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A REVIEW ON PHARMACOLOGICAL ACTIVITIES OF ANNONA SQUAMOSA

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Abstract:

Plants have been used widely in traditional medicine by a range of nations since ancient times and more research into their quality, safety, efficacy value is needed. One of the plants that have been used widely by society in traditional medicine is Annona squamosa. The roots, seeds, and leaves of Annona squamosa contain many medicional properties like antimicrobial, antifungal, anti-inflammatory, anticancer, antiulcer, antidiabetic, antidiarrheals, antiplatelet, antioxidant, hepatoprotective, neuroprotective and cytoprotective. This review will be definitely useful for the researchers as well as the clinicians dealing with Annona squamosa to know its proper usage,as the plant appears to be highly important due to its medicinal properties.

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INTRODUCTION:

Annona squamosa is also known as custard apple belongs to the family Annonaceae family.The genus 'Annona' came from the latin term 'anon' which means 'annually produce'.It grows well in many parts of the world which includes Asia,Africa,Australia & America.It can grow upto 3-8m tall & is a subtropical small deciduous spreading tree with large green dropping leaves,trumpet shaped light yellow flowers and a cone shaped fruit.

This review covers the pharmacological aspects of different parts of Annona squamosa and biologically active constituents responsible for treatment potentials.

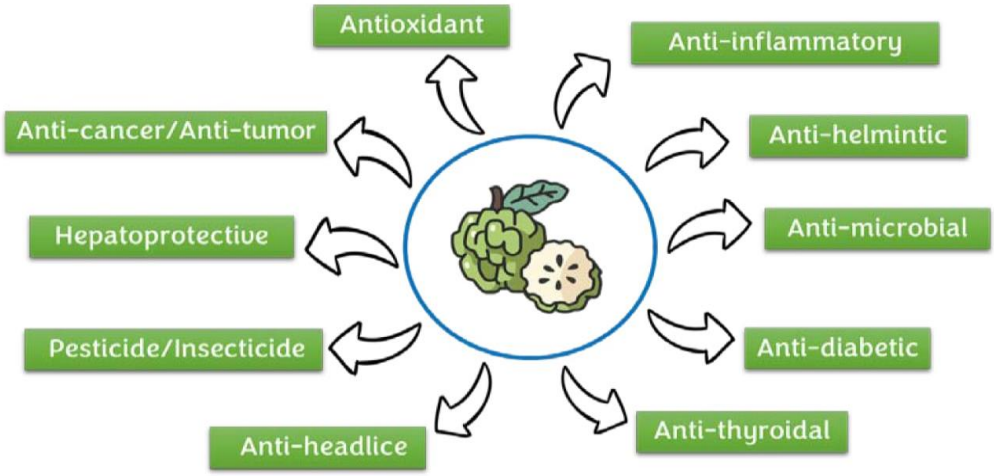
Taxonomical characterization:

Kingdom	**Plantae**
Subkingdom	Tracheobionta(vascular plants)
Superdivision	Spermatophyta(seed plants)
Division	Magnoliophyta(flowering plants)
Class	Magnoliopsida(dicotyledons)
Subclass	Magnoliidae
Order	Magnoliales
Family	Annonaceae(custard apple family)
Genus	Annona
Species	squamosa

Chemical composition of Annona squamosa:

PLANT PARTS	**CHEMICAL COMPOSITION**
Seeds	Annonastatin,asimicin,squamocin,essential oils like β farnesene,β-pirene,α pirene,limorene etc.
Roots	Liriodenine,norcorydine,isocorydine,norushinsunine etc.
Bark	Acetogenins like 4-deoxyannoreticuline,annoreticuline-9,annosquamosins A,B cyclopeptide, squamone, squamotacin, 2,4 cis and trans squamoxinone.
Leaves	Alkaloids like Aporphine,roemerine,norisocoryline etc, rhamnoside,quercetin-3-o-glucoside
Fruits	Liriodenine,norcorydine,isocorydine,norushinsunine etc.

Pharmacological activities of Annona squamosa:



Antimalarial activity:
→Leaf ethyl extract of Annona squamosa has antimalarial activity against chloroquine sensitive and chloroquine resistant strains of Plasmodium falciparum.N-Nitrosoxylopine,roemerolidine and Duguevalline alkaloids isolated from Annona squamosa leaf extract are responsible for antimalarial properties.
→The bark extract exhibit IC50 of 30µg/ml against blood stage Plasmodium falciparum.
→The all compounds present in Annona squamosa shows moderate antiplasmodial activity against chloroquine resistant strain (Dd2) and chloroquine sensitive strain (D10).

Antioxidant activity:
→Antioxidants are the compounds which inhibits the protection for living organisms from damage which is a manifestation of uncontrolled Reactive oxygen species(ROS) production.
→Antioxidants plays a major role to fight oxidative stress by scavenging free radicals.
→Different parts of Annona squamosa possess antioxidant activity.
→Organic & aqueous extracts Annona squamosa leaves showed dose dependent free radical(1,1 diphenyl-2-picrylhydrazyl,hydrogen peroxide,nitric oxide) scavenging activity and reducing power activity.
→THDMF-Rha(5,7,4' trihydroxy-6,3' dimethoxyflavone 5-O-α- I-rhamnopyranoside) isolated from Annona squamosa leaf extract upon oral admistration reduced cellular oxidative stress and raised antioxidant activities in animal models.
→Quercetin-3-O glycoside isolated from Annona squamosa has antioxidant activity as intake of 15mg/kg/day for 10days significantly raised the activities of catalase,superoxide dismutase and reduced glutathione.
Antiulcer activity:
→The twigs of Annona squamosa contain active constituents that protects peptic ulcer.

» (+)-O-methylarmepavine,N-methylcorydaldine and isocorydine

Anti secretory property

Reduce gastric acidity,pepsin & gastrin level and also inhibits H^+ -K^+ ATPase pump

» Leaf extract of Annona squamosa protective against

Aspirin induced ulcer & pyloric ligation induced ulcers in mice

Antidiabetic activity:
→Annona squamosa plant posses an antihyperglycemic effect(hypoglycemic effect – reduces blood glucose levels).
»Diabetes was induced into male albino wistar rats by using streptozotocin

Oral administration of aqueous extract of Annona squamosa plant in diabetic rat for 30 days

Reduced blood glucose,urea but increased the activities of insulin,c-peptide,albumin and restored all marker enzymes to near control levels

Anti – inflammatory activity:

→Inflammation is the pathological process that involves cellular components and pro inflammatory cytokines which are responsible for the development &progression of various diseases.

→Leaves,bark,seeds & pericarp of Annona squamosa consists of anti-inflammatory chemicals.

»Leaf aqueous extract of Annona squamosa counteracted acetic acid induced colitis in mice by oral treatment with 300mg/kg for a month

Significantly reduced MDA(colonic malondialdehyde),increased GSH(colonic glutathione),GPx(glutathione peroxidase) & CAT(catalase).

»Two new cyclic peptides isolated from the pericarp of Annona squamosa were fanlizhicyclopeptide A&B Diminish the generation of TNF-α and IL-6 in activated macrophages.

»Cyclosquamosin D & Cherimolacyclopeptide B isolated from Annona squamosa seeds .
Inhibits the generation of proinflammatory cytokines such as IL-6 &TNF-α in activated macrophages.

→18-acetoxy-ent-kaur-16-ene & Caryophyllene oxide isolated from Annona squamosa bark exerts analgesic & anti-inflammatory action.

»16β,17-dihydroxy-ent-kauran-19-oic acid isolated from Annona squamosa bark

Inhibits superoxide production & release elastase from activated neutrophils

By inhibition of rapid calcium release from cellular calcium reserve in neutrophils.

Antimicrobial activity:

→Methanolic extract of bark of Annona squamosa possesses the invitro antimicrobial activity against gram positive & gram-negative strains such as Bacillus coagulans and Escherichia coli bacteria.

Antibacterial activity:

→Organisms of food borne diseases like Bacillus cereus, Listeria monocytogenes, Staphylococcus aureus & Campylobacter jejuni are sensitive to leaf extract of Annona squamosa.

→Annona squamosa leaf extract is active against Klebsiella pneumoniae, Streptococcus pneumoniae, Enterococcus faecalis, Staphylococcus epidermis, Vibrio alginolyticus & proteus species.

→Annona squamosa seed extract are active against Pseudomonas aeruginosa & Escherichia coli.

→The bark of Annona squamosa is active against bacteria.

Antifertility activity:

→Ethanol extract of Annona squamosa seed powder was reported to have anti-ovulatory activity in rabbits. when given 200mg/kg seed extract for 2days for rabbits inhibits ovulation per 40%.

→It has abortifacient activity but the seed powder has no effect on pregnancy.

→It exhibited contraceptive action in male rats but on stoppage of the intake of extract the action is reversible.

Wound healing activity:

»Topical application of ethanolic extract of Annona squamosa leaves

Enhances wound healing

By increasing collagen synthesis, glycosaminoglycan synthesis, cellular proliferation at injury sites.
→This evident the ancient topical use of Annona squamosa leaves for wounds.

Anticancer activity:

Seeds

Consists of Squadiolins A&B

High potency against human Hep G2 hepatoma cells & cytotoxic against human MDA-MB231 breast cancer cells.
→Acetogenin squamotacin isolated from the bark of Annona squamosa showed selective cytotoxicity for PC-3 with a potency greater than 100 million times that of Adriamycin.

Antitumor activity:

The effect of aqueous and organic extracts from defatted seeds of Annona squamosa was studied on a rat histiocytic tumour cell line AK-5

Showed significant apoptotic tumour cell death with enhancing caspase -3 activity.

→Some studies like DNA fragmentation & annexin-V staining confirmed that the extract induce apoptosis in tumour cells by means of oxidative stress.
→Aqueous extract of Annona squamosa seeds has antitumor activity invivo against AD-5 tumour.

Insecticidal activity:

→ Botanicals have a high potential as an alternative to synthetic pesticides.

→Due to the presence of ACGs, Annona plant like Annona squamosa have been shown to be promising biological pesticide among tropical plants.
→Annona squamosa showed the strong growth inhibition effect against Chrysanthemum aphis.

Anti-headlice activity:

→Seed extract of Annona squamosa in coconut oil at the ratio 1:2 killed 98% of headlice within 2hours.
→ Antiheadlice activity of leaf extract of Annona squamosa is less potent than the seed extract.

→Active components from Annona squamosa seeds which tools between 30 & 62 min to cause 100% mortality according to the method developed by McCage.

Anti genotoxic activity:

The antigenotoxic effect of aqueous and ethanolic bark extract of Annona squamosa in DMBA induced genotoxicity in golden Syrian hamsters was assessed by determining the frequency of MnPCEs(micronucleated polychromatic erythrocytes) & chromosomal aberrations.Oral administration of aqueous and ethanolic bark extract of Annona squamosa significantly reduced the frequency of MnPCEs & chromosomal aberration in DMBA treated hamsters.

Anti-hyperlipidemic activity:

Aqueous extract of polyherbal formulation of Annona squamosa was administered orally(200mg/kg body weight) into streptozotocin induced diabetic rats for 30days

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Different doses of polyherbal formulation on blood glucose,plasma insulin in diabetic rats were studied & the level of lipid peroxides and tissue lipids were estimated in streptozotocin induced diabetic rats

↓

Effects were compared with tolbutamide

↓

Treatment with polyherbal formulation & tolbutamide resulted in significant decreased in lipid peroxides,tissue lipids & blood glucose and increase in plasma insulin

↓

Showed antihyperlipidemic & antiperoxidative effect

Anti-plasmodial activity:

the antiplasmodial activity of methanolic extract of annona squamosa plant was tested on chloroquine sensitive strain 3d7 & chloroquine resistant strain dd2 of plasmodium falciparum.the methanolic extract of annona squamosa leaves showed high antiplasmodial activity than stem bark extract(moderate activity).

Anti-viral activity:

16 beta ,17-dihydroxy-ent-kauran-19-oic acid extracted from annona squamosa fruit has antiviral activity against hiv replication in h9 lymphocyte cells.

Antifungal activity:

→Annona squamosa has antifungal activity against Alternaria alternate, Candida albicans,Fusarium solani,Microsporum canis &Aspergillus niger.

→The active anti-fungal constituents of leaves are 16-hentriacontanone(palmitone) & 10-hydroxy-16-henriacontanone.

→The antifungal chemicals present in seeds are squamocin A&G.

Anti thyroid activity:

THDMF-Rha(5,7,4' trihydroxy-6,3' dimethoxy-flavone 5-O-α- I-rhamnopyranoside) isolated from Annona squamosa leaves has shown anti thyroid activity.

→Oral administration of THDMF-Rha into rats shown diminished I-thyroxine-induces thyrotoxicosis.

Hepatoprotective activity:

→Methanol extract of Annona squamosa leaves was found to hepatoprotective against isoniazid-rifampicin induced hepatotoxicity.

→Annona squamosa leaf extract was found to be hepatoprotective against CCL-4 induced hepatotoxicity.

Immunomodulatory activity:

Annona squamosa bark contains Linuginosine (+)-O-methylarmepavine,Lanuginosine (+)-anomuricinem,Isocorydine & N-methyl-6,7-dimethoxyisoquinolone which can modulate immune response by induction of T&B cells to proliferate,stimulation of macrophages,upregulation of CD4+,CD8+ & CD19+ cell population and stimulation of IL-2 & IFN-Y production.

Vasorelaxant activity:

Cyclosquamosin B isolated from Annona squamosa seeds possesses vasorelaxant activity through inhibition of calcium release from extracellular compartment via voltage gated calcium channels. The therapeutic potential of cyclosquamosinB is currently under investigation.

Cytotoxic activity:

→The aqueous extract of defatted seeds of Annona squamosa were tested for
antitumoural activity by testing on different human tumour cell lines.

Aqueous extract of defeated seeds of Annona squamosa was induced in MCF-7 & K-562 cells

Induced Apoptosis by nuclear condensation, DNA fragmentation, induction of reactive oxygen species (ROS) generation, reduced intracellular glutathione levels.

→Aqueous extract of deffated seeds of Annona squamosa failed to induce apoptosis in COLO-205 cells.

→The aqueous extract of Annona squamosa selectively induces apoptosis in certain types of cancerous cells.

Reno protective activity:

→Aqueous leaf extract of Annona squamosa has proved to have renoprotective activity.

→300mg/kg of aqueous extract of Annona squamosa taken orally for one month significantly restored the previously raised urea,creatinine and uric acid levels in streptozocin-induced diabetic rats and also increases superoxide dismutase activity.

Anti atherogenic activity:

→ The fresh fruit pulp of Annona squamosa can modify the plasma lipids which may show beneficial effects for cardiovascular diseases.

→Oral administration of 5g/kg body weight reduced total cholesterol by 45 to 46% in healthy animal & 32.4% in alloxan-induced diabetic rabbits.

→The acids present in Annona squamosa stem like Ent-kaur-16-en-19-oic acid and 16alpha-hydro-19-al-ent-kauran-17-oic acid have antiplatelet property which can inhibit the platelet aggregaration process.

Anti diarrheal activity:

→Annona squamosal leaves contain alkaloids, tannins, steroids, flavonoids and saponins.

→Tannins have astringent property that can treat diarrhea and dysentery.

→the aqueous extract of Annona squamosa leaves were effective as antidiarrheal.

CONCLUSION:

Different parts of Annona squamosa possess many pharmacological activities like Antimalarial, Antioxidant, Antiulcer, Antidiabetic , Anti-inflammatory, Antimicrobial, Antibacterial, Antifertility, Wound healing , Anticancer, Antitumor, Insecticidal, Anti-headlice,Anti genotoxic, Antihyperlipidemic, Antiplasmodial, Antiviral, Antifungal, Antithyroid, Hepatoprotective, Vasorelaxant, Immunomodulatory, Cytotoxic, Reno protective, Antiatherogenic, Antidiarrheal properties. The isolation and identification of the active chemical constituents have put forward the pharmacological and medicinal importance of Annona squamosa.

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