- Insecticide, anti-ovulatory, haematinic, sedative, stimulant, expectorant, and abortifacient are some of its uses. This perennial, procumbent plant, which is found all throughout India, contains liriodenine, moupinamide, anonaine, squamosamide, and sachanoic acid as its primary active ingredients (Shah, 2011).
- The custard apple family includes the Annona species, which is grown across India. The Annona plant has been extensively utilized for medicinal purposes in many indigenous and traditional medical systems.
- A variety of plant components, including leaves, fruits, bark, roots, and even seeds, are used to prepare medicines. Many cultures also make considerable use of Annona squamosa as a traditional remedy (Ashok, 2004).
- Ethanolic extract of leaves & stem are reported to have an Anti cancerous activity.

II. PLANT PROFILE

A. Botanical Classification:

These are small trees that grow to a height of 3 to 6 meters. They have elliptic oblong dark green leaves (10 to 15 cm long and 3 to 5 cm wide) that have an odd smell, pear-shaped yellowish green fleshy fruit (5 to 20 cm in diameter) that is covered in a green, thick, round coating on the outside and edible pulp on the inside, and they produce sweet fruits, also called sweet sugar, every year.

Common Names:

Sithaphal, Custard apple, Sharifa.

Synonyms:

Sugar apple, Sithaphalam, Custard apple.

Taxonomical Classification:

- Kingdom:Plantae
- Class Angiosperms
- Division:Magnolids
- Order:Magnoliales
- Family: Annonaceae
- Genus Annona
- Species: Annona squamosa

A. Description:

The tree is around six meters tall. Petioles are 12 mm long, and the leaves are oblong, lanceolate, sub acute, and globous above where lateral nerves 8–11 pairs are located. Sepals are pubescent, triangular, and tiny. About 25 x 6 mm pubescent petals are present on both sides. When mature, the globose fruits break easily and have a glaucous bloom on the surface. They are yellowish-green in color. The silky, brownish-black seeds.

B. Ecology:

Sitaphal is found throughout the tropics. Trees thrive in hot, dry regions; at 30˚C, seedlings exhibit significant levels of photosynthetic activity. Pollination is enhanced by a minimum temperature of 25˚C and a high relative humidity of 70%. For custard apples, a pH of 6 to 6.5 is ideal.

C. Morphology:

Often referred to as a sugar apple or custard apple, Annona squamosa Linn is a member of the Annonaceae family. An explanation of Annona squamosa's morphology is provided below:

General Structure and Habitat:

- *Type*: Little shrubs or trees that is deciduous.
- *Height*: Usually reaches 3 to 8 meters in height.
- *Bark*: Grayish-brown, thin, and somewhat cracked is the bark's texture.
- *Leaves*:
- *Arrangement*: On branches, they are placed alternately.
- *Shape*: simple, pointed-tipped, lanceolate, or oblong leaves.
- *Dimensions*: 3-5 cm in width and 6-15 cm in length.

- *Color*: Both sides have a smooth texture and range from light to dark green.
- *Surface:* The bottom surface may be somewhat pubescent (hairy), while the upper surface is glabrous (smooth).
- *Aroma:* The leaves have a faintly fragrant scent when crushed.

D. Flowers:

- Blooming alone or in clusters of two to four on the leaf axils.
- Actinomorphic (radially symmetric) and bisexual in structure.
- *Dimensions:* compact, with a diameter of 2-3cm.
- *Petals*: Petals are three greenish-yellow, thick, meaty petals with inner and outer whorls.
- *Sepals:* Three small green sepals attached at the base.
- *Stamens:* Numerous stamens with long anthers and short filaments.
- *Pistils:* The superior ovary consists of many carpals.
- *Blooming Season:* Depending on the location, it often blooms throughout the warmer months.

E. Fruit:

- An aggregate fruit is formed when multiple small individual fruits (syncarp) fuse together.
- *Shape:* 5-10 cm in diameter, ranging from spherical to heart-shaped.
- Several knobby segments cover an uneven surface.
- *Color:* When young, it is green; as it ripens, it turns yellow or brown.
- *Pulp:* A delicious, custard-like, creamy-white pulp is found inside.
- *Seeds:* A large number of 1-2 cm long, dark brown or black seeds imbedded in the pulp.

III. THE ROOT SYSTEM:

- *Type:* Taproot system with outspreading lateral roots.

A. Distribution:

- Found in areas that are tropical and subtropical.
- Prefer places with enough sunshine and soil that drains properly.
- A popular food product, Annona squamosa grows in a range of settings with moderate rainfall, although its shape makes it well-suited to arid circumstances.

B. Cultivation and Habitat:

Custard apple is originated from West Indies and South America. It is commonly cultivated in Thailand and India.

C. Rationale of work:

- Based on past research investigations it has been proved offers various pharmacological effects that are helpful for the body.
- Custard apple leaves have been found to be a popular dietary supplement for the treatment of diabetes, as functional food, and daily tea for boosting digestion, enhancing sleep, and treating diabetes.
- Roots are used internally to treat spiritual depression and spinal ailments. Bark is known to be a strong astringent.
- Fruits are regarded a good tonic in Ayurveda because they enrich the blood, act as an expectorant, promote muscular strength, cool the body, reduce burning sensations, increase biliousness, act as a cardiac sedative, and relieve vomiting.
- Ripe fruit is maturing, and the combo, combined with salt, is employed against malignant tumors to accelerate suppuration.
- Almost all plant extracts are practically utilized for treatment & prevention of diseases.

D. Traditional and culinary uses:

Epilepsy, diarrhea, heart problems, worm infestation, constipation, bleeding, fever, ulcers, and antibacterial properties are among the traditional uses of the plant. It also possesses anticancer and ant fertility properties. With seed extract, photochemical, pharmacological, antibacterial, and anti-ovulatory properties have been investigated. Additionally, it has been found that the aqueous leaf extract can help with hyperthyroidism. It has been claimed that ethanolic extract of leaves and stems has anti-cancer properties. Numerous researchers have looked at it and found that it works as an insecticidal agent (JA, 2004) (Bechan Sharma). Annona squamosa leaf extract has

been shown to have hepatoprotective activity (Gauthaman K, 2008). Hypoglycemic anti-diabetic effect (Murthy PS, 2005). and free radical scavenging activity (Kulkarni VR, 2011).It was from this plant that apomorphine alkaloids (16), flavonoids (13), glycosides (17), terpine derivatives, and a new diazepine, squamoline (13), were identified.
According to a review of the literature, no research has been done on the antidepressant properties of Annona squamosa leaf extract. The usage of natural medications is growing in popularity. The purpose of this study is to assess the antidepressant properties of Annona squamosa leaf extract.

E. Initial photochemical examination of plant extracts:
Anona squamosa leaf ethanolic extract was tested using standard protocol for the presence of phytoconstituents such as alkaloids, tannins, glycosides, flavonoids, and saponins, among others described by Jeevalatha *etal.* (2022) (Loganathan T, 2022).

Clitoris ternatea belonging to Fabaceae family and the Papilionaceous subfamily. This perennial leguminous plant grows as vines or creeper in tropical climates, bearing deep roots and elliptic to obtuse leaves. Some of its flowers are white toblue. It is propagated by seed and produces significant yields in a short amount of time following grazing, with great regrowth. Many naturally occurring antioxidants and bioactive components, including phenolics, flavonoids, cyan pigments, flavanol glycosides and kaempferol glycosides, flavanol glycosides, terpenoids, myricetin with glycosides, tannins, and steroids, are present in the flower. The potential of these substances to combat oxidative stress there has beenwell investigated. The root part of the CT has been used as an anthelmintic, laxative, purgative, a diuretic inflammation, constipation, urinary tract infections, and fever, arthritis, and eye conditions.

F. Test for ferric chloride and phenol:
3 ml of distilled water and a few drops of a 10% aqueous ferric chloride solution were added to 1 ml of the extract. Green color formation is a sign that phenols are present.

G. Look for flavonoids - Shinoda examination:
1 ml of a 1% ammonia solution was added to 2 ml of the extract. When flavonoids are present, they appear yellow in color.

H. Do a Tannin Test - The ferric chloride test:
1 ml of 0.008 M potassium ferricyanide and 1 ml of 0.02 M ferric chloride with 0.1 N HCl were added to 1 ml of the extract. A blue-black appearance suggests the presence of tannins

I. Check for saponins - Test of foam:
Five milliliters of distilled water and two milliliters of crude extract were combined in a test tube and shaken vigorously. Pour in a few drops of olive oil. The development of steady foam is seen as a sign that saponins are present.

J. Tannin detection test - Ferric chloride test:
To 1 ml of extract, 1 ml of 0.008 M potassium ferricyanide was added, followed by 1 ml of 0.02 M ferric chloride containing 0.1 N HCl. The presence of tannins is indicated by the appearance of blue-black.

K. Examine for saponins - Foam tests:
In a test tube, 2mL of crude extract was combined with 5mL of distilled water and forcefully shaken. Add a couple of drops of olive oil. Stable foam development is thought to indicate the presence of saponins

IV. PHARMACOLOGICAL ACTIVITIES:

A. Antioxidants and Anti-lipidemic activity:
The substances known as antioxidants and anti-lipidimic activity are in charge of shielding living things from harm brought on by the aberrant generation of reactive oxygen species, which also causes lipid per oxidation, protein degradation, DNA strand breakage, and other issues. According to ethno medical research, there are several plants, such as Annona squamosa, that can be used to treat diabetes, a condition in which free radicals and ROS are crucial. The lipid profile and antioxidant enzymes of animal models of type 2 non-insulin-dependent diabetic mellitus (NIDDM) were assessed in relation to the aqueous extract of Annona squamosa leaves. Reduced glutathione (GSH), catalase (CAT), superoxide dismutase (SOD), and enhanced

scavenging enzyme activities were the characteristics taken into consideration as the assessment of the aforementioned activities. Several tissues showed substantial reductions in malondialdehyde levels together with decreased glutathione (GSH), glutathione reductase (GR), and glutathione-stransferase (GST). Comparing the treated diabetic rats to the untreated diabetic rats (control), the aqueous extract of Annona squamosa markedly decreased the triglyceride and total cholesterol levels while gradually raising the HDL cholesterol level. It has been discovered that these modifications help to enhance lipid metabolism in diabetics (Achyut Narayan Kesari, 2008).and reduce diabetes complications.

B. Analgesic and Anti-inflammatory activity:

The analgesic and anti-inflammatory properties of caryophyllene oxide, which was extracted from an unsaponified petroleum ether extract of Annona squamosa bark, were investigated. Significant central and peripheral analgesic and anti-inflammatory action was seen for caryophyllene oxide at dose levels of approximately 12.5 and 25 mg/kg body weight and unsaponified petroleum ether extract at dosage levels of around 50 mg/kg body weight. A dosage-dependent and statistically significant analgesic effect was induced by caryophyllene oxide. Additional pharmacodynamic studies were necessary to comprehend the anti-inflammatory and analgesic properties of caryophyllene oxide (Wakte PS, 2010).

C. Anti-bacterial and cytotoxic activity:

Petroleum ether extract (PE), CHCl3 extract (CE), EtOH extract (EE), annotemoyin-1, annotemoyin-2, squamocin, and cholesteryl glucopyranoside are examples of plant compounds that exhibit antibacterial and antifungal properties. They exhibit the greatest inhibition of gram-positive organisms, including B. subtilis, B. cereus, B. megaterium, Staphylococcus aureus, S. b-haemolytica, and Sarcina lutea, while gram-negative organisms, including E. coli, S. dysenteriae, S. shiga, S. flexneriae, S. sonnei, Salmonella typhi, P. aeruginosa, and Klebsiella spp. The LC50 values of the petroleum ether and chloroform extracts were computed (Mukhlesur Rahman M, 2004).and the cytotoxicity of the plant extracts was investigated using the brine shrimp lethality assays.

D. Anti-Ulcer activity

Peptic ulcers, which are mostly caused by stomach lesions that arise when a delicate balance between specific gastro protective and aggressive substances is upset, affect a great number of individuals globally. Proton pumping H+ K+ ATPase is the primary source of uncontrolled hydrochloric acid secretion, a pathological condition known as excessive stomach acid output. Models of stomach ulcers brought on by alcohol (AL), histamine (HA), pyloric ligation (PL), cold restraint (CRU), aspirin (ASP), and alcohol (PL) were utilized to evaluate the plant extract's anti-ulcer qualities. An in vitro test of H+K+-ATPase activity and plasma gastrin level was subsequently performed on these animals to validate the extract's anti-ulcer qualities. shown anti-secretary efficacy in vivo with a reduction in plasma gastrin level and inhibited the development of ulcer in the CRU, PL, and HA models. With protection in AL and ASP models and an increased mucin content in PL, Annona squamosa demonstrated cytoprotection. N-methylcorydaldine, lanuginosine, and (+)-Omethylarmepavine were identified as the plant's active principles. These might be the starting point for the development of new synthetic and semi-synthetic chemicals that will be used as antiulcer medicines in the future (Rakesh Maurya, 2011).

E. Hypoglycemic and anti-diabetic activity:

Diabetes has been treated orally with a variety of medicinal herbs or their preparations since ancient times. Compared to other synthetic hypoglycemia oral medications, these herbal therapies have been proven to be less expensive and to have no negative side effects. When given orally to both normal and streptozotocin (STZ)-induced diabetic rats and alloxan-induced diabetic rabbits at varying doses, the ethanolic extract of Annona squamosa leaves demonstrated that a dose of 350 mg/kg body weight decreased the fasting blood glucose (FBG) level by 6.0% and the peak blood glucose during the glucose tolerance test (GTT) by 17.1% in the normal rats. The FBG level was lowered by 26.8% with the same dosage of the ethanolic extract**.** It also increased the animals' glucose tolerance by 38.5 and 40.6% during the GTT in rabbits with alloxan-induced diabetes. Rats with STZ diabetes showed improvements in glucose tolerance of 37.2 and 60.6% during GTT (Geeta Watal, 2005) [23] and a 13.0% decrease in

FBG. Similarly, the ant diabetic activity of an aqueous extract of Annona squamosa L. roots at 250 and 500 mg/kg body weight was evaluated in rats with hyperglycemia induced by streptozotocin (STZ), which lowers blood glucose levels in STZ-induced diabetic rats from 285.52 to 208.81 mg/dl (Khan, 2009).

F. Anti-tumor activity:

Asimicin18, squamocin18, squamocinD18, desacetyluvaricin18, isodesacetyluvaricin18, squamostatin-D18, squamostatin-E18, squamostatin-B18, squamostatinA18, 12, 15cisquamostatinA19, 4deoxyannoreticuin20, and cis-4-deoxyannoreticuin20 were evaluated for their ability to suppress the growth of cancer cell lines using the MTT method. The findings demonstrated that, regardless of whether the investigated compounds had nonadjacent bis-THF ACGs or bis-adjacent THF ACGs, the stereo chemical factor should be considered an essential element for their potent action. The ACGs with the S configuration at C24 showed higher selective cytotoxicity than the ACGs with the R configuration at C24. Strong growth-inhibiting capabilities have been demonstrated by ACGs against a range of tumor cell lines, including several drug-resistant (MDR) tumor cell lines. As a result, ACGs might be considered promising. Consequently, ACGs may be regarded as a potential anticancer candidate for upcoming therapeutic use (Jianwei Chen, 2009).

G. Hepatoprotective activity:

For the treatment of liver toxicity, natural therapies made from medicinal plants are regarded as a safe and efficient substitute. To investigate its potential use in treating hepatotoxicity in humans, the hepatoprotective efficacy of Annona squamosa's alcoholic and water extract was assessed in rats that had been given hepatotoxic treatments. According to the experimental investigation, Annona squamosa extracts could only lessen the effects of isoniazide and rifampicin on the liver, but they were unable to totally reverse the hepatic damage caused by these medications. The antioxidant action of the flavonoids found in Annona squamosa leaves may be the source of their protective function (21)**.** Rats were used to test the protective impact of the methanolic extract of Annona squamosaon isoniazid-rifampicin-induced hepatotoxicity, and it was discovered that the rats also showed a protective effect against liver injury (Gauthaman Karunakara, 2011).

V. CONCLUSION

An ethanolic extract of Annona squamosa leaves was subjected to a preliminary photochemical study, which verified the existence of the flavonoid component rutin and identified alkaloids, flavonoids, tannins, phenols, and triterpenoids. The ethanolic extract of Annona squamosa leaves revealed the presence of several photochemical, with rutin (a flavonoid component) being the one responsible for the analgesic effect of Annona squamosa, according to the observational record of our current study project.

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