

**ANNONA MURICATA: A PLANT REVIEW****Harshith Kumar K. N.\*, Suresha B. S. and Balasubramanian T.**

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**ABSTRACT**

*Annona muricata* is a member of the Annonaceae family and is a fruit tree with a long history of traditional use. *A. muricata*, also known as soursop, graviola and guanabana, is an evergreen plant that is mostly distributed in tropical and subtropical regions of the world. The fruits of *A. muricata* are extensively used to prepare syrups, candies, beverages, ice creams and shakes. A wide array of ethnomedicinal activities is contributed to different parts of *A. muricata*, and indigenous communities in Africa and South America extensively use this plant in their folk medicine. Numerous investigations have substantiated these activities, including anticancer, anticonvulsant, anti-arthritis, antiparasitic, antimalarial, hepatoprotective and antidiabetic activities. Phytochemical studies reveal that annonaceous acetogenins are the major constituents of *A. muricata*. More than 100 annonaceous acetogenins have been isolated from leaves, barks, seeds, roots and fruits of *A. muricata*. In view of the immense studies on *A. muricata*, this review strives to unite available information regarding its phytochemistry, traditional uses and biological activities.

**KEYWORDS:** *Annona muricata* ; section snippets Biodiesel production, Anti diabetic activity.**INTRODUCTION**

All over the world the herbal medicine acts as the representative of the most important fields of traditional medicine. The study on the medicinal plants is essential to promote the proper use of herbal medicine in order to determine their potential as a source for the new drugs.<sup>[1]</sup> Medicinal plants have been used for the treatment of illness since before recorded history. The sacred Vedas dating back between 3500 B.C and 800 B.C gives many references of the utilization of the medicinal plants. “Virikshayurveda” is one of the remotest works in the traditional herbal medicine which was compiled even before the beginning of Christian era. “Rig Veda” is one of the oldest literatures which was written around 2000 B.C. and mentions the use of Cinnamon (*Cinnamomum verum*), Ginger (*Zingiber officinale*), Sandalwood (*Santalum album*) etc was used not only in the religious ceremonies but also in the medical preparations.<sup>[2]</sup> The relationship between food and medicine was quoted as “Let food be thy medicine and medicine be thy food”.<sup>[3]</sup> Plants and plant-based medicaments are used as the basis of many of the modern pharmaceuticals that we use today in order to treat our various ailments.<sup>[4]</sup> The better understanding of the plant derived medicine depends mainly on two factors that have gone hand in hand. One criterion involves the proof to show that the formulated medicine does what it is claimed to do and other is the identification of the active compound by means of the chemical analysis.<sup>[5]</sup>

**VERNACULAR NAMES**

- Kannada - Mulluramaphala, Hanumaphala, Lakshmanaphala.
- English - Brazilian pawpaw, Graviola, Prickly custard apple, Soursop
- Tamil - Mullu-sitha-pazham, Pulippu Palam
- Latin American Spanish – Guanábana
- Malayalam – Mullatha
- Assam - Ata-phal, Atlas.<sup>[6]</sup>

**TAXONOMY**

- Kingdom: Plantae
- Subkingdom: Trecheobonta -vascular plants
- Division: Mangoliophyta-flowering plants
- Super division: Spermatophyte-seed bearing plant
- Class: Mangoliopsida
- Subclass: Mangoliidae
- Order: Mangoliales
- Family: Annonaceae
- Genus: *Annona*
- Species: *Muricata*<sup>[7]</sup>

**CHEMICAL CONSTITUENTS:**

Alkaloids, anthocyanins and betacyanin's, coumarins, glycosides, phenols, quinones, saponins, flavonoids, tannins, terpenoids, triterpenoids, steroids, and It is also an ample source of iron, calcium, vitamins, and antioxidants.

## USES

Traditional medicinal uses of *Annona muricata* have been identified in tropical regions to treat diverse ailments such as fever, pain, respiratory and skin illness, internal and external parasites, bacterial infections, hypertension, inflammation, diabetes and cancer. *Annona muricata* have been characterized as an antimicrobial, anti-inflammatory, anti-protozoan, antioxidant, insecticide, larvicide, and cytotoxic to tumor cells.<sup>[6]</sup>

## SECTION SNIPPETS

### Fruit composition and description

The height of a soursop tree varies from 3 up to 10 m tall, possess oval leaves with axillary buds, reaching a full size of 6 cm wide and 12 cm long (Jiménez-Zurita et al., 2017a). The soursop is a spiny aggregate fruit constituted of a berry product of multiple ovaries (Thompson, 2003). The fruits can have a length of 30 cm with a weight up to 5 kg. Phenotypically, is a dark-green shell with an oval, conical or irregular heart form, which is the product of an inadequate development of the.

### Fruit growth and ripening

Soursop needs a warm and tropical climate for its development. The pollination in soursop is complex, causing low fruit set and in consequence low yield. Climate conditions of 25 °C temperature and 80% of relative humidity (low temperature, high humidity) can improve the pollination process (Janick and Paull, 2008). The soursop is a climacteric fruit and the time of harvesting is established based on the skin color of the fruit. According to Worrell et al. (1994), after the soursop flowers are.

### Postharvest handling and technology

The soursop is a very perishable fruit, and that is why it requires a careful handling from harvest to consumption (de Lima and Alves, 2011). Probably, the most important factor that affects the quality of the soursop is the precise time in which the fruit is physiologically mature. For instance, a fruit harvested immature will show an irregular maturation and a bad taste in the pulp as a consequence. Furthermore, when the fruits are harvested ripe, they show a reduced postharvest shelf life in.

### Soursop postharvest diseases

Soursop fruits are infected by numerous fungi species, which have been isolated, identified and characterized. Cyriacus and Kingsley (2010) identified several fungi on the exocarp and mesocarp of mature green soursop fruits from Nigeria, namely: *Aspergillus flavus*, *Aspergillus niger*, *Botryodiplodia theobromae*, *Colletotrichum* sp., *Fusarium solani*, *Mucor* sp., *Penicillium chrysogenum*, *Penicillium* sp., *Rhizopus stolonifer* among others. Moreover, Nweke and Ibiam (2012) found that soft-rot disease.

### Micropropagation

Soursop propagation is usually carried out by seed (Paull and Duarte, 2011). In Mexico, the large existing

genotype variability of soursop fruits had been generated by seed propagation (Evangelista-Lozano et al., 2003). The multiplication of *Annona muricata* L. by seed is preferred because propagation through traditional methods such as layering, budding, grafting, shoots and root cuttings are very slow and expensive (Zobayed et al., 2002). For this reason, the micropropagation techniques by.

### Genetic diversity

The molecular diversity of the specie *Annona muricata* soursop is still largely unknown. The evaluation of genetic variation of crop species is fundamental for the design of a successful plant breeding program because it helps to choose parental lines for the genetic crosses with the goal to induce a much larger variation in the progeny (Boora and Dhillon, 2010). Nowadays, there is a lack of information about the genetic characteristics of soursop commercial varieties partially due to the very.

### Genomic sequencing

Since the first plant genome sequence was published (Arabidopsis-Genome-Initiative, 2000), the number of plant genomes sequenced has increased continuously. This has been possible thanks to the improvement in the sequencing technologies in terms of cost and speed; the storage capacity and the bioinformatics tools for sequence analysis. All of this gave rise to the plant genomics era, which has brought great advances in agronomic sciences (Bolger et al., 2014). Currently, there are few genomic.

### Future perspectives

Even when during the last years, studies of the *Annona muricata* L. had increased, major efforts are required to uncover the transcriptomic and genomic sequences of the specie. The improvement of DNA sequencing technologies and the advances in genomics and transcriptomics will make possible to obtain a better understanding of the *Annona muricata* L. genes expression patterns, which will provide a large amount of valuable biological information that can be used in several ways. For instance, it.<sup>[8]</sup>

### BIODIESEL PRODUCTION FROM SOURSOP (*ANNONA MURICATA* L.) SEED OIL

This study investigated the optimal reaction conditions for biodiesel production from soursop (*Annona muricata*) seeds. A high oil yield of 29.6% (w/w) could be obtained from soursop seeds. Oil extracted from soursop seeds was then converted into biodiesel through two-step transesterification process. A highest biodiesel yield of 97.02% was achieved under optimal acid-catalyzed esterification conditions (temperature: 65 °C, 1% H<sub>2</sub>SO<sub>4</sub>, reaction time: 90 min, and a methanol: oil molar ratio: 10:1) and optimal alkali-catalyzed transesterification conditions (temperature: 65 °C, reaction time: 30 min, 0.6% NaOH, and a methanol: oil molar ratio: 8:1). The properties of soursop biodiesel

were determined and most were found to meet the European standard EN 14214 and American Society for Testing and Materials standard D6751. This study

suggests that soursop seed oil is a promising biodiesel feedstock and that soursop biodiesel is a viable alternative to petrodiesel.<sup>[9]</sup>



## PRODUCTION OF BIODIESEL THROUGH TWO-STEP PROCESS:

### • Esterification Step

An  $\text{H}_2\text{SO}_4$ -catalyzed pretreatment was employed to reduce the oil's acidity and convert its FFAs into biodiesel. To study the influence of reaction factors on esterification, several experimental trials were conducted in a sealed reactor with stirring under different conditions: molar ratios of methanol to oil (4:1–12:1), temperatures (45–85 °C), catalyst amounts (0.25–2.0%), and reaction times (30–150 min). After each reaction, the samples were withdrawn to evaluate the FFA conversion.<sup>[10]</sup>

### • Transesterification Step

The oil pretreated through  $\text{H}_2\text{SO}_4$ -catalyzed esterification was used for the transesterification step. The esterified reaction mixture was kept in a funnel for phase separation. After two phases were completely separated, the crude oil and biodiesel (upper layer) was poured into a sealed reactor and subsequently transesterified into biodiesel using NaOH as catalyst. A set of experiments with various methanol to oil molar ratios (4:1–12:1), temperatures (45–85 °C), catalyst amounts (0.4–1.2%), and reaction times (15–75 min) were studied for their effects on the conversion yield. After each reaction, the reactor was placed at room temperature for phase separation. The mixture's upper layer containing biodiesel was collected to determine the biodiesel yield.<sup>[11]</sup>

## ROLE OF HERBAL DRUGS IN PREVENTION AND CURE OF DIABETICS

Diabetic is a serious of metabolic disorder and plenty of medicinal plants are used in traditional medicines to treat diabetes. These plants have no side effects and many existing medicines are derived from the plants. Diabetic is mainly due to oxidative stress and an increase in reactive oxygen species that can have major effects. Many plants contain different natural antioxidants, in particular tannins, flavonoids, vitamins C and E that have the ability to maintain  $\beta$ -cells performance and decrease glucose levels in the blood. Nowadays, different treatments, such as insulin therapy, pharmacotherapy and diet therapy are available to control diabetes. There are several types of glucose lowering drugs that exert anti-

diabetic effects through different mechanisms. These mechanisms includes stimulation of insulin secretion by sulfonylurea and meglitinides drugs, increasing of peripheral absorption of glucose by biguanides and thiazolidinediones<sup>[12]</sup>, delay in the absorption of carbohydrates from the intestine by alpha glucosidase and reduction of hepatic gluconeogenesis by biguanides.<sup>[13]</sup>

**Different pharmacological action of herbal antidiabetic remedies:** Mechanism of action of herbal antidiabetic is depending on presence of active chemical component in plant material. Different mechanism of action of herbal medicine is given below.

- Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger) stimulation.<sup>[14]</sup>
- Stimulation of insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes.
- Prevention of pathological conversion of starch to glucose.<sup>[15]</sup>
- Stimulation of insulin secretion.<sup>[16]</sup>
- Preventing oxidative stress that is possibly involved in pancreatic  $\beta$ -cell dysfunction found in diabetes.<sup>[17]</sup>
- Reduction in insulin resistance.<sup>[18]</sup>
- Providing certain necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells, Regenerating and/or repairing pancreatic beta cells, Increasing the size and number of cells in the islets of Langerhans.<sup>[19]</sup>
- Inhibition in renal glucose reabsorption.<sup>[20]</sup>
- Protective effect on the destruction of the beta cells.<sup>[21]</sup>
- Inhibition of  $\beta$ -galactosidase and  $\alpha$ -glucosidase.<sup>[22]</sup>
- Improvement in digestion along with reduction in blood sugar and urea.<sup>[23]</sup>
- Cortisol lowering activities.<sup>[24]</sup>
- Stimulation of glycogenesis and hepatic glycolysis.<sup>[25]</sup>
- Inhibition of alpha-amylase.<sup>[26]</sup>

## DIFFERENT TYPES OF INDUCTION OF DIABETICS IN ANIMAL MODELS

### • Alloxan

Diabetogenic action of alloxan is mediated by reactive oxygen species. Alloxan and the product of its reduction, dialuric acid, establish a redox cycle with the formation of superoxide radicals. These radicals undergo

dismutation to hydrogen peroxide. Thereafter highly reactive hydroxyl radicals are formed by the Fenton reaction. the action of reactive oxygen species with simultaneous massive increases in cytosolic calcium concentration causes rapid destruction of  $\beta$  cells. The action of alloxan in the pancreas is preceded by its rapid uptake by the  $\beta$  cells.<sup>[27]</sup>

- **Streptozotocin**

Streptozotocin 2-deoxy-2-[3-[methyl-3-nitrosourea]-d-glucopyranose]] is synthesized by streptomyces's a chromogen's and is used to induce both type-1 and type-2. Streptozotocin induces diabetes in almost all the species. diabetes dose varies with the species and the optimal dose required to produce diabetes in rat was found to be [50-60mg/kg i.p. or i.v], in mice 9175-200mg/kg i.p. or i.v] and in the dogs [15 mg/kg for 3 days]. Due to its low solubility the rapid i.v; injection appears to be best route of administration.<sup>[28]</sup>

- **Ferric nitrilotriacetate induction of diabetes mellitus**

This rarely used procedure. Rats and rabbit's parenterally treated with a large daily dose of ferric nitrilo acetate manifested diabetic symptoms such as hyperglycemia glycosuria ketonemia and ketonuria after approximately 60 days of treatment the blood insulin response to oral glucose loading poor.<sup>[28]</sup>

- **Non-insulin dependent diabetes mellitus [NIDDM] resembling animal models**

By altering the dose and the dose of the STZ injection, the n-STZ models exhibit various stages of type-2 diabetes mellitus, such as impaired glucose tolerance, mild, moderate and severe hyperglycemias neonatal STZ-induced rat model of type 2 diabetes mellitus model is generated by injecting Wistar rats on the day of their birth intravenously<sup>[28]</sup> [saphenous vein] or intraperitoneal with 100mg/kg of STZ.

- **Hormone induced diabetes**

Growth hormone induced diabetes; in intact adult dogs and cats repeated administration of growth hormone induces an intensively diabetic condition with all symptoms of diabetes including severe ketonemia and ketonuria, corticosteroid induced diabetes: hyperglycemia, glycosuria, are observed in forced fed rats treated with cortisone, in guinea pig and rabbit.

- **Insulin deficiency due to insulin antibodies**

Bovine insulin [1mg] is injected subcutaneously to guinea pig at monthly intervals and is bleed by cardiac puncture two weeks after the second and subsequent doses of antigen. Intravenously injection [0.25-1.0ml] of guinea pig anti insulin serum to rats induces aldose of dependent increase of blood glucose. This effect is due to neutralization by insulin antibodies secreted by the injected animal.

- **Virus induced diabetes**

Type-1 diabetes may due to virus infection and  $\beta$ - cell specific autoimmunity. The d-variant of the encephalomyocarditis virus [EMC-d] selectively infects and destroys the  $\beta$  cells in the male ICR Swiss mice similar to the human insulin dependent diabetic.<sup>[19]</sup>

- **Genetically diabetic animals**

Several animal species, mostly rodents have been described to exhibit spontaneous diabetes mellitus on a hereditary basis E.g.; spontaneously diabetic rats like BB rat WBN/KOB rat etc.<sup>[28]</sup>

- **Models of diabetes accelerated atherosclerosis**

Accelerated cardiovascular disease is leading cause of both morbidity and mortality in diabetic patients. Aggressive therapy of dyslipidemia is necessary since the risk of myocardial infarction is the same as in non-diabetic patients with previous myocardial infarction. Currently rats and mice are the most widely used models to study diabetes and atherosclerosis.

- **Genetic models of diabetes**

**A) Spontaneously develop diabetic rats:** These models permit the evaluation of the effect of the natural product on an animal without an interference of the side effects induced by the chemical drugs like alloxan and STZ reported above. Several recent publications summarized the major advances in this field (ex; spontaneously diabetic Gotokakizakhi rat which is a genetic model of type-2 diabetes originating from selective breeding over many generations of glucose-intolerant non diabetic wistar rats.

**B) Genetically engineered diabetic mice:** In this case, rodents may be produced to over or under express proteins thought to play an keyrole in the glucose metabolisms although significant advances in this field have arisen in recent years, especially with the advent of transgenic mice, there have been no studies carried out involving natural products on this models.<sup>[28]</sup>

## DISCUSSION

Diabetes mellitus is spreading in an alarming way throughout the world and three fourth of the world populations and considered as a major cause of high economic loss which can in turn impede the development of nations. Moreover, uncontrolled diabetes leads to many chronic complications such as blindness, heart disease, and renal failure, etc. For this, therapies developed along the principles of western medicine (allopathic) are often limited in efficacy, carry the risk of adverse effects, and are often too costly, especially for the developing world. Therefore, treating diabetes mellitus with plant derived compounds which are accessible and do not require laborious pharmaceutical synthesis seems highly attractive. The study revealed that 64 plant species were generally used for treatment of diabetes. The www.wjpr.net Vol 7, Issue 07, 2018. 2029 Mekala. World Journal of Pharmaceutical Research



majority of the experiments confirmed the benefits of medicinal plants with antidiabetic effect in the management of diabetes mellitus. The detailed natural plants not only used for the treatment of diabetes, but also treated for other ailments also. The fruits were most commonly used plant parts and other parts (leaf, root, stem, bark, flower, and whole plant) were also useful for curing. However, the diabetic model that was most commonly used was the streptozotocin and alloxan-induced diabetic mouse or rat as diabetic models. In this study, most commonly used animal model was STZ rat. The most commonly involved active constituents are Flavonoid, Tannin, Phenolics, and Alkaloid. Numerous mechanisms of actions have been proposed for these plant extracts. Some hypotheses relate to their effects on the activity of pancreatic  $\beta$  cells (synthesis, release) or the increase of the insulin sensitivity or the insulin-like activity of the plant extracts. All of these actions may be responsible for the reduction or abolition of diabetic complications.

### CONCLUSIONS AND FUTURE PERSPECTIVE

In conclusion, *A. muricata* is widely used in traditional medicine to treat a variety of ailments, such as hypertension, diabetes, and cancer. Research also stated that these plants contain various types of bioactive compounds from certain classes, such as acetogenins, flavonoids, phenols, alkaloids, and megastigmane. In vivo and in vitro research showed that it has potential to treat various conditions, such as wound healing, ulcer, inflammation, cancer, diabetes, and hypertension. In this review, we summarized the traditional uses, medicinal uses, chemical constituents, and pharmacological effects of *A. muricata*. In addition, we also emphasized the effect of *A. muricata* towards an anti-diabetic effect. There is still a significant research gap, and future studies are required to conduct detailed investigations and better understand *A. muricata*'s anti-diabetic potential. In addition, the biological studies conducted by using this crude extract are still limited to anti-diabetic effects. Meanwhile, there is no thorough metabolomic study carried out for this potential effect. The metabolite changes that are revealed from the effect of bioactivities have not been identified. Hence, the mechanisms of action cannot be well determined. Finally, *A. muricata* has a bulk of evidence on the anti-diabetic effect and the potential as an alternative diabetes mellitus treatment. However, major steps to conduct more metabolomic studies to advocate for pharmaceutical development are needed. We also hope that the information offered in this review may encourage clinical studies to be conducted on this potential.

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