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Review Paper

Phytochemical and Pharmacological Review on *Annona squamosa* Linn

Neha Pandey*, Dushyant Barve

T.I.T. College Of Pharmacy, Anand Nagar, Bhopal (M.P)

ABSTRACT

Plants been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. *Annona squamosa Linn* is a multipurpose tree with edible fruits & is a source one of the medicinal & industrial products. *Annona squamosa Linn* is used as an antioxidant, antidiabetics, hepatoprotective, cytotoxicactivity, genetoxicity, antitumour activity, antilice agent. It is related to contain alkaloids, carbohydrates, fixed oils, tannins & phenolic. A review of chemical constituent present in various parts of *A.squamosa Linn* & their pharmacological actions in given in the present article.

Keywords:- *Annona squamosa Linn* phytochemical constituent, pharmacological actions, toxicity.

INTRODUCTION

According to the WHO survey 80% populations living in the developing countries rely almost exclusively on traditional medicine for their primary health care needs. Exploration of the chemical constituents of the plants & pharmacological screening may provide us the basis for developing the leads for development of novel agents. In addition, herbs have provided us some of the very important life saving drugs used in the armamentarium of modern medicine. However among the estimated 250,000-400,000 plant species, only 6% have been studied for biological activity and about 15% have been investigated phytochemically (1,2). This shows a need for planned activity guided phyto-pharmacological evaluation of herbal drugs.

Annona squamosa Linn is a small ever green tree is cultivated throughout india for its fruits, different parts of *Annona squamosa Linn.* are used in folkloric medicine for the treatment of various disease (3). This plant is commonly called custared apple in english & sharifa in hindi & sitaphalam in telgu in india (4). Annona squamosa linn. is an a shrub or small tree 7 m hight & is cultivated throughout india. This article intends to provide an overview of the chemical constituents present in various parts of *Annona squamosa Linn* & their pharmacological actions (5).

GENERAL INFORMATION:-

Annona squamosa Linn, belonging to family *Annonaceae* is commonly found in India & cultivated in Thailand & originates from the West Indies & south America. It is mainly grown in gardens for its fruits & ornamental value.

It is known as custard apple, sugar apple, sweet après in english, & sharifa in hindi & sitaphalam in telugu in india & corossolier & cailleux, pommier cannelle in french (5).

It is considered beneficial for cardiac disease, diabetes hyperthyroidism & cancer. The root is considered as a drastic purgative(4). An infusion of the leaves is considered efficacious in prolapsusani of children, the crushed leaves are sniffed to over come hysteria & fainting spells, they are also applied on ulcer & wounds. The ripe fruits of this plant are applied to malignant tumors to hasten suppuration. The dried unripe fruit powder is used to destroy vermin The seeds are acrid & poisonous . Powdered seeds serve as fish poison and insecticides . A paste of seed powder has been applied to the head to kill lice. It is also used for destroying worm in the wound of cattles (6).

PHYTOCHEMICAL EVALUATION

The plant is reported to contain glycoside, alkaloids, saponins, flavonoids, tannins, carbohydrates, proteins, phenolic compounds, phytosterols, amino acids .The various chemical constituents isolated from leaves, stems and roots of the plant including anonaine, aporphine, coryeline, isocorydine, norcorydine, glaucine. Leaves contains 4-(2-nitro-ethyl 1)-1-6-((6-o-β-D-xylopyranosy1-β-D-glucopyranosyl)-oxy)benzene, Anonaine, Benzyltetrahydroisoquinoline, Borneol, Camphene, Camphor, car-3-ene, Carvone, β-Caryphyllene, Eugenol, Farnesol, Geraniol, 16-Hetriacontanone, Hexacontanol, Higemamine, Isocorydine, Limonine, Linalool acetate,

***Address for correspondence:**
E-mail: gauripanday@yahoo.co.in

Menthone, Methyl anthranilate, Methylsalicylate, Methylheptenone, p-(hydroxybenzyl)-6,7-(2-hydroxy,4-hydro)isoquinoline, n-Octacosanol, a-Pinene, b-Pinene, Rutin, Stigmasterol, β-Sitosterol, Thymol and n-Triacontanol. Alkaloids ,proteins & amino acids are absent in the leaf extract (7).

The volatile constituents of *Annona squamosa.Linn*. bark were identified from the essential oil obtained by the steam distillation and studied by GC/MS. The bark contain annonaine, an alkaloid which is found to posses many of the properties. Six major components were identified as 1H-cycloprop(e) azulene(3.46%), germacrene D (11.44%), bisabolene (4.48%), caryophyllene oxide(29.38%), bisabolene epoxide(3.64%) and kaur-16-ene(19.13%). The oil was also screened for its antimicrobial activity which exibited a significant antimicrobial activity against Bacillus subtills & staphylococcus aureas (8). Isolation of about 30 acetogenins from the seeds of *A.squamosa Linn* .eg Squamocins B toN, Coumarinoligans. Annotemoyin-1, Annotemoyin-2, squamocin & cholesteryl, glucopyranoside are isolated from the seeds of *A.squamosa Linn* These compounds shows remerkable antimicrobial & cytotoxic activities (9). Roots contain an essential oil(0.15%) ;β caryophyllene ,α pinene, α-humulene, α gurjunene. Chloroform extract of the plant *A.squamosa Linn* contain a active constituents Annotemoyin. Flavonoids isolated from aqueous extract of *Annona squamosa Linn.* has been showed antimicrobial activity. Bullatacin is one such compound that possessed antitumoral and pestici dal activity in vitro. The ethanolic extract of leaves and stem is reported to have anticancer activity (4). There are some of the chemical constituents of pharmacological importance are presented in table 1.

PHARMACOLOGICAL INVESTIGATION

Antibacterial Activity:-

The antibacterial screening by agar cup method indicates that highest zone of inhibition was shown by the methanol extract followed by petroleum ether and aqueous extracts for *Annona squamosa* leaf. Extracts of *Annona squamosa* inhibited the growth of all test strains except Salmonella typhimurium. Aqueous extracts showed less activity than methanol extracts possibly because i) the same active substances were present in water extracts, but in low concentrations ii) active substances were soluble in organic solvents and therefore, not present in water extracts . The antibacterial action of the extracts is more pronounced on Gram-positive than on Gram-negative bacteria, and these findings correlate to the observations of previous screenings of medicinal plants for antibacterial activity . Bacillus subtilis, Staphylococcus epidermidis, Staphylococcus aureus and Vibrio alginolyticus were the most sensitive bacterial strains in the present experiments. Annona squamosa had strong antibacterial activity against these bactirial stains. (10).

Antidiabetic Activity :-

The present work has detected the antidiabetic activity of A. squamosa root extract in STZ-induced hyperglycemia in rats. STZ induced diabetes mellitus and insulin deficiency lead to increased blood glucose level. When A. squamosa root extract was administered to diabetic rats, hypoglycaemia was observed after 2 hrs, with the maximum effect being seen at 6 h.From the results it is assumed that the root extractcould be responsible for stimulation of insulin release and observed restoration of blood glucose level. Further, the observed decreased blood glucose lowering effect of the extract in STZ- induced diabetic rats could also possibly be due to increased peripheral glucose utilization. It has been reported that using medicinal plant extract to treat STZ-induced diabetic rats results in activation of ß-cells and insulinogenic effects.

The antihyperglycemic activity of the Aq. extract of Annona squamosa roots was comparable with glibenclamide, a standard hypoglycaemic drug.(11). The ethanolic extract of *Annona squamosa Linn* leaves posses considerable hypoglycemic activity in normal rats. The dose of 350 mg/kg body weight reduced the fasting blood glucose level by 6.0% within 1 h, whereas, the peak blood glucose at 1 h during glucose tolerance test was reduced by 17.1% in normal rats. Treatment of alloxan-induced diabetic rabbits for 15 days with a dose of 350 mg/kg of extract reduces fasting blood glucose by 52.7 % and urine sugar by 75%. The dose of 350 mg/kg body weight of ethanolic extract in 10-day treatment of a group of STZ-diabetic rats produced 73.3% fall in FBG level and no sugar was observed in fasting urine. (31). An aqueous extract of *A. squamosa* leaves found to lower considerable fasting plasma glucose level in streptozotocin-nicotinamide induced type 2 diabetic rats. The findings of the study support the antidiabetic claims of *A. squamosa*.(32).

Anti Genotoxic Agent:-

The antigenotoxic effects of aqueous and ethanolic bark extracts of Annona squamosa was assessed by determining the frequency of micronucleated polychromatic erythrocytes (MnPCEs) and chromosomal aberrations. The frequency of

MnPCCs and chromosomal aberrations in bone marrow were higher in DMBA treated animals as compared to control animals. Oral administration of aqueous and ethanolic brark extracts significantly reduced the frequency of MnPCEs and chromosomal aberration in DMBA treated hamsters. Although both extracts have shown antigenotoxic effects, the effects of ethanolic extract was found to be more prominent than the aqueous extract. The present study thus demonstrate the antigenotoxic effects of Annona squamosa brak extracts in DMBA induced genotoxicity in golden Syrian hamsters.(12).

Antihyperlipidemic Activity:-

This study shows the effect of Polyherbal formulation of Annona squamosa on blood glucose, plasma insulin, tissue lipid profile, and lipidperoxidation in streptozotocin induced diabetic rats. Aqueous extract of Polyherbal formulation of Annona squamosa was administered orally (200 mg/kg body weight) for 30 days. The different doses of Polyherbal formulation on blood glucose and plasma insulin in diabetic rats were studied and the levels of lipid peroxides and tissue lipids were also estimated in streptozotocin induced diabetic rats. The effects were compared with tolbutamide. Treatment with Polyherbal formulation and tolbutamide resulted in a significant reduction of blood glucose and increase in plasma insulin. Polyherbal formulation also resulted in a significant decrease in tissue lipids and lipid peroxide formation. The decreased lipid peroxides and tissue lipids clearly showed the antihyperlipidemic and antiperoxidative effect of Polyherbal formulation apart from its antidiabetic effect.(13).

Anti-Head lice effect :-

The present study focused on the separation and identification of the active compounds against head lice from the hexane extract of Annona squamosa L seed Chromatographic ad spectroscopic techniques revelated that two major compounds of the hexane seed extract were oleic acid and triglyceride with one oleate ester. The yields of these compounds were 12.25 % and 7.74 % dry weight respectively . The compounds were tested in vitro againt head lice. comparing to the crude hexane of tahe seed . The triglycride with one oleate ester and the crude hexane extract diluted with coconut oil 1.1 .These compounds were found to kill all tested head lice in 49,.11 and 30 minutes respectively. The triglyceride ester can be used as a marker for quantitative analysis of the active compound for quality control of the raw material A. squamosa seed and its extract. This first finding will be useful for quality assessment and the chemical stability of the anti head lice preparation from this plant.(14).

Antimicrobial activity :-

Four different solvent extracts of leaves of Custard apple (Annona squamosa L.) were studied for its antibacterial activity. Agar diffusion method was selected to check antibacterial activity. Two Gram positive (Staphylococcus aureus and Bacillus subtilis) and two Gram negative (Escherichia coli and Pseudomonas aeruginosa) bacteria were selected for screening. The screening results showed that highest zone of inhibition was observed in methanol extract against Ps. aeruginosa(MIC: 130µg/ml) followed by petroleum ether extract against Ps. aeruginosa (MIC: 165 µg/ml) and methanol extract against E. coli (MIC: 180 µg/ml). phytochemical studies showed that Linalool, Borneol, Eugenol, Farnesol, and Geraniol present in extracts which provide antibacterial activity.A.squamosa contains flavonoids which expoes strong antibacterial activity.Volatile compound of this plant were also stuied for its antibacterial activity.(7).

Antioxidant – Activity:-

The free radical scavenging potential of the leaves of *A. squamosa Linn* was studied by using different antioxidant models of screening. The ethanolic extract at 1000 microg/ml showed maximum scavenging of the radical cation, 2,2-azinobis- (3-ethylbenzothiazoline-6-sulphonate) (ABTS) observed upto 99.07% followed by the scavenging of the stable radical 1,1-diphenyl, 2-picryl hydrazyl (DPPH) (89.77 %) and nitric oxide radical (73.64%) at the same concentration. However, the extract showed only moderate scavenging activity of superroxide radicals and antilipid peroxidation potential, which was performed using rat-brain homogenate. The findings justify the antioxidant activity of *A. squamosa*.(33), (34).

A study was carried to analyse the antioxidant effect of oral administration of aqueous extract of *A. squamosa Linn* leaf on blood glucose, haemoglobin, glycosylated haemoglobin, plasma insulin, antioxidant enzymes and lipid peroxidation in liver and kidney to streptozotocin (STZ)-induced diabetic rats. Oral administration of *A. squamosa* aqueous extract to diabetic rats for 30 days significantly reduced the levels of blood glucose, lipids and lipid peroxidation, but increased the activities of plasma insulin and antioxidant enzymes, like catalase, superoxide dismutase, reduced glutathione and glutathione peroxidase. It conclude that the *A. squamosa* aqueous extract supplementation is useful in controlling the blood glucose level, improves the plasma insulin, lipid metabolism and is beneficial in preventing diabetic complications from lipid peroxidation and

antioxidant systems in experimental diabetic rats.(15).

Antitumour Activity

The plant Annona squamosa traditionally known as custard apple possesses potent bioactive principles in all its parts . The effectof aqueous and organic extracts from defatted seeds of A. squamosa was studied on a rat histiocytic tumour cell line AK-5. Both the extracts caused significant apoptoic tumour cell death with enhance caspase-3 activity. down regulation of antiapoptotic genes Bcl-2 and Bcl_{xi} and enhance the generation of intracellular ROS , which correlated well with the decreased levels of intracellular GSH. In addition DNA fragmentation and annexin – V staining confirmed that the extracts induced apoptosis in tumour cells through the oxidative stress. Aqueous extrats of A. squamosa seeds possessed significant antiumor activity in vivo against AD-5 tumor.(16)

Cytotoxic Activity

Annonaceous acetogenins are a new class of compounds that have been reported to have potent pesticidal, parasiticidal, antimicrobial, cell growth inhibitory activities. In this study, organic and aqueous extracts from the defatted seeds of annona squamosa (custard apple) were tested on different human tumour cell lines for antiumoural activity. While organic and aqueous extracts induced apoptosis in MCF-7 and K-562 cells they fails to do so in COLO-205 cells. Treatment of MCF-7 and K-562 cells with organic and aqueous extracts resulted in nuclear condensation , DNA fragmentation, induction of reactive oxygen species (ROS) generation and reduced intracellular glutathione levels. In addition down regulation of Bcl-2 and PS externalization by Annexin – V staining suggested induction of apoptosis in MCF-7 and K-562 cells by both the extracts through oxidative stress. On the contrary, COLO-205 cells showed only PS externalization but no change in ROS and glutathione levels. These observations suggest that the induction of apoptosis by A. squamosa extracts can be selective for certain types of cancerous cells.(17).

Chemoprevantive & Antilipidperoxidative:-

The chemopreventive and antilpidperoxidative potential of Annona squamosa bark extracts in DMBA induced hamster buccal pouch carcinogenesis. Oral squamous cell carcinoma was induced in hamster buccal pouches by painting with 0.5% 7, 12-dimethylbenz (a) anthracene (DMBA) three times per week for 14 weeks. We observed 100% tumor formation in DMBA patient hamsters. Oral administration of aqueous & ethanolic bark extracts of Annona squamosa at a dose of 500 mg kg -1 body weight & 300 mg kg -1 body weight, respectively prevented the tumor formation as well as decreased the levels of lipid peroxidation by products & enhanced the antioxidants defens mechanism in DMBA painted hamsters. The effect of ethanolic bark extract is however more potent than aqueous extract of Annona squamosa barks. Our results suggest that Annona squamosa bark extracts exert their anticarcinogenic effect by modulating the status of lipid peroxidation & antioxidants in DMBA painted hamsters.(3)

Hepatoprotective :-

The extracts of *Annona squamosa* (300 & 350 mg/kg bw) were used to study the hepatoprotective effect in isoniazid + rifampicin-induced hepatotoxic model in albino Wistar rats. There was a significant decrease in total bilirubin accompanied by significant increase in the level of total protein and also significant decrease in ALP, AST, and ALT in treatment group as compared to the hepatotoxic group. In the histopathological study, the hepatotoxic group showed hepatocytic necrosis and inflammation in the centrilobular region with portal triaditis. The treatment group showed minimal inflammation with moderate portal triaditis and their lobular architecture was normal. In another study, the protective effect was eva- luated in diethylnitrosamine induced hepatotoxicity. This study revealed that the extracts of *Annona squamosa* exerted hepatoprotective effect and the plant extract could be an effective remedial for chemical- induced hepatic damage.(18).

Insecticidal Activity:-

The present study investigatied Insecticidal activity of ethanolic extract of Annana squamosa. The preliminary phytochemical investigation was carried out to identify the various constituents present in the extract. It was found that the Annana squamosa contain alkaloids, protein, amino acid, carbohydrate, glycosides, phytosterols, tannins and phenolic compounds. The ethanol extract of Annona squamosa produced significant Knockdown" (KD_{50}) in the concentration 1% w/v and 5% w/v tested 23.1 min and 11.4 min for respectively. The mortality(100%) was achieved at 39.6±1.4 and 14.5±1. 1min for 1% w/v and 5% w/v concentration respectively. No mortality of the insects was found in any of the controls u"p to 100 hours.The ethanolic Annana squamosa extract showed potent activity against Sitophilus oryzae pest. The finding of new insecticidal activity is of great economic importance both from the agronomic and preventive medicine point of view. The reason for using new natural insecticides is that these are active at highly acceptable levels, biodegradable and do not leave

toxic residues while the commonly used phosphorous and chlorinated insecticides contaminate the environment.(19)

Mosquitocidal activity:-

The significant activity demonstrated by extracts of Annona squamosa suggest that the two plants may have strong killing effects against insects particularly mosquitoes, hence giving a promising source of larvicidal agents. The EtOAc fractions of Annona squamosa were the most active achieving 100 to 90% mortality at 50µg/ml. In order to determine the active principles in the EtOAc fraction further larvicidal testing of the three sub fractions Sq-1, Sq-2, Sq-3, for A.Squamosa showed a dose dependant ($p \geq 0.05$) but also significantly a decreased activity from its parent fraction at the same concentration levels. This indicates that , several medium polar compounds in the extract are acting synergesitically or competitively at the active sites. A. squamosa plant collected from brazil indicated larvicidal effect against Aedes adopictus and C. quinquefascinits and against Anopheles stephensi. Present larvicidal activity result supports the reports and demonstrated that extract of Annona species are potential anti-mosquito agents.(20).

Pesticidal activity :-

The pure compound annotemoyin-1 isolated from the chloroform extract of the seeds of Annona squamosa Linn was evaluated for its pesticidal activity against both adults and different instars of Tribolium castaneum (Herbst) under laboratory condition. The LD_{50} values of the compound were 579.67, 394.89, 24.10, 612.92, 366.95, 315.18, 636.12, 423.30, 333.67, 684.88, 449.28, 101.68, 742.69, 525.93, 199.41, 792.38, 609.08, 191.70, 827.43, 615.36, 221.13, 920.54, 693.10 and 423.12. These results demonstrated that the earlier instars were more sensitive to the compound than those of late instars as well as adults. (21).

Antithyroidic activity

The methanoli extract of seeds of *A. squamosa Linn* shows ameliorative effect in the regulation of hyperthyroidism in mouse model. Hyperthyroidism produced by L-Thyroxine (L-T_4) administration (0.5 mg/kg/d for 12 days, i.p.), which increased the levels of serum triiodothyronine (T_3) and thyroxine (T_4), activity of hepatic G-6-Phospatase, 5'-mono-deiodinase (5'DI) and peroxidation (LPO) with a parallel decrease in superoxide dismutase (SOD) and catalase (CAT) activities. However, simultaneous administration of the Annona seed extract (200 mg/kg) to L-T_4 induced hyperthyroid animals for 10 days, reversed all these effects indicating their potential in the regulation of hyperthyroidism. Further, the seed extract did not increase, but decreased the hepatic LPO suggesting its safe and antiperoxidative nature.(22).

Molluscicidal activity

In search for plant molluscicides for the vector control of schistosomiasis, Ethanolic extracts from *A. squamosa Linn* root was evaluated against adult forms and egg masses of *Biomphalaria glabrata*. Results from accurate experiments indicate that the analyzed extracts possess properties lethal to *Biomphalaria glabrata*.(23).

The molluscicidal activity of leaves, bark and seed of *A. squamosa* against the snail *Lymnaea acuminata* was studied. The toxicity of powder from leaves, bark, and seed of custard apple against the snail was time - and dose -dependent. After 24 h the toxicity of the seed (LC50=377.8 mg/litre) was higher than that of the leaf (LC50=381 mg/litre) and bark (LC50=458 mg/litre). The acetogenins extracted from the seed were highly toxic against the snail (LC 50=2 mg/litre at 96 h).(24).

Antiplasmodial activity

The antiplasmodial activity of methanolic extract of plant *A. squamosa Linn* was tested on chloroquine sensitive strain 3D7 and chloroquine resistant strain Dd2 of *P. falciparum*. The methanolic extract of *A. squamosa* leaves showed high antiplasmodial activity with IC50 values of 2 and 30 microg/ml on 3D7 and Dd2, respectively. While stem bark showed moderate activity with IC50 values of 8.5 and 120 microg/ml on Dd2.(25).

Vasorelaxant activity

A cyclic octapeptide, cyclosquamosin B, isolated from the seeds of *A. squamosa Linn* showed a vasorelaxant effect on rat aorta. It showed a slow relaxation activity against norepinephrine (NE)-induced contractions of rat aorta with/without endothelium. It showed inhibition effect on vasocontraction of depolarized aorta with high concentration potassium, but moderately inhibition effect on NE-induced contraction in the presence of nicardipine. These results showed that the vasorelaxant effect by cyclosquamosin B might be attributed mainly to inhibition of calcium influx from extra cellular space through voltage-dependent calcium channels.(26).

Anti-platelet activity

The ent-kaurane diterpenoids, which are isolated from stem of *A. squamosa Linn* are investigated for anti-platelet activity. The ent-kaurane diterpenoids 'ent-Kaur-16-en-19-oic acid' and '16alpha-hydro-19-al-ent-kauran-17-oic acid' showed complete inhibitory effects on rabbit platelet aggregation at 200 microM. (27).

Anti-inflammatory activity

The analgesic and anti-inflammatory properties of aqueous and ethanolic extracts of leaves of *A. squamosa Linn* (1000, 2000 and 3000 mg/kg) were tested on male and female adult Wistar albino rats. The rats exhibited marked analgesia, although mortality was not observed 72 h after treatment with the extracts. The aqueous extracts of A. squamosa exhibited anti-inflammatory properties against carrageenan - and histamine - induced oedema , as well as analgesic properties against thermal and chemical stimuli as evidenced by the significant reduction in the number of acetic acid-induced writhing and increase in the reaction time by the thermal stimuli. The ethanolic extracts of the plant had no significant analgesic or anti-inflammatory properties.(28).

Antifertility activity

The seed extract of *A. squamosa Linn* was investigated for post coitus antifertility activity. The seed extract of *A squamosa Linn* shows antiimplantational and abortifacient activities.(29).

Antiviral activity

A kaurane diterpenoid 16β, 17-dihydroxy-ent-kauran-19-oic acid was isolatedfrom *A. aquamosa Linn* and investigated for their activity against HIV virus. The 16β, 17-dihydroxy-ent-kauran-19-oic acid showed significant activity against HIV replication in H9 lymphocyte cells.(30).

Anthelmintic activity

Annona squamosa seeds extracts showed anthelmintic activity against *Haemonchus contortus*, the main nematode of sheep and goat in Northeastern Brazil. A compound **1** was isolated from ethyl acetate extract and inhibited the egg hatching of *H. contortus* at 25 mg ml−1. The structure of **1** was determined as a C37 trihydroxy adjacent bistetrahydrofuranacetogenin based on spectroscopic analysis.(35).

CONCLUSION

The extensive survey literature reviewed that *Annona squamosa Linn*, is an important medicinal plant with diverse pharmacological spectrum. Few novel chemical constituent isolated from the *A. squamosa* showed anti –cancer , anti-HIV and anti-diabetic(type 2 diabetic) properties too. Further evalution need to be carried out on A. squamosa in order to explore concealed areas and their practical clinical application, which can be used for the welfare of the mankind.

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List of various chemical constituents present in various parts of *Annona Squamosa* Linn.

TABLE NO. 1.

S.No.	Constituents isolated	Parts	Reference
	Alkaloids		36, 37.
1	Anonaine	Leaves, tender stem, bark, roots, seeds.	37
2	Anolobine	Roots.	36
3	Aporphine	Leaves, tender stem.	36
4	Corydine	Leaves, tender stem, bark.	36
5	Isocorydine	Leaves, tender stem, bark, roots.	36
6	Norcorydine	Leaves, tender stem.	36
7	Norisocorydine	Leaves, tender stem.	36
8	Glaucine	Leaves, tender stem, bark.	37
9	Liriodenine	Roots.	36
10	Norlaureline	Leaves, tender stem.	37
11	Norushinsunine	Roots.	37
12	Reticuline	Roots.	36
13	Roemerine	Leaves, tender stem.	38
14	Samoquasine A	Seeds.	39
15	Annosqualine	Stem.	

	Cyclopeptides		
			40, 41
16	Cyclosqamosin A	Seeds.	40, 41
17	Cyclosqamosin B	Seeds.	40, 41
18	Cyclosqamosin C	Seeds.	40, 41
19	Cyclosqamosin D	Seeds.	40, 41
20	Cyclosqamosin E	Seeds.	40, 41
21	Cyclosqamosin F	Seeds.	40, 41
22	Cyclosqamosin G	Seeds.	42
23	Cyclosqamosin H	Seeds.	42
24	Cyclosqamosin I	Seeds.	43
25	Squamtin A	Seeds.	44
26	Annosquamosin A	Seeds.	
	Acetogenines		
27	Annonacin	Seeds.	47
28	Annonacin A	Seeds.	47
29	Annonastatin	Seeds.	48
30	Squamocin	Seeds.	46
31	Squamocin-O_1	Seeds.	45
32	Squamocin-O_2	Seeds.	45
33	Bullatacin	Stem bark.	49
34	Bullatacinone	Stem bark.	49
35	4-deoxyannoreticuin	Bark.	50
36	cis-4-deoxyannoreticuin	Bark.	50
37	(2,4-cis and trans)-squamoxinone	Bark.	50
38	(2,4-cis and trans)-Mosinone A	Bark.	51
39	Mosin B	Bark.	51
40	Mosin C	Bark.	51
41	Squamotacin	Bark.	52
42	Molvizarin	Bark.	52
43	(2,4-cis and trans)-squamolinone	Bark.	53
44	(2,4-cis and trans)-9-oxoasimicinone	Bark.	53
45	Bullacin B	Bark.	53
46	Squamostatin D	Seeds.	54
47	(2,4-cis- and trans)-bullatacinone	Seeds.	54
48	Squamostatin C	Seeds.	55
49	Annonin I	Seeds.	56, 57
50	Annonin VI	Seeds.	56
51	Squamostene-A	Seeds.	58
52	Reticulacin-1	Seeds.	59
53	Squamosinin-A	Seeds.	60
54	Annotemoyin-1	Seeds.	61
55	Annotemoyin-2	Seeds.	61
	Ent-kaurane Diterpenoids		
56	Annomosin A	Stems.	59
57	Annosquamosins A		62
58	Annosquamosins B		62
59	Annosquamosin C	Stems.	63
60	Annosquamosin D	Stems.	63
61	Annosquamosin E	Stems.	63
62	Annosquamosin F	Stems.	63
63	Annosquamosin G	Stems.	63

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