Guyabano (*Annona Muricata*): A review of its Traditional uses Phytochemistry and Pharmacology

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Abstract

Guyabano*(Annona muricata*) which belongs to the family of Annonaceae is an evergreen tree species used as traditional medicines. Extracts and metabolites from this plant exhibit pharmacological properties such as anti-inflammatory, antiulcer, anthelmintic, antibacterial, and free radical scavenging activity. Beside medicinal uses, this plant has high economic value due to its edible and nutritive fruit, leaves, bark and provides substantial livelihood support to local inhabitants. A wide range of chemical compounds including Alkaloids(acetogenins), lipids, isoquinoline, lactones, Annomuricatina (protein), Bullatacin, Muricoreacinetc. have been isolated from this species. The present review summarizes the information concerning the traditional uses, phytochemistry and biological activity of Annonaceous acetogenins.

Keywords: Annona muricata, Annonaceous acetogenins; Medicinal properties; Phytochemical constituents; Pharmacological actions.

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Introduction

Annonaceae, the custard apple family[1]is a family of flowering plants consisting of trees, shrubs, or rarely lianas[2]. With about 2300 to 2500 species and more than 130 genera, it belongs to the genus *Annona* and the family are concentrated in the tropics, with few species found in temperate regions[3]. About 900 species are Neotropical, 450 are Afrotropical, and the other species Indomalayan. Guyabano tree, or soursop in English (Scientific Name: *Annona muricata Linn*.) is ethno medicinally important species from this family. Guyabano is adaptable to tropical climate and are currently cultivated for its fruit in most Southeast Asian countries such as Malaysia, Indonesia and Philippines[4]. It is also known as*guanabana*(Spanish, El Salvador)*huanaba*(Guatemala),*zopote de viejas*(Mexico), or *cabeza de negro*(Venezuela) , *catoche* or *catuche*(Argentina),*anona de puntitas* or *anona de broquel*; (Bolivia)*sinini*; (Brazil), *araticum do grande*, *graviola*, or *jaca do Para*; (Netherlands) amongst a few. It is a small, upright tropical evergreen, low-branching and bushy but slender tree, which can reach a height of 7.5-9 m. The large evergreen leaves are smooth and glossy and have a dark green upper surface. The fruits are usually oval or heart-shaped and 10-30 cm long and up to 15 cm in width. The skin of the fruit is leathery and covered with curved, soft, pliable spines. The inside of the fruit is cream-colored and is divided into segments. Closely-packed segments are seedless and other segments have a single oval, smooth, hard black seed. One piece of large fruit can contain a dozen to 200 or more seeds [5].

The bark, leaves, fruit, roots, and fruit seeds of the Guyabano tree are known since long for various medicinal uses. The fruit and juice is used against worms and parasites, to cool down fevers, to increase lactation after childbirth. The seeds can be crushed and then used against internal or external parasites, head lice, and worms[6].The tea prepared from the leaves are used as a sedative and a soporific (inducer of sleep) in the West Indies and Peruvian Andes. This infusion is also used to relief pain or for antispasmodic purposes. For

liver problems a leaf tea is used in the Brazilian Amazon[7]. Traditionally it isused in medicinal herbal drugs to cure various diseases such as for diarrhea (fruit), cough, hypertension, rheumatism, tumors, cancer, asthma, childbirth, lactagogue (fruit), malaria, tranquilizer, skin rashes, parasites (seeds), worms (seeds), liver problems, arthritis (used externally) etc[8]. It contains a variety of components which attribute to the various biological activities. The roots and bark can be of aid for diabetes, but can also be used as a sedative. The purpose of the present review is to highlight the various traditional uses, phytochemistry and pharmacological reports on Guyabano (*A. muricata*).

1. Use in traditional medicine

Ethno pharmacological studies show that Guyabano is used in many countries for the treatmentof number of diseases (Table1). Some of these uses are outlined in Table No1.

Table No.1:- Ethnomedical Information for Gayubano (Adapted from Technical Data Report for Graviola (Annona muricata) Inc. 2002)

Country	Part Used	Ethno medical use	Preparation	Ref. No.
Amazonia	Leaf	Used as a strong diuretic for swollen feet (edema) and as a tonic	Infusion Oral	[9]
	Seed	Used as a carminative	Dried Oral	[9]
Brazil	Fruit	Used for dysentery, mouth sores, fever and	Juice Oral	[10]
	Leaf	Used for liver problems, for an anthelmintic and antirheumatic, for neuralgia, rheumatism, arthritis pain and as an antiparasitic, for dysentery, intestinal colic,	Extracted in hot water	[11]
	Root Bark	Considered calmative, antispasmodic, and antidiabetic.	Decoction Oral	[12-14]
Malaysia	Leaf	Used for high blood pressure and diarrhea. Used as an astringent and a styptic.	Decoction Oral	[15-16]

Peru	Leaf	Used to treat catarrh, liver disorders, diarrhea, dysentery, fevers,hypertension, sores, internal ulcers, diabetes. Used as a sedative and antispasmodic.Used for	Decoction Oral Decoction Oral	[17]
	Seed	Used to kill parasites. Crushed seeds and seed oil used as an insecticide, for skin parasites and lice.	Decoction Oral Maceration	[18]
	Bark	Used to treat diabetes. Used as a sedative and antispasmodic.	Decoction Oral	[19]
	Root	Used to treat diabetes. Used as a sedative and antispasmodic.	Hot water Ext Oral	[19]
Togo	Leaf	Used for malaria	Hot water Ext Oral	[20]
West Indies	Leaf	Used for hypertension, worms and diarrhea and also Used for difficult childbirth, asthma, hypertension,	Hot water Ext Oral	[21]
	Fruit	Used for fevers, parasites, diarrhea and as a lactogogue	Fruit Oral	[21]
	bark	Used for hypertension and parasites.	Hot water Ext Oral	[21]

2. Phytochemical

Much of the cancer research on Guyabano focuses on a novel set of phytochemicals called Annonaceous acetogenins. Guyabano produces these natural compounds in its leaf, stem, bark, and fruit seeds. 350 annonaceous acetogenins have been isolated from 37 species, wherein 50% of over 80 of them are found to be significantly bioactive and can be fractationated[22].The Annonaceous acetogenins are a rapidly growing class of compounds whose true anticancer potential as ATP inhibitors is currently being investigated. Bullatacin (**1**), one of the most potent acetogenins, is effective in these *in vivo* models at only 50 *í*g/kg/day (which is 300 times the *in vivo*potency of taxol).The long-chain fatty acids of the acetogenins mimic their recognition by the P-gp, and hence are not effectively eliminated from the multi drug resistant (MDR) cells. The potent and unique activity of the acetogenins seems to be very effective, especially against resilient cell lines such as MCF-7/Adr, P3887 and L121026 murine leukemias in normal mice and against A278026 human ovarian

carcinoma xenographs in athymic mice[23]. Thus, a thorough *in vivo* study is augmented to support the *in vitro* data.

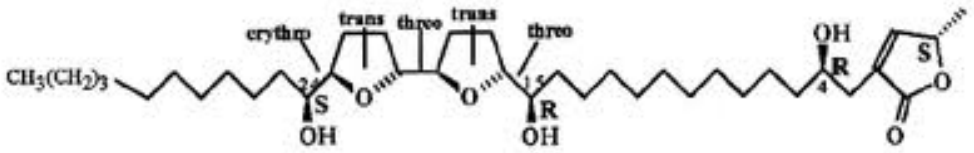


Figure 1: **Structure of Bullatacin (1).**

3. Phytochemical constituents:

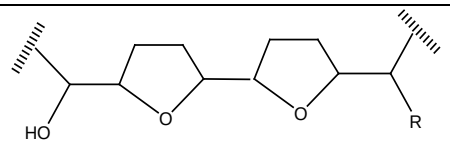
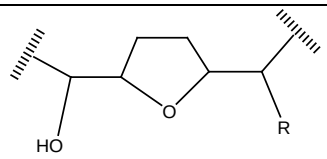
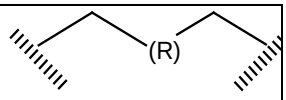
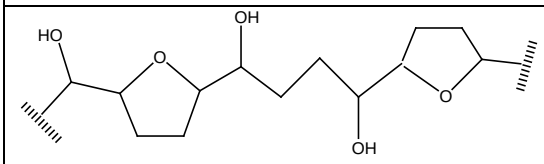
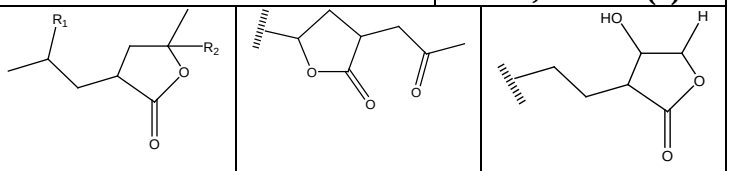
Phytochemical screening of the plants showed the presence of alkaloids, carbohydrates, coumarins, flavonoids, glycosides, phenolic compounds, phytosterols, proteins, quinones, saponins, steroids and terpenoids[24].The ethanolic leaf extract shows high phosphorous and iron content of 128 mg%and 1.075 mg% respectively. The ethanolic root extract shows highest calciumcontent of 22 mg% and the aqueous extract of seed contains high carbohydratecontent of 11.025 mg% respectively[25].

Most acetogenins are white waxy derivatives of long-chain fatty acids (C32 or C34), and theterminal carboxylic acid is combined with a 2-propanol unit at the C-2 position to form a methylsubstitutedα,β-unsaturated-γ-lactone. One of their interesting structural features is a single, adjacent or nonadjacent tetrahydrofuran (THF) or tetrahydropyran (THP) system with one or two flankinghydroxyl group(s) at the center of a long hydrocarbon chain. The THF or THP cores are biogenetically generated by polyepoxidation of an unconjugated polyene followed bydomino cyclizations.The Annonaceous acetogenins are classified according to their relative stereostructures across the THF rings. They classified into mono-THF (2), adjacent bis-THF (3), nonadjacent bis-THF(4), non-THF ring(5), tri- THF, and nonclassical

acetogenins (THP and ring-hydroxylated THF compounds), followed by subclassification of the γ-lactone, substituted γ-lactone, or ketolactone variations(6)[26].

Few of the annonaceous acetogenins in graviola include annocatalin, annohexocin, annomonicin, annomontacin, annomuricatin A & B, annomuricin A thru E, annomutacin, annonacin, annonacinone, annopentocin A thru C, cis-annonacin, cis-corossolone, cohibin A thru D, corepoxylone, coronin, corossolin, corossolone, donhexocin, epomuricenin A & B, gigantetrocin, gigantetrocin A & B, gigantetrocinone, gigantetronenin, goniothalamicin, iso-annonacin, javoricin, montanacin, montecristin, muracin A thru G, muricapentocin, muricatalicin, muricatalin, muri-catenol, muricatetrocin A & B muricatin D, muricatocin A thru C muricin H, muricin I, muricoreacin, murihexocin 3, murihexocin A thru C, murihexol, murisolin, robustocin, rolliniastatin 1 & 2, solamin, uvariamicin I & IV, xylomaticin.[27]]

Table 2: Core units for classification of Annonaceous acetogenins

		
Mono THF acetogenins(2)	**Adjacent bis-THF acetogenins(3)**	**R= (CH2) epoxide, ketone, CH-OH(5)**
		
Non-adjacent bis THF acetogenins(4)	**Sub-types of the terminal lactone R1 & R2 =H,OH cis or trans ketolactone (6)**	

A new acetogenin, sabadelin, has been isolated from the roots of *A.muricata* and characterized using tandem mass spectrometry (MS/MS). Sabadelin (**7**) is probably an intermediate in the biosynthetic pathway of mono-THF acetogenins, and it is proposed as a biogenetic precursor of cis-panatellin.[28]

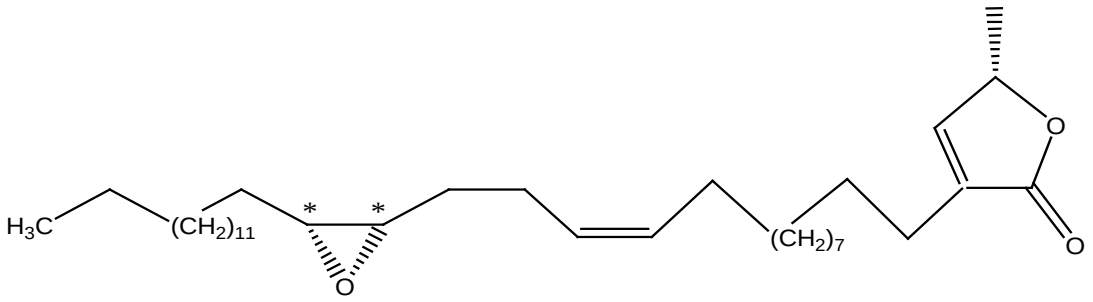


Figure 2: Structure of Sabadelin (7).

A methylene chloride extract of the pulp of *Annonamuricata* L. was fractionated in search for scarcely functionalized Annonaceous acetogenins (type E).Previously known C-35 and C-37 mono-epoxy unsaturated compounds, epomuricenins-A and -B (**1+2**) and epomusenins-A and -B (**3+4**), were obtained. Two new mono-epoxysaturated C-35 representatives, epomurinins-A and -B (**5+6**) were also isolated by Melot et.al[29].

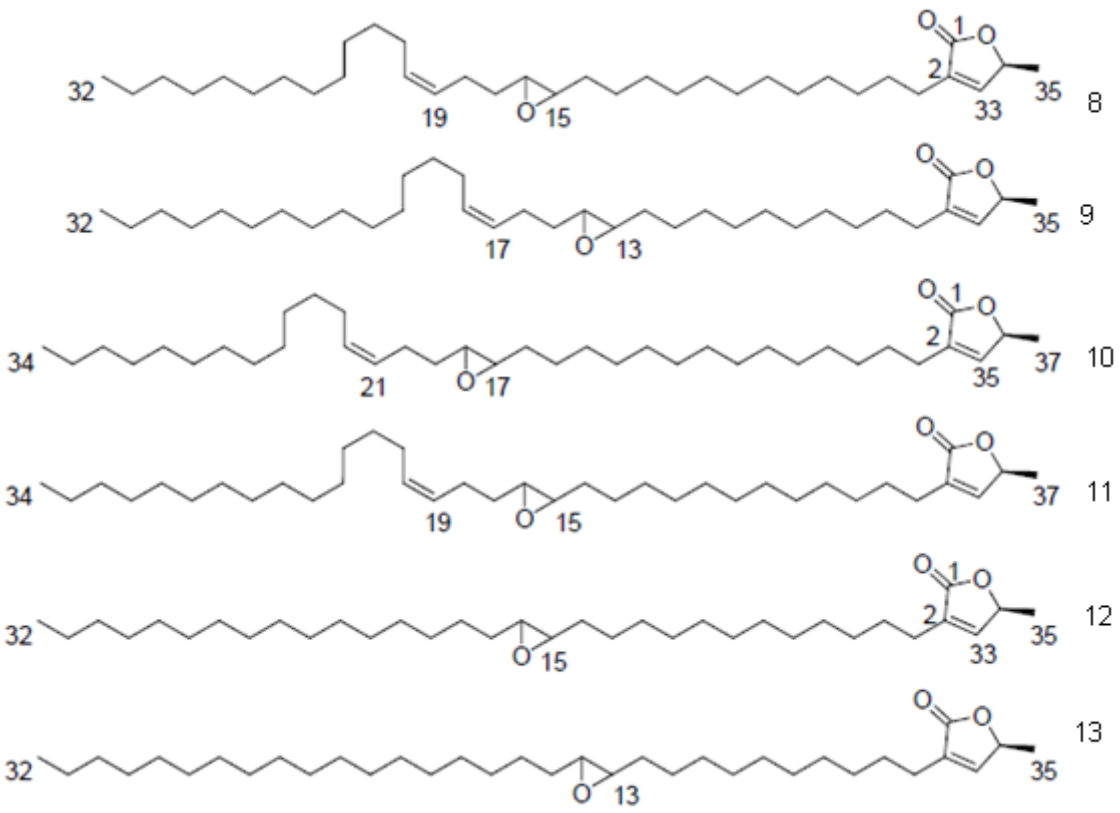


Figure 3:-Obtained ACGs: Epomuricenins-A (8), epoxymurin-A) and -B (9); Epomusenins-A (10) and -B (11); Epomurinins-A (12) and -B (13) \.

4. Pharmacological activity

Several pharmacological activities and medicinal applications of Gayubano are widely known. Whole plant parts extract have been used for various medicinal purposes. A summary of the biological studies on Gayubano are presented below.

i. Anti-hyperglycemic activity

Olawale et.al studied the anti-hyperglycemic activity of the methanolic extract of *A. muricata*on streptozotocin-induced diabetic Wistar rats.A mean blood glucose concentration of 3.78 + 0.190 mmol/L, 21.64 + 2.229mmol/L and 4.22 + 0.151mmol/L for the control, untreated diabetic and treated diabetic groups respectively were selected. A significant difference in the blood glucose concentrations of the treated and untreated hyperglycemic groups of rats was observed [30].

ii. Diabetes and ß-cell Integrity

The methanolic extracts of *A.muricata* leaves were investigated to observe the microanatomical changes in the pancreatic islet cells of streptozotocin induced Diabetic Wistar rats. Three groups viz control, untreated diabetic group, and *A. muricata*-treated diabetic group consisted of ten adult rats each. Diabetes mellitus (DM) was induced by a single intra-peritoneal injection of 80 mg/kg streptozotocin dissolved in 0.1 M citrate buffer wherein, equivalent volume of citrate buffer was treated to the control group. Histomorphological and morphometric examination of the stained pancreatic sections showed a significant increase in the number, diameter, and volume of the β-cells of pancreatic islets of the *A. muricata*-treated group (5.67 ± 0.184 N/1000 µm2, 5.38 ± 0.093 µm and 85.12 ± 4.24 µm3, respectively) when compared to that of the untreated diabetic group of rats (2.85 ±

0.361 N/1000 µm2, 2.85 ± 0.362 µm and 69.56 ± 5.216 µm3, respectively).The results reveal regeneration of the β-cells of islets of pancreatic islet of rats treated with extract of *A. muricata*[31]

Similar studies were carried out by Adewole et.al[32]on rat experimental paradigms of DM. Further their antioxidant activities were estimated wherein AME-treated Groups C and D rats showed significant decrease ($p<0.05$) in elevated blood glucose, reactive oxygen species (ROS), thiobarbituric acid reactive substances (TBARS), triglycerides (TG), total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL), respectively. *A. muricata* extract has a protective, beneficial effect on hepatic tissues subjected to STZ-induced oxidative stress, possibly by decreasing lipid peroxidation and indirectly enhancing production of insulin and endogenous antioxidants [33].

No significant toxicity was observed in animal tissues at low and moderate doses but the leaf extractcould cause kidney damage in higher doses. Lowering of plasma glucose level and positive effects on cardiovascular risk factors suggest good antidiabetic activity [34].

iii. Hepatoprotective activity

The alcoholic extract of *A.muricata* renders an overall protection against CCl_4 induced toxicity by scavenging the free radicals produced by CCl_4 metabolism. Thus it provides protection against increase in serum glutamic oxaloacetic transminase (SGOT), serum glutamic pyruvic transaminase (SGPT),serum alkaline phosphatase (SALP), liver and brain lipid peroxidation (LOP)levels and decrease in liver and brain protein levels. All these data suggest that the plant drugs possess possible antihepatotoxic activity. Traditional medical practitioners in India administer the decoction against liver disorders[35].

iv. Antinociceptive and Anti-Inflammatory Activities

A. muricata leaf (AML) also exerted antinociceptive effect in the hot plate test. This effect is antagonized by naloxone, an opioid antagonist. Vieira de Sousaet.al reported that the antinociceptive effect is viacentral opioid receptors or promoted release of endogenous opiopeptides [36]. In addition, AML has been observed to exhibit its antiulcerogenic effect in dose dependent manner which relates to cytoprotective and antioxidant properties. Furthermore, the gastroprotective effect of AML in ethanol-induced ulcer model is mediated by the involvement of endogenous sulfhydryl that increase the defense mechanism of the gastric mucosa against aggressive factor in the stomach. This might be due to the similar antioxidative compounds reported in the plant previously [37].

In another study the extract delivered per oral route (p.o.) reduced the number of abdominal contortions by 14.42% (at a dose of 200 mg/kg) and 41.41% (400 mg/kg). Doses of 200 and 400 mg/kg (p.o) inhibited both phases of the time paw licking: first phase (23.67% and 45.02%) and the second phase (30.09% and 50.02%), respectively. The extract (p.o.) increased the reaction time on a hot plate at doses of 200 (30.77% and 37.04%) and 400 mg/kg (82.61% and 96.30%) after 60 and 90 minutes of treatment, respectively. The paw edema was reduced by the ethanol extract (p.o.) at doses of 200 (23.16% and 29.33%) and 400 mg/kg (29.50% and 37.33%) after 3 to 4 h of application of carrageenan, respectively. Doses of 200 and 400 mg/kg (p.o.), administered 4 h before the carrageenan injection, reduced the exudate volume (29.25 and) and leukocyte migration (18.19 and 27.95%) significantly[36].

The ethanol extract from guyabano leaves were investigated in animal models. In a chemically induced edema to the rat paw, the guyabano ethanol extract was found to significantly reduce the exudates volume suggesting its antinociceptive and inflammatory activities.

v. Anticancer

a. Pancreatic cancer

The extract from *Annona muricata*induced necrosis of pancreatic cancer (PC) cells by inhibiting cellular metabolism. The expression of molecules related to hypoxia and glycolysis in PC cells (i.e. HIF-1α, NF-κB, GLUT1, GLUT4, HKII, and LDHA) were down-regulated in the presence of the extract. *In vitro*functional assays further confirmed the inhibition of tumorigenic properties of PC cells. Overall, the compounds present in the whole extract inhibited multiple signaling pathways that regulate metabolism, cell cycle, survival, and metastatic properties in PC cells[37].

The presence of Annonaceous acetogenins in the extract was evident bythe depletion of ATP production in PC cells. Current studies are undergoing to ensure that the cytotoxic effects are specific to tumorigenic cells only, by including the non-transformed immortalized pancreatic epithelial cell line HPNE, which is derived from pancreatic duct.

b. Skin Papillomagenesis

The chemopreventive effects in a two-stage model of skin papillogenesis were investigated by Sulaiman Hamizah et.al (2012) [38]. Chemopreventive effects of an ethanolic extract of *A. muricata* leaves (AMLE) was evaluated in 6-7 week old ICR mice given a single topical application of 7,12-dimethylbenza(α)anthracene (DMBA 100ug/100ul acetone) and promotion by repeated application of croton oil (1% in acetone/ twice a week) for 10 weeks. Morphological tumor incidence, burden and volume were measured, with histological evaluation of skin tissue. Topical application of AMLE at 30, 100 and 300mg/kg significantly reduced DMBA/croton oil induced mice skin papillomagenesis in (i) peri-initiation protocol (AMLE from 7 days prior to 7 days after DMBA), (ii) promotion protocol (AMLE 30 minutes after croton oil), or (iii) both peri-initiation and promotion protocol (AMLE 7 days prior to 7 day after DMBA and AMLE 30 minutes after croton oil throughout the

experimental period), in a dose dependent manner ($p<0.05$) as compared to carcinogen–treated control. Furthermore, the average latent period was significantly increased in theAMLE-treated group. Interestingly, at 100 and 300 mg/ kg, AMLE completely inhibited the tumor development in all stages. Histopathological study revealed that tumor growth from the AMLE-treated groups showed only slight hyperplasia and absence of keratin pearls and rete ridges. The results, thus suggest that the *A.muricata* leaves extract is able to suppress tumor initiation as well as tumor promotion even at lower dosage[38].

c. Cytotoxicity studies

The aqueous extract of Guyabano leaves on T47D cells were effective at high doses (mean IC_{50} = 31,384 µg/ml). A previous study with soursop leaf butanol extract obtained an IC_{50} value of 29.2 µg for MDA-MB-435S cells and 30.1 µg for HaCaT cells, while the IC_{50} value of the leaf ethanol extract was 17,149 for T47D cells. A higher dose of soursop leaf extract is required to get any cytotoxic effect since the aqueous extract contains less acetogenins[39].

In another study the cell inhibition activities of several Annonaceous acetogenins, covering the three major structural classes of bisadjacent, bis-non-adjacent, and single tetrahydrofuran (THF) ring compounds and their respective ketolactone rearrangement products, were tested in an *in vitro* disk diffusion assay against three murine (P388, P03, and M17/Adr) and two human (H8 and H125) cancerous cell lines as well as a non-cancerous immortalized rat GI epithelial cell line. The results demonstrate a dose-dependent inhibition of cancerous cell growth, while non-cancerous cell growth is not inhibited by the same dosages. All of the acetogenins, irrespective of their various structural types, inhibit the growth of adriamycin resistant tumor cells and non-resistant tumor cells at the same levels of potency. These results show that the Annonaceous acetogenins are an extremely potent class of compounds, and

their inhibition of cell growth can be selective for cancerous cells while effective for drug resistant cancer cells, and exhibit minimal toxicity to 'normal' non-cancerous cells.

A crude hexane extract of *A. muricata* gave a significant activity with an IC_{50} value of 0.8 pg/ml against CEM-SS cell line while the crude ethyl acetate (EA) extract also gave a significant activity with an IC_{50} value of 0.5 pg/ml but against HL-60 cell line. Over all, the ethanolic extract exhibit significant activity in MDR breast cancer cells than all three of the standard drugs viz. adriamycin, vincristine, and vinblastine[40].

d. Mitochondrial Complex I inhibitor

Acetogenins are potent inhibitors of NADH ubiquinone oxidoreductase, which is an essential enzyme in complex I of the electron transport system (ETS) which eventually leads to oxidative phosphorylation in mitchondria. A recent report showed that they act directly at the ubiquinone catalytic site(s) within complex I and in microbial glucose dehydrogenase. They also inhibit the ubiquinone-linked NADH oxidase that is peculiar to the plasma membranes of cancerous cells and functions to permit cytosolic phosphorylation (substrate levelphosphorylation) by restoration of NAD levels. Thus, the end result of both of these mechanisms is ATP deprivation.

Five annonaceous acetogenins, rolliniastatin-1 (14), rolliniastatin-2 (15), laherradurin (16), squamocin (17), annonacin (18), and rotenone as a reference, differing in their NADH oxidase inhibition activity, have been evaluated for antifeedant, insecticidal, trypanocidal and cytotoxic effects on insect, mammalian and tumor cells. All the test compounds were toxic to *Leptinotarsadecemlineata*, demonstrated selective cytotoxicity to insect Sf9 cells and a panel of tumor cell lines with the multidrug-resistant SW480 (P-glycoprotein+, Pgp+) being the most sensitive one. Compounds 14,15, 17, and rotenone had post-ingestive effects against *Spodoptera littoralis* larvae while 14, 17, 18, and rotenone were active against *Trypanosoma cruzi*. Based on their biochemical properties (inhibition of the mitochondrial NADH oxidase

activity), the *in vivo* effects of these compounds on *S. littoralis* and their cytotoxic effects on Sf9 and tumor cells were more predictable than their effect on *T. cruzi* and mammalian cells[41].

vi. Anti-Herpes Simplex Virus

Studies showed the extract of *A. muricata* inhibit the cytopathic effect of HSV-1 on vero cells indicating an anti-HSV1 potential[42].

vii. Anti-depression

A. Muricata may have antidepressive activity due to its ability to stimulate serotonin receptors. The fruit and the leaf extracts of Guyabano contains three alkaloids, annonaine , nornuciferine and asimilobine , that upon tests have shown to inhibit binding of [3H]rauwolscine to 5-HTergic 5-HT1A receptors in calf hippocampus. These results imply that Guyabano fruit (*A. muricata*) possesses anti-depressive effects[43].

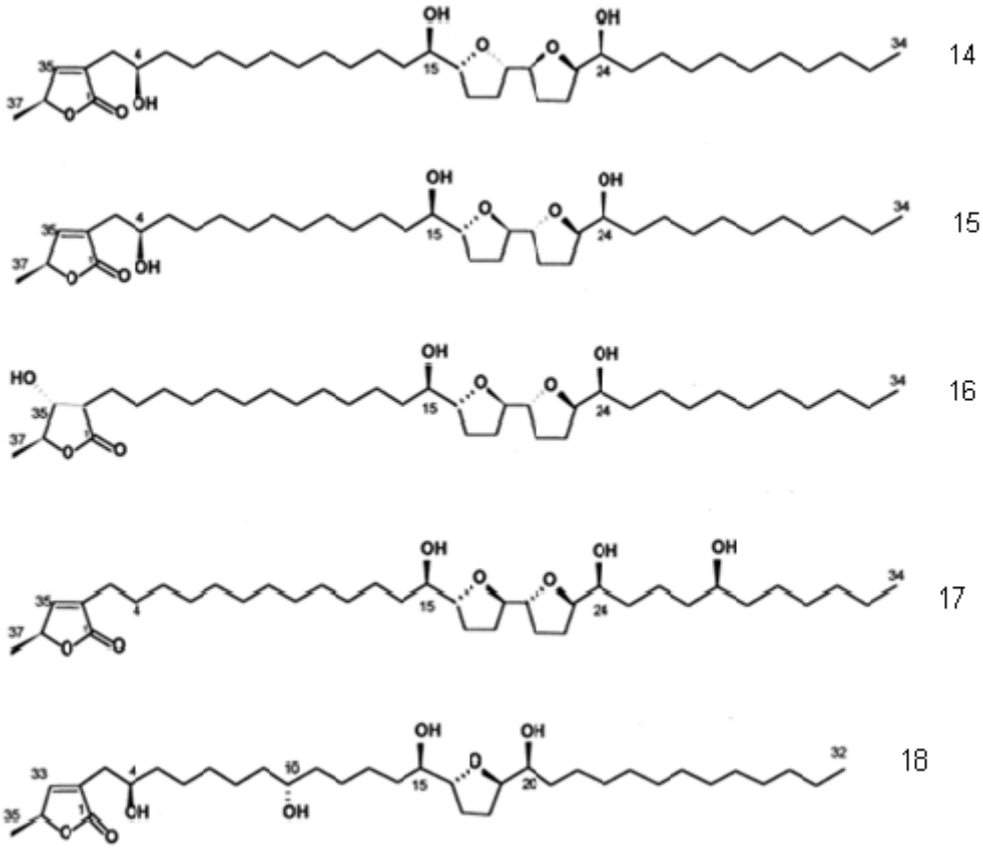


Figure 4 : -Molecular structures of the test compounds.

viii.Anti-Hyperlipidemia

Study of methanolic extracts of *A.muricata* on serum lipid profiles in experimentally-induced diabetic Wistar rats showed antihyperlipidemic activities with significant reductions in total cholesterol, LDL and VLDL and a significant increase in HDL and antiatherogenic index[44].

ix.Antimicrobial

A. muricata leaf extract exhibit a broad spectrum of activity against a panel of bacteria (B. subtilis, Staph aureus, K. pneumonia, P. vulgaris, etc.) responsible for common bacterial diseases like pneumonia, diarrhea, UTIs and skin infections[21]Aqueous extracts of *A.muricata* exhibit an antibacterial effect against *S. Aureus* and *Vibrio Cholerae*.The ethanolic extract of leaf shows highest antibacterial activity towards *Pseudomonas aeruginosa* and *Staphylococcus aureus.*[45]

x.Antioxidant Activity / Comparative Study

The aqueous leaf extract contains a high protein andphenol content of 36.66 mg% and 134.28 mg% respectively. The non-enzymatic antioxidant components like Vitamin-C and Vitamin-E of aqueous leaf and seedextract contains 66.6 mg% and 26.68 mg% respectively. The enzymatic antioxidantcomponents like Super Oxide Dismutase (SOD) and Catalase of aqueousleaf and seed extract contains 255 U/mg and 83.4 µmol of /min/mg respectively[46].

Study evaluated the antioxidant potential of leaves of three different species of Annona using different in vitro models. Results indicates that the extracts of *A. muricata* possess potent *in vitro* antioxidant activity as compared to other *Annona* species, suggesting a role as an effective free radical scavenger [47].

xi. Anti-hypertensive

A. muricata(9.17–48.5 mg/kg) cause significant ($p < 0.05$) dose-dependent reduction in blood pressure without affecting the heart rates. The hypotensive effects were unaffected by atropine (2 mg/kg), mepyramine (5 mg/kg), propranolol (1 mg/kg) and l-NAME (5 mg/kg). *A. muricata* leaf aqueous extract significantly *($p < 0.05$)* relax phenylephrine (10–9–10–4 M) and 80 mM KCl induced contractions in endothelium intact and denuded aortic rings; and cause a significant *($p < 0.05$)* rightward shift of the Ca^{2+} dose response curves in Ca^{2+}-free Kreb's solution containing 0.1 mM EGTA[48].

Conclusion

Plant extracts of *A. muricata* exhibit diverse categories of pharmacological activities such as Antihyperglycemic**,** Anti-Herpes Simplex Virus**,** Anticancer / Acetoginins**,** Anti-Hyperlipidemia, Anti-depression**,** Antimicrobial**,** Cytotoxicity, Chemopreventive / Skin Papillomagenesis, Antioxidant, Antibacterial, Antiproliferative etc. Cancer research is ongoing on these important plants and plant chemicals, as several pharmaceutical companies and universities continue to research, test, patent, and to synthesize these chemicals into new chemotherapeutic drugs. In addition, researchers have reported that NADH dehydrogenase inhibitors can suppress HIV infection. As this is a familiar property of Annonaceous acetogenins, several acetogenins found in the *Annona* plants have been submitted to the NIH anti-AIDS screening program by Purdue University.

However, only a small proportion has been investigated both phytochemical and pharmacologically. There are gaps in the studies, which need to be bridged in order to exploit the full medicinal potential of *A. muricata*. This plant also has widespread use with

extraordinary medicinal potential which should be better explored to find new biological properties which may increase its importance as efficient medicinal plant in biodiversity.

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