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TRADITIONAL USES OF *ANNONA SQUAMOSA* –A REVIEW

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ABSTRACT

Natural remedies and alterative medication 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* is the best example of it. The leaves are used as a vermicide, for treating cancerous tumors and are applied to abscesses, insect bites and other skin complaints. The fruit of this plant is commonly known as custard apple which is eatable. Powdered seeds are used to kill head-lice and fleas but care should be taken that the powder does not come in contact with the eyes as this causes great pain. Scrapings of root-bark are used for toothache. This review article is a sincere effort to put traditional uses of *Annona squamosa*.

Keywords: *Annona squamosa*, custard apple, traditional uses.

INTRODUCTION

Annona squamosa L. (*Annonaceae*), commonly known as the custard apple tree is a native of West Indies. But the cultivation is present throughout India, because of its edible nature. It is a fruit tree considered as a native of Central America also and hence have a wider cultivation throughout the regions of tropics. The taste of the pulp of the fruit is really sweet because of its higher sugar content of about 58% of dry mass, and hence it is found clear that the fruit pulp possess a high calorie value. This plant was reputed to contain several medicinal properties [1].

Scientific Classification:

Kingdom : Plantae – Plants

Division : Magnoliophyta – Flowering Plants

Family : Annonaceae, Custard apple

Family Genus : *Annona* L – *Annona*

Species : *Annona squamosa* L – Sugar apple

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Plant of *Annona squamosa* *Annona squamosa* fruit and seeds

Plant of *Annona squamosa*



***Annona squamosa* fruit and seeds**



Traditional uses of *Annona squamosa*

The plant is traditionally used for the treatment of dysentery, epilepsy, cardiac problem, constipation warm infection, hemorrhage, antibacterial infection, dysuria, fever constipation and ulcers. It also has anti fertility, anti tumor and abortifacient properties [2-5] . In Ayurveda, Fruits are considered as a good tonic, enriches food, used as an expectorant, increases muscle strength, cooling, lessens burning sensation and tendency to biliousness, sedative to heart and relieves vomiting. Ripe fruit mixture along with salt is used against malignant tumours to hasten suppuration. Dried unripe fruit is used to destroy vermin Seeds are used as an abortifacient and good to destroy lice in hair in Unani medicine. Seeds are powerful irritant of conjunctivitis and produce ulcers in the eye. Leaves are used as polutice over boils and ulcers and also to kill lice. The whole tree is a good source of fire wood [6] Roots are traditionally used as a purgative [7] .

Antiulcer activity

Peptic ulcer is a disease that affects a 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 .Increased 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⁺-ATPase. 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. The plant and its chloroform and hexane fraction attenuated the formation of ulcer in CRU, PL, HA model and also displayed anti-secretory activity in vivo with the decrease in plasma gastrin level. Cytoprotection of *Annona squamosa* was apparent with protection in AL, ASP models and enhanced mucin level in PL. (+)-Omethylarmepavine, N-methylcorydaldine, lanuginosine, were found to be the active principles of the plant which may serve as the initial point for the designing of novel semi-synthetic and synthetic compounds as the antiulcer agents in the future [8] .

CNS

Plant is traditionally used in the treatment of CNS disorder epilepsy. Chemical constituent Corydine, Magnine shows CNS depressant activity, Borneol, Camphor, Reticulline act as an CNS Stimulant .One of the active constituent Tryptophan possess antimanic, antidepressant property, Thiamine possess anti alzimer activity[9] . Studies revealed that *Annona squamosa* is potentially used in Parkinsonian diseases .Hydroalcoholic extract of *Annona squamosa* shows neuroprotective effect against 6-

hydroxydopamine induced Parkinsonian disease at a dose of 200 and 400 mg/kg and significantly increase the dopamine level [10].

Blood and Haemopoetic tissue

Fruits of *Annona squamosa* is considered as a good tonic to enriches the blood [11]. Anti diabetic It has been shown through research that *Annona squamosa* exhibit potential antidiabetic activity. Oral administration of hot water extract of leaves of *Annona squamosa* at a dose of 350 mg/kg body weight reduce the fasting blood glucose level by 6.5% in the STZ induced diabetes rats. The same dose shows significant reduction in Fasting Blood Glucose level by 24.4% in alloxan induced diabetes rabbits. It seems to act by enhancing insulin level from pancreatic islets, increasing the utilization of glucose in muscle and inhibition of glucose output from live. Water extract inhibit the activity of glucose 6phosphatase in isolated rat microsomes. *Annona squamosa* act more than site pancreas, muscle and intestine. The margin of safety is also high [12].

It has been observed through various literatures that the Antidiabetic effect of *Annona squamosa* leaf extract is possibly mediated through the insulin stimulating and free radical scavenging properties of its active constituents Quercetin-3-O-glucoside[13].Streptozotocin inhibit the free radical scavenging enzymes causing β cell cytotoxic effect .It has also been observed that young leaves of the plant contain phenol and flavonoid which possess an antioxidant and free radical scavenging ability. Antihyperglycemic activity of the plant may be due to the antioxidant activity of phenol and flavonoid which reduces β cell cytotoxicity and restores the β cell.

Reduced glutathione is a potent free radical scavenger GSH within the islet of β cell and is an important factor against the progressive destruction of the β cell following partial pancreatectomy .Depletion of GSH result in enhanced lipid per oxidation. This can cause increased GSH consumption and can be corelated to the increase in the level of oxidized Glutathione (GSSG).Treatment with *Annona squamosa* resulted in elevation of GSH levels which protect cell membrane against oxidative damage by regulation the redox status of proteins in the membrane [14]

Anthelmintic activity

Among the gastrointestinal nematodes, *Haemonchus contortus* is found to be the most frequent and pathogenic species that causes the high mortality rate in young animals mainly during the rainy season. Synthetic anthelmintics are often used to reduce the above losses. *Annona squamosa* seed powder is used against the insects in Northeast of Brazil due to the presence of active substances with parasitocidal effects. The anthelmintic activity of the extracts and the isolated compounds of *A. squamosa* seeds were evaluated on the egg hatching of *H. contortus*. Compound one which was isolated from the

ethyl acetate extract inhibited the egg hatching of *H. contortus* at the concentration of about 25 mg/ml and the structure of compound one was determined as a C37 trihydroxy adjacent bistetrahydrofuran acetogenin by the spectroscopic analysis [23]. The anthelmintic activity of the *Annona squamosa* seed extract against the adult earthworm, *Pheritima posthuma* was also investigated and was found that the methanolic extract showed the effective anthelmintic activity causing the death of earthworms [15].

Liver and Biliary system

Leaves of the plant are used in sub acute cases of liver. Further studies reported that Alcoholic and water extract of leaves shows potential hepatoprotective activity in rats [16]. It has been clinically demonstrated that administration of methanolic extract of *Annona squamosa* at a dose of 250 and 500 mg/kg significantly prevented the isoniazid-rifampicin induced elevation in level of serum marker enzyme, ALT, AST and ALP & γ GT serum bilirubin in rats. The effect of extract was compared with standard drug Silymarin [17]. Studies reported that hepatoprotective effect of the extract may be due the flavonoid component having free radical scavenging activity lead to hepatoprotection so it could be due to anti oxidative effect of flavonoid present in leaf of *Annona squamosa*. Research studies also shows that *Annona squamosa* is potential hepatoprotective drug against diethylnitrosoamine induced liver injury in Swiss albino mice [18].

Anti-malaria

In vitro plant leaf methanol extract exhibited potent inhibition against the chloroquine-sensitive strain 3D7 and chloroquine-resistant strain Dd2 of malignant plasmodium, and the stem skin methanol extract had moderate inhibitory effect against Dd2 [19].

Antitumor activity

Twelve different acetogenins with diverse stereo chemical structures and configurations namely asimicin18, squamocin18, squamocin-D18, desacetylvaricin18, Iso desacetylvaricin18, squamostatin-D18, squamostatin-E18, squamostatinB18, squamostatin-A18, 12,15-cis-squamostatin-A19, 4-deoxyannoreticuin20, and cis-4-deoxyannoreticuin20 were evaluated for their ability to inhibit the growth of cancer cell lines using MTT method which indicated that the stereochemical factor is to be considered as an essential factor for the potent activity of the tested compounds irrespective of their bis-adjacent THF ACGs or the nonadjacent bis-THF ACGs. The ACGs with S configuration at C-24 possessed more selective cytotoxicity than the ACGs with the R configuration at C24. ACGs showed the significant inhibitory activities against the growth of various tumor cell lines and also against the multiple drug resistant (MDR) tumor cell lines.

Thus, ACGs might be considered as a promising antitumor candidates for the future clinical application [20].

Anticancer

As it is known that oxidative stress have been implicated in the pathology of many diseases such as cancer, diabetes, because *Annona squamosa* shows effective antioxidant activity. So it may possess anti carcinogenic property [21]. Extract of *Annona squamosa* fruit pericarp was tested for cytotoxic activity against Dalton's lymphoma cells and He La cells. The chloroform extract was found to be cytotoxic to different cell lines tested and suggested the potential for *Annona squamosa* fruit pericarp for the development of anticancer activity. It has been shown in research in literatures that active constituent Bullatacin possess anticancer activity in the treatment of breast and kidney [22]. Other phytochemical that have been documented with antitumor activity are Limonene, Liridenine, β -carotene, citric acid, corydiene, mallic acid and tannin [23]. There has been no dearth of scientific literature that genotoxic agents have a causative effect in the pathogenesis of carcinomas. 7,12-dimethylbenz (a) anthracene (DMBA) which is, a potent organ specific carcinogen has been found to produce mutagenic effects on cells. *Annona squamosa* has a long history in traditional Indian medicine for being used to treat several diseases including cancer. Genotoxicity was induced in golden Syrian hamsters by single intraperitoneal injection of DMBA (30 mg/kg body weight). The antigenotoxic effect of aqueous and ethanolic bark extracts of *Annona squamosa* was assessed by determining the frequency of micro nucleated polychromatic erythrocytes (MnPCEs) and chromosomal aberrations. The frequency of MnPCEs and chromosomal aberrations in bone marrow were higher in DMBA treated animals as compared to control animals [24]. Oral administration of aqueous and ethanolic bark extracts significantly reduced the frequency of MnPCEs and chromosomal aberration in DMBA treated hamsters. Although both extracts have shown antigenotoxic effect, the effect of ethanolic extract was found to be more prominent than the aqueous extract. The functional groups of Annonaceous acetogenins include the terminal lactone ring and the tetrahydrofuran ring, which could inhibit cell energy metabolism by inhibiting the respiratory chain of cellular mitochondria. Annonaceous acetogenins could inhibit cancer cell growth, but at the same dose, could not inhibit the growth of non-cancer cells [25]. In vivo and in vitro Annonaceous acetogenins had antitumor effects against leukemia, liver, prostate, pancreatic, and cervical carcinoma, with the constituent polyphosphorus bullatacin G having the most potent activity. In cell growth inhibition experiments, in vitro Annonaceous acetogenins and polyphosphorus bullatacin G had potent anti-tumor effects against larynx and breast cancer cells in human. In addition, Annonaceous acetogenins also inhibited mitochondrial NADH oxidoreductase and the transmission of the

respiratory chain of mitochondria, resulting in the rapid decrease of cell energy, causing function loss of P-glycoprotein, overcoming multidrug resistance (MDR) [26].

Antioxidant activity

For the study of antioxidant activity the leaves extract were used. The chemical constituent were isolated and was subjected to IR, LC-MS and the compound was confirmed flavones type compound on the basis of spectral data. The in vitro antioxidant activity of isolated compound *Annona squamosa* L was evaluated by free radical scavenging activity of different concentrations (10µg, 50 µg, and 100 µg) using 1, 1-diphenyl-2 picryl hydrazil method (DPPH). The results of assay were then compared with synthetic antioxidant Butylated hydroxyl anisole (BHA).The isolated compound exhibit (9.62, 24.28, and 45.62%) significant free radical scavenging activity [27].

Anti HIV

There was a positive result exhibited by the extract of *Annona squamosa* when evaluated for anti HIV screening. In the above study new chemical compound have been named and isolated. The structures of the new compounds were established by spectral analyses and chemical evidence. Among the 14 isolated compounds in the study , 16β,17-dihydroxy-ent-kauran-19-oic acid showed significant activity against HIV replication in H9 lymphocyte cells with an EC50 value of 0.8 µg/ml [28].

Cytotoxic activity

Two new compounds have been isolated and were evaluated for the above activity. The extract of seed was used for the isolation of the compound. The study was carried out against HCT, human lung carcinoma (A-549), human breast carcinoma (MCF-7), and human prostate adenocarcinoma (PC-3) with Adriamycin as positive standard using MTT method [29].

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Respiratory Diseases

The fruits has expectorant properties and used to treat productive cough in India.[30] Alkaloids in the roots has bronchodilatory properties. In Brazil the leaves forms part of a cough remedy syrup [31].

Anti-inflammatory & analgesic activity

Caryophyllene oxide was isolated from the unsaponified petroleum ether extract of bark of *A. squamosa*. This compound exhibit analgesic and anti-inflammatory activities in doses of 12.5 and 25mg/kg body weight. The analgesic activity seems to be both centrally and peripherally mediated. [32] The seeds on the other hand contain cyclic peptides cyclosquamosin A, B, D, E, and H. The compound cyclosquamosin D was found to inhibit the production of pro-inflammatory cytokines within the lipopolysaccharide and Pam3Cys-stimulated J774A.1 macrophages. [33, 34] isolated 11 ent-kauranes from the stem of *A. squamosa* which showed immunomodulating effects in leukocytes. In another study they isolated 16β,17-dihydroxy-ent-kauran-19-oic acid. This compound show antioxidant along with anti-inflammatory activities. [35]

Warning:

Pregnant women should not eat Sugar apple as it may abort the foetus

CONCLUSION

We concluded from above review studies that *Annona squamosa* is a potential plant in the world. Further studies are required.

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