


A Review on Marvel Fruit: *Annona muricata* [†]

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Abstract: The purpose of this review is to delve into the essence of *Annona muricata* Linn. *A. muricata*, also known as soursop, guanabana, and graviola, is a member of the *Annonaceae* family and has a long history of traditional uses. This is an evergreen plant that grows in the tropical and subtropical regions of the world, primarily in Africa, South America, and Southeast Asia. The medicinal properties of the *A. muricata* plant are a blessing for humanity, and it has been widely used in folk medicine. *A. muricata* preparations on the market include candies, syrups, beverages, ice creams, and shakes. Several studies have concluded that the plant contains over 212 chemical constituents such as acetogenins, alkaloids, and phenols. The plant has antibacterial, antiviral, antifungal, antitumor, anthelmintic, analgesic, antiarthritic, hypotensive, anti-inflammatory, and immune-enhancing effects, as well as anti-diabetic activity. Although some toxicities have been reported, the extract of *A. muricata* has been found to be effective and safe. This review attempts to bring together the majority of the available information on *A. muricata*'s phytochemistry, traditional uses, biological activities, and toxicity.

Keywords: *Annona muricata*; Annonaceae; annonaceous acetogenins; cytotoxicity; neurotoxicity

1. Introduction

Natural products, particularly those derived from plants, have been used to help humankind maintain its health since the dawn of medicine. Over the last century, plant phytochemicals have been an important pipeline for pharmaceutical discovery. The value of active ingredients and the use of plants in agriculture and medicine have piqued scientists' interest [1].

According to the World Health Organization (WHO), more than 80% of the world's population relies on traditional medicines to meet their primary health care needs. The primary characteristics of these medicines are medicinal plant chemical substances that exert a physiologic action on the human body. The most important plant bioactive compounds are thought to be alkaloids, flavonoids, tannins, and phenolic compounds. New anti-infective drugs can be discovered from higher plants using the plant chemical phytochemical ethnopharmacological approach [2].

Intensive chemical studies of these species' leaves and seeds have resulted in the isolation of a large number of acetogenins. Some of the isolated compounds exhibit interesting biological or pharmacological activities, such as antitumoral, cytotoxic, antiparasitic, and pesticidal properties. Because of their anti-parasitic and pesticidal properties, the roots of these species are used in traditional medicine [3].

The extract of *A. muricata*'s fruits, seeds, bark, roots, and pericarp contains over 212 phytochemical varieties that are used to treat a variety of ailments. According to historical records, *A. muricata* has been used as an insecticide and parasiticide. Fever, pain, respiratory illness, sedative, malaria, gastrointestinal problems, arthritis, and liver and kidney problems have all been treated with fruit juice and leaf and bark infusions. *A. muricata* has also been shown to have anti-diabetic and anti-tumor activity in recent studies (Figure 1) [4].



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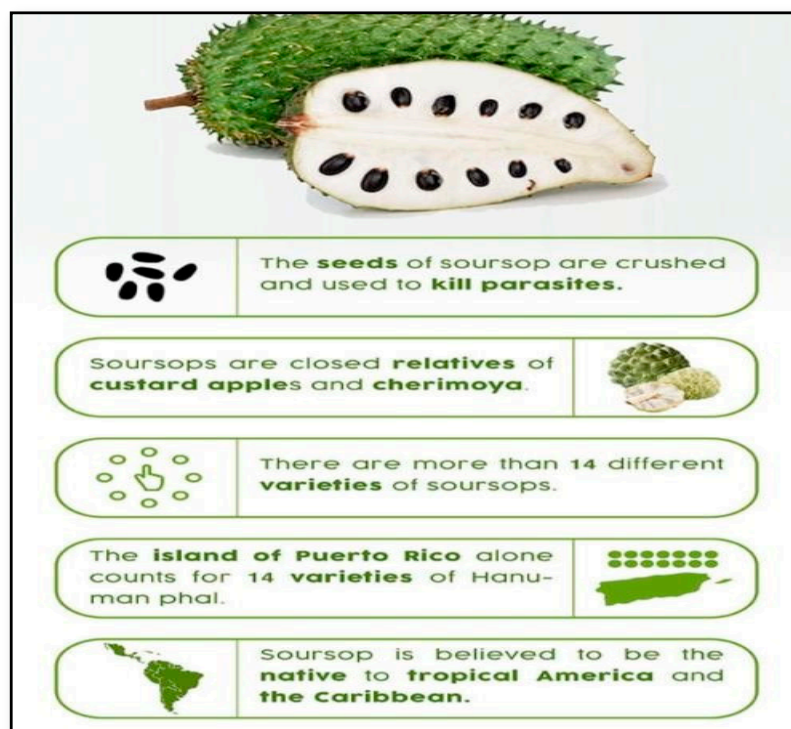


Figure 1. Properties of Soursop [4].

The hepatoprotective effects of AM leaf extracts were effective in the normalization of function after liver damage, as determined by biochemical and histological tests [5].

Because the fruit has economic value, it is widely cultivated and consumed as edible food. The plant's major pharmacological activities include cytotoxicity, antileishmanial activity, wound healing, and antimicrobial activity. It also has anticarcinogenic and genotoxic properties. The presence of tannins, steroids, and cardiac glycosides, which are the major phytochemical compounds, was revealed via phytochemical analysis of the plant [6].

2. Drug Profile

Synonyms: *Annona Macrocarpa* Wercle

Kingdom: plantae

Clade: magnoliids

Order: magnoliales

Family: annonaceae

Genus: *Annona*

The petals are yellowish and thick. The outer petals are broadly ovate, 2.8 cm (1.1 in) to 3.3 cm (1.3 in) by 2.1 cm (0.83 in) to 2.5 cm (0.98 in), tapering to a point with a heart-shaped base. They are evenly thick and covered with long, slender, soft hairs on the outside and finely matted soft hairs on the inside. The inner petals are oval and overlap. They are sharply angled and tapered at the base, measuring approximately 2.5 cm (0.98 in) to 2.8 cm (1.1 in) by 2 cm (0.79 in). The margins are thin, with fine matted soft hairs on both sides. The receptacle is hairy and conical. The stamens are 4.5 mm (0.18 in) long [7]. Its pollen is shed in the form of permanent tetrads [8].

The fruits are prickly and dark green as shown in Figure 2. They are ovoid in shape and can grow to be up to 30 cm (12 in) long, with a moderately firm texture. Their flesh is juicy, acidic, whitish in color, and aromatic [9].



Figure 2. *Annona muricata*: (A) whole plant, (B) leaves, (C) flower, (D) fruit, (E) seeds [8].

A. muricata is a member of the *Annonaceae* family, which includes approximately 130 genera and 2300 species.

A. muricata is common in the West Indies and northern South America. It has recently spread throughout the West Indies, as well as from southern Mexico to Peru and Argentina [10,11].

3. Cultivation

The plant is cultivated for its 20–30 cm (7.9–11.8 in)-long prickly green fruit, which can weigh up to 6.8 kg (15 lb), making it the second largest *Annona*. Away from its native range, some limited production occurs as far north as southern Florida within USDA Zone 10, but this is mostly for garden plantings for local consumption. It is also grown in parts of Southeast Asia and is widely in Mauritius. Mexico is the primary supplier of the fruit, followed by Peru, Brazil, Ecuador, Guatemala, and Haiti [12]. *Annona suricata*'s complete genome was sequenced in 2021 to aid soursop breeders and stimulate further development of genomic resources for this globally important plant family [13].

4. Ethnomedicinal Uses

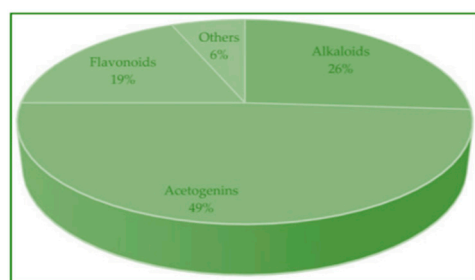
All parts of the *A. muricata* tree, like those of other *Annona* species such as *A. squamosal* and *A. reticulata*, are widely used as traditional medicines for a variety of human ailments and diseases, particularly cancer and parasitic infections shown in Table 1. The fruit is used as a natural remedy for arthritis, aches and pains, neuralgia, arthritis diarrhea, dysentery, fever, malaria, parasites, rheumatism, skin rashes, and other symptoms, as well as to induce a mother's milk after childbirth. The leaves are used to treat cystitis, diabetes, headaches, and insomnia. Furthermore, internal administration of the decoction of the leaf is thought to have anti-rheumatic and neuralgic properties, whereas the cooked leaves are topically applied used in the treatment of abscesses and rheumatism [14].

Table 1. Medicinal uses of *A. muricata*.

| Plant Part | Medicinal Use | Preparation/Application |
|------------|--|----------------------------------|
| Leaf | Insomnia, febrifuge, catarrh, snake bites, analgesic, arthritis pain, rheumatism, neuralgia, weight loss, malaria, digestive, typhoid fever, antimicrobial | Oral |
| Fruit | Hypertension, diarrhea, dysentery, febrifuge, inflammation, lactagogue, astringent | Juice/oral |
| Bark | Helminthiasis, diarrhea, stomach ulcer, sedative, vermifuge, antidot | Decoction |
| Root | Dysentery, vermifuge, antidote, insomnia, catarrh, febrifuge, spasms, parasites | Decoction /oral |
| Seed | Sedative, cardi tonic, convulsion, renal and skin disorder, vaginal infection | Plaster/topical Infusion/oral |

5. Phytochemistry

The extract of *A. muricata* contains over 212 different phytoconstituents [15]. The chemicals most abundant and contributing to bioactivity are acetogenins, alkaloids, phenols, and flavonoids (Figure 3). Several studies have revealed the presence of flavonol triglycerides, alkaloids, phenolics, megastigmanes, cyclopeptides, and essential oils. Minerals such as calcium, sodium, iron, potassium, copper, and magnesium are obtained by the body through consumption [16].

**Figure 3.** Phytochemicals present in *A. muricata* [17].

The presence of various major minerals such as K, Ca, Na, Cu, Fe, and Mg suggests that eating *A. muricata* fruit regularly can help provide essential nutrients and elements to the human body [17].

5.1. Acetogenesis

Acetogenins are a distinct class of compounds that are thought to be the primary bioactive compound of the *Annonaceae* family, and are thus also known as annonaceous acetogenins. More than 120 acetogenins have been identified in plant parts such as the leaves, stem, bark, seed, pulp, and fruit peel. The structure of the acetogenins determines *A. muricata*'s bioactivity. Annonacin is an important acetogenin found in abundance in the fruit and leaf, as well as in lesser amounts in the seeds, roots, and peel. According to some studies, acetogenins are more cytotoxic than alkaloids [18].

5.2. Alkaloids

Muricata contains two important alkaloids: reticuline and coreximine (Figure 4). The alkaloids are more abundant in the leaves and less so in the roots, stems, and fruits, in that order. Isoquinoline, apomorphine, and protoberberine are the most important alkaloids found. The alkaloids extracted from *A. muricata* have an affinity for 5-HT_{1A} receptors, which participate in dopamine synthesis and thus have antidepressant and cytotoxic effects in the body [19].

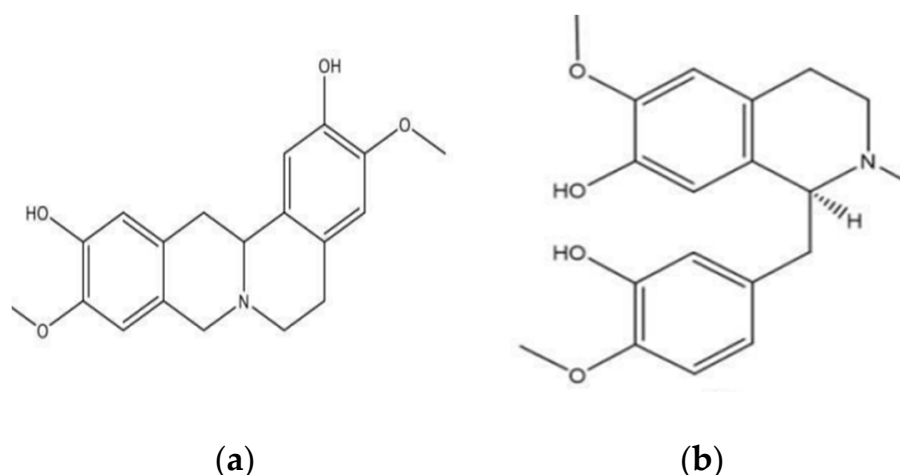


Figure 4. The most abundant alkaloids in *A. muricata*: (a) coreximine; (b) reticuline [19].

5.3. Flavonoid

The most abundant flavonoids in *A. muricata* are kaempferol, quercetin and rutin (Figure 5). According to reports, *A. muricata* contains up to 37 phenolic compounds. The two most important are quercetin and gallic acid. Tocopherols and tocotrienols are abundant in the fruit's pulp. According to research, the majority of phenols are soluble in aqueous extracts. Antioxidant properties have been reported for phenolic compounds [20].

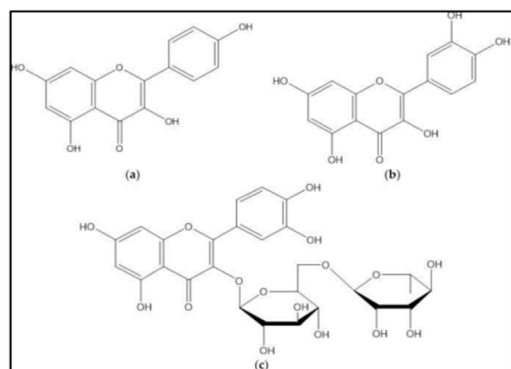


Figure 5. Flavonoids in *A. muricata*: (a) kaempferol (b) quercetin (c) rutin [20].

5.4. Essential Oil

GC and GC-MS analyses of *A. muricata* leaf oil from Cameroon revealed the presence of mostly sesquiterpenes, with caryophyllene being the most abundant compound. Another study on *A. muricata* from Vietnam discovered significant pinene volatile oil constituents, including geracene D (20.6%), mentha-2,4(8)-diene (9.8%), pinene (9.4%), and elements (9.1%) derived from leaf oil. Other important compounds include cadinene, epicasinol, and cardinal compounds allegedly discovered in leaf oil extracts. The essential oil extracted from fruit pulp was discovered to have aliphatic acid esters containing the major compounds 2-hexenoic acid methyl ester and 2-hexenoic acid ethyl ester. High concentrations of mono- and sesquiterpenes, including caryophyllene were observed, while the fruit pulp also yielded 1,8-cineole and linalool [21].

5.5. Other Compounds

Several studies have found the presence of other compounds in the leaves, seeds, and fruit pulp, such as vitamins, carotenoids, amides, and cyclopeptides. The seeds contain anti-inflammatory and anti-tumor amides called N-p-coumaroyl tyramine and cyclopeptides. Around 37 volatile compounds have been identified in the fruit pulp, and sesquiterpene

derivatives have been discovered in the leaf. Soursop pulp also contains enzymes such as pectinase, catalase, and peroxidase. During ripening, the enzyme amylase is detected, and its activity increases approximately 18-fold as the ethylene level in the fruit increases [21].

6. Pharmacological Activities

6.1. Anticancer

A. suricata's anticancer activity is linked to its cytotoxic activity against cancer cells. The effects of *A. muricata* on cancer cells. Extracts from various parts of *A. muricata* act as anticancer agents through a variety of mechanisms. Extracts of the fruit, stems, seeds, and twigs of *A. muricata* were reported to inhibit matrix metalloproteinases (MMPs) such as MMP-2 and MMP-9, which play important roles in cancer progression. Extracts from the leaves, twigs, and roots inhibited the proliferation of the human leukemia cell line HL-60 by disrupting MMPs, reactive oxygen species (ROS), and G0/G1 cell cycle arrest, resulting in cancer cell growth inhibition [22].

The A549 lung cancer cell line was treated with an ethyl acetate extract of *A. muricata* leaves, which induced apoptosis by increasing Bax expression and decreasing Bcl-2 expression. Apoptosis induced by an ethyl acetate extract of *A. muricata* leaf has also been linked to cell cycle arrest at the G0/G1 phase in the colorectal cancer cell line COLO-205 [23] and the breast cancer cell line MDA-MB-231. Another study found that *A. muricata* leaf ethanol extract and ethyl acetate fractions were active against MCF7 cells via an apoptosis mechanism mediated by decreased Bcl-2 expression and increased caspase-3 and caspase-9 expression [24].

6.2. Antiulcer

Flavonoids, tannins, and phenolic acids are abundant in *A. muricata* and have therapeutic effects due to their antioxidant, anti-inflammatory, and gastroprotective properties. According to a survey, the leaves and bark of *A. muricata* are commonly used to make tea to treat gastrointestinal problems such as gastritis and poor digestion [25].

6.3. Antidiabetic

A. muricata also exhibits antidiabetic activity. It contains flavonoids that inhibit α -glucosidase activity through hydroxylation bonding and substitution. This inhibition suppresses carbohydrate hydrolysis and glucose absorption and inhibits carbohydrate metabolism into glucose [26].

In vitro, *A. muricata* fruit extracts were found to have antioxidant and anti-diabetic effects by inhibiting key enzymes involved in type 2 diabetes mellitus, such as amylase and glucosidase. According to one study, *A. muricata* pericarp has the best inhibitory enzyme and antioxidant properties. When compared to the standard drug, the fruit pulp and leaf extract inhibited amylase and glucosidase and reduced the rate of glucose assimilation into the blood after feeding [27].

The antidiabetic effects of *A. muricata* aqueous extract are mediated by antioxidant mechanisms. In streptozotocin-induced diabetic mice, *A. muricata* leaf extract reduced lipid peroxidation processes, which are a sign of oxidative stress, and indirectly affected insulin production and endogenous antioxidants [28].

6.4. Antibacterial

When compared to the standard antibiotic streptomycin, *A. muricata* extracts demonstrated antibacterial activity against Gram-positive and Gram-negative bacteria. However, the solvent used for extraction can have an impact on the bioactive efficacy of the extracts. The combination of *A. muricata* ethanolic extract and antibiotic treatment reduced the potential of antibiotic multidrug-resistant *Escherichia coli* and *Staphylococcus aureus* strains. Another study found that bioactive compounds in *A. muricata*, such as alkaloids (annonaine, asimilobine, liriodenirine, nornuciferine, and so on), attack the bacterial membrane (plasma and outer membrane), resulting in broad-spectrum antibacterial activity [12].

6.5. Antiviral

Antiviral activity of *A. muricata* extract has been reported, for example by interfering with the replication process of HIV-I. In another study, ethanolic extracts of *A. muricata* stem and bark demonstrated in vitro antiviral activity against the herpes simplex virus. Another study found that after 1 h of contact time, an acidified ethanolic extract of *A. muricata* reduced viral replication [13]. This activity could be attributed to the presence of phenolic compounds such as rutin. Acetogenins with good inhibitory activity against SARS-CoV-2 spike proteins include annonamuricin a, annonamuricin b, annonamuricin c, muricatocin c, Suricata in, cis-annonacin, annonacin-10-one, cis-goniothalamycin, Ariana can, and javoricin (in silico) [29]. Cis-annonacin had the lowest binding energy and the greatest ability to form hydrogen bonds, indicating that it was the most potent of the acetogenins tested in the study. This finding suggests that annonaceous acetogenins have the potential to be anti-SARS-CoV-2 agents and should be studied in vitro and in vivo [30].

7. Nutritional Facts

One cup (225 g) of soursop pulp contains 148 calories, 2.3 g of protein, 37.8 g of carbohydrates, and 0.7 g of fat. *Annona muricata* is high in vitamin C, fiber, and potassium [31].

Calories: 148;

Fat: 0.7 g;

Carbohydrates: 37.8 g;

Fiber: 7.4 g;

Sugars: 30.5 g;

Protein: 2.3 g;

Vitamin C: 46.4 mg;

Potassium: 626 mg.

7.1. Crabs

Annona muricata has nearly 38 g of carbohydrates per cup. Soursop's carbs come from naturally occurring sugars, and it has more than 7 g of fiber per serving (about a quarter of your recommended daily intake). Sorrel has a low glycemic index [32].

7.2. Fats

This fruit contains very little fat, with less than one gram per serving.

7.3. Protein

Annona muricata, like most fruits, contains little protein. A single serving contains only 2.3 g of protein. To meet one's daily protein requirements, one would need to include other protein sources in one's diet, such as salmon, lean meats, and legumes [32].

8. Conclusions

A. muricata is an evergreen plant that is found almost everywhere. *A. muricata* extract contains over 212 different phytoconstituents. Annonaceous acetogenins are important chemical constituents found almost everywhere in plants that contribute to human health problems. This plant's alkaloids, flavonoids, and phenols exhibit a wide range of activity. People all over the world use a decoction of the plant's fruit, leaves, roots, and bark for a variety of purposes. The plant's cytotoxic, antiparasitic, anti-inflammatory, and antioxidant properties are the most promising. Previous studies focused primarily on the biological activity of this plant's extract. More research is needed on the biochemical and physiological functions of its active compounds, as well as the detailed mechanisms underlying these activities. Several reports suggest that the important constituent annonacin has a neurotoxicological effect. A clear distinction between chemical constituents, dose, and toxicity is critical. Future research and clinical trials must focus on the compounds that contribute to toxicity, as well as their dose and effect on the body. This article is intended to provide researchers with information and motivation to continue studying this plant.

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