Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Issue 2, 2012

Review Article

PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *ANNONA MURICATA*: A REVIEW

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Received: 20 Oct 2011, Revised and Accepted: 28 Nov 2011

ABSTRACT

In the present review, an attempt has been made to congregate the traditional, phytochemical and pharmacological studies done on an important medicinal plant *Annona muricata,* (Family annonaceae). Cyclo hexapeptides, acetogenins, annonaceous acetogenins were the major phytochemical compounds studied from this medicinal plant. The fruit is of economic value and hence cultivated and used widely as an edible food. The plant possess the major pharmacological activities includes cytotoxic, antileishmanial, wound healing, anti-microbial activity. It also has the anti-carcinogenic and genotoxic effect. Phytochemical analysis of the plant revealed the presence of tannins, steroids and cardiac glycosides which are the major phytochemical compounds. The pulp obtained from the plant shows the thermal diffusivity property. This review encompasses the potential application of the above plant in the pharmaceutical field due to its wide pharmacological activities. As the fruit of this plant is highly nutritious this paves the ways to work in future on its potential to serve as an edible vaccine.

Keywords: *Annona muricata*, Phytochemical compounds, Pharmacological activities.

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[1]. 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[2]. The relationship between food and medicine was quoted as "Let food be thy medicine and medicine be thy food".[3]

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[4]. 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[5].

According to world health organization (WHO), greater than 80% of the total world's population depends on the traditional medicines in order to satisfy their primary health care needs. It also suggested in improving the technologies for cultivation of medicinal plants[6]. The chemical substances of the medicinal plants which have the capacity of exerting a physiologic action on the human body were the primary features. The bioactive compounds of plants such as alkaloids, flavonoids, tannins and phenolic compounds were considered to be most important. The phytochemical research that has been done based on the ethno-pharmacological information forms the effective approach in the discovery of new anti-infective agents from higher plants[7].

Annona muricata L. belongs to the family of Annonaceae has a widespread pantropical distribution and has been pridely known as corossol. It is a widespread small tree and has its native in Central America[8]. The fruit of *Annona muricata* Linn. is found to be edible in Yunnan province of China[9] and their fruits is used commercially for the production of juice, candy and sherbets . Intensive chemical investigations of the leaves and seeds of this species have resulted in the isolation of a great number of acetogenins. The isolated compounds display some of the interesting biological or the pharmacological activities, such as antitumoral, cytotoxicity, antiparasitic and pesticidal properties. Roots of these species are used in traditional medicine due to their antiparasitical and pesticidal properties[10].

Annona muricata which is also called as the so ur-sop, sir sak or guanabana has been named as popular fruit tree that is cultivated throughout the tropical regions of the world .The seeds and leaves of these species was found to contain more than 50 mono-THF acetogenins. Some of the key intermediates that are involved in the biosynthesis of these acetogenins has been isolated from this species recently and were named as epomuricenins-A and B, montecristin, cohibins-A and B, muridienins-1 and 2, muridienins-3 and 4, muricadienin and chatenaytrienins-1, 2 and 3 and also a new compound called as sabadelin which might be a biogenetic precursor of cis-panatellin[11].

Guanabana is found to grow more in many of the regions of the tropical world was extensively studies for the exploration of the new Annonaceous acetogenins from its bark, seeds and leaves which possess much of the diverse biological activities. Studies done on the leaves of A. muricata has been resulted in the isolation of eight cytotoxic acetogenins[12].

Fruit Description

The soursop from the Annonaceae family is found to be the most important tropical fruit that contributes much to the wider economic growth of some of the tropical countries such as tropical America, Australia, Africa and Malaysia. The soursop flavor possess a maximum of 114 volatile compounds that is found to be responsible for the whole aroma profile, 44 esters, 25 terpenes, 10 alcohols, 9 aldehydes and ketones, 7 aromatic compounds, 5hydrocarbons, 3 acids, 3 lactones and 8 other miscellaneous compounds .

Soursop gives a flavor of custard when it is ripen condition and hence has a pleasant, distinctive aroma and fibrous pulp that can be consumed because of its very juicy, creamy and sweet character. The fruit has a weight of about four kilograms and it is found to be the largest in its family that lends itself to be the processed into various other products such as juice blends, nectars, syrups, jams, jellies and ice-creams. This unique flavor of soursop increases its processed products to possess much potential in the international market.

Esters were found to be the dominant compounds regardless of the soursop's origin, with methyl (E)-2-hexenoate, methyl (E)-2-butenoate, methyl butanoate and methyl hexanoate being the four principal compounds. There are different methods that have been employed for the flavor compounds analysis, among which the most common methods are solvent- and steam distillation–extraction[13].

Starch which has been isolated from the sweetsop and soursop fruits was also characterized and was found that both the starches isolated possess small granules of about 2.49–2.76 lm and the similar amylose composition of about 19% and gelatinization temperatures of about 64.12–72.99°C for sweet and 65.67–75.30°C for soursop[14].

Guanabana seed meal is found to be a richest source of (*S*)-oxynitrilase which is used as a biocatalyst and it is responsible for catalyzing the enantio selective addition of HCN to aromatic, heteroaromatic and other alpha beta-unsaturated aldehydes to produce cyanohydrins[15].

Phytochemical Constituent

Type of compound	Constituent	Extract tested	Part used	Techniques involved-structural elucidation	Structure of the compound
Cyclohexapeptide[8]	annomuricatin C	methanol extract	Seeds	MS/MS fragmentation using a Q-TOF mass spectrometer equipped with an ESI source, chemical degradation and extensive 2D-NMR	*cyclo*(Pro1–Gly2–Phe3–Val4–Ser5–Ala6–)
Cyclopeptide[9]	annomuricatin B	alcohol extract	Seeds	chemical and spectral methods	cyclo-(prolyl-asparaginyl-alanyl-tryptophyl-leucyl-glycyl-thryl
Acetogenins[10]	-Cohibins A and B	methanol extract	Roots	characterized by tandem mass spectrometry (MS/MS)	-
Acetogenin[11]	Sabadelin	methanolic extract	Roots	characterized by tandem mass spectrometry (MS/MS)	-
Annonaceous acetogenins[12]	muricoreacin and murihexocin C	ethanol	leaves	MS\ 1H and 13C NMR\ COSY and Single-relayed COSY experiments	-
Acetogenin[16]	Murihexol, donhexocin, annonacin A and Annonacin	defatted with hexane and percolated with 95% EtOH	Seeds	FAB-MS\ 1H and 13C NMR\ COSY	-
Acetogenins[17]	murihexocins A and B	-	Leaves	MS, 1H NMR, and 13C NMR	-
Acetogenins[18]	Annohexocin	ethanolic	leaves	planar structure of 1 was determined by MS, IH and tSc NMR, HMQC, COSY, and carefully designed single-relayed COSY experiments	-
Cyclic hexapeptide[19]	annomuricatin A	ethanolic	Seeds	types and sequence of the amino acids were confirmed by X-ray diffraction analysis	-

The table gives the information about the phytochemical constituents that has been isolated from different parts of the plant with different solvents.

Annonaceous acetogenins are a series of polyethers which contains either the adjacent or the non adjacent tetrahydrofuran (THF) or tetrahydropyran (THP) ring and also an a, b-unsaturated c-lactone ring. They possess the most beneficial antitumor, cytotoxic, antimalarial and antifeedant properties. Acetogenins gets interacted with the NADH–ubiquinone oxidoreductase (complex I) in mammalian and in the insect mitochondrial electron transport systems and/or with ubiquinone-linked NAD (P)H oxidase in the cancer cells cytoplasmic membranes[20].

The first cyclopeptide gramicidin S has been discovered in almost 20th century of around 1940s. Naturally occurring cyclopeptides has been usually isolated from various sources which includes marine invertebrates and higher plants and their characteristic structure and stability to enzyme offered them with the extensive and remarkable biological activities such as anti-tumor, antifungal, antivirus, enzyme inhibition, etc. that is closely associated to their molecular conformation.

The cyclopeptides three-dimensional molecular conformation structures in the solid state and many other studies on the crystal structures have been reported by the technique of X-ray diffraction analysis eventhough most of the structures of cyclopeptides were also clarified by spectrum method. But, the amino acid sequence is not determined properly everytime[21].

Pharmacological Activities

Cytotoxicity and antileishmanial activity of *Annona muricata* pericarp

When the hexane, ethyl acetate and methanol extracts of *Annona muricata* pericarp were tested in vitro against *Leishmania braziliensis* and *L. panamensis* promastigotes and also against the cell line U 937, ethyl acetate extract was found to be more active than GlucantimeW which was used as the reference substance and the other extracts. Further fractionation of the extract has resulted in the isolation of three acetogenins namely annonacin, annonacin A and annomuricin A[22].

Anti-viral activity

Annona muricata extract was screened against Herpes simplex virus-1 (HSV-1) and clinical isolate (obtained from the human keratitis lesion) in order to check whether they inhibit the cytopathic effect of HSV-1 on vero cells which is the indicative of anti-HSV-1 potential. The minimum inhibitory concentration of ethanolic extract of *A. muricata* was found to be 1 mg/ml which shows that the *A. muricata* could be used as the potential antiherptic drugs[23].

Anticarcinogenic and genotoxic effects

Acetogenins (Ace) are the chemicals whish possess various biological properties including the cytotoxic effect against the neoplasic cells which suggests their potential usage as the antitumoral agents. Acetogenins also possess the capacity to reduce the mouse colon crypts that is induced by azoxymethane (Azo) and was found that 50% reduction in the amount of crypts in the animals treated with acetogenin when compared with the level determined in mice treated with Azo[24].

Wound Healing Activity

Wound is the first medical problem that is faced by the human race. The knowledge about wounds and their management remains still in the primitive and stunted stage. A wound is a disrupted state of tissue that is caused by the physical, chemical, microbial or immunological insult which heals either by the regeneration or fibroplasias finally. The wound healing activity of alcoholic extract of stem and bark of *Annona muricata* was found to show the marked reduction in area of the wound which was tested in the albino rats which proves their possible use in the healing the wound[25].

Anti-microbial activity

The antibacterial effect of the methanolic and aqueous extract of the leaves of *Annona muricata* was tested against various bacterial strains such as *Staphylococcus aureus* ATCC29213, *Escherichia coli* ATCC8739, *Proteus vulgaris* ATCC13315,*Streptococcus pyogenes* ATCC8668, *Bacillus subtilis* ATCC12432, *Salmonella typhimurium* ATCC23564, *Klebsiella pneumonia* NCIM No.2719 and *Enterobacter aerogenes* NCIM No. 2340.Among the above organisms tested, *B. subtalis* and *S.aureus* was found to be the most susceptible Gram-positive bacteria while *K. pneumoniae* and *P. vulgaris* was found to be the most susceptible Gram-negative bacteria . Leaf extract of *Annnona muricata* is used in the treatment of various bacterial infectious diseases such as pneumonia, diarrohea, urinary tract infection and even some skin disease. *Annona muricata* extract contains a wide spectrum of activity against a group of bacteria that are responsible for the most common bacterial diseases. Thus, the plant possesses an abundant of the antibacterial compounds[25].

Other Studies

Phytochemical analysis

Phytochemical analysis of the leaf extract of the above plant revealed the presence of secondary metabolites like tannins, steroids, cardiac glycosides, etc. were present in very trace amounts. Secondary plant metabolites which are called as the phytochemicals possess some of unknown pharmacological activities. Phytochemicals with adequate antibacterial efficacy can be used for the treatment of bacterial infections[25].

Thermal diffusivity of soursop (*Annona muricata L.*) pulp

Studies on the thermal diffusivity of foods are very much essential for the designing and optimizing of every process that is involved in heat transfer at the unsteady state. The thermal diffusivity of soursop pulp was determined by means of the usage of the heat penetration curves in 8Z short cans that is considered as the cylindrical objects. The pulp that is obtained from fruits were tested in both ripen and in the unripe condition at three different temperature ranges including the freezing zones. The study conducted showed no difference in the thermal diffusivity values at a 5% significance level[26].

CONCLUSION

Medicinal plants were the potent source of human health due its active compounds that is responsible for its various pharmacological activities. *Annona muricata,* a traditional medicinal plant was investigated and showed that the phytochemical constituents and the bioactive compounds posses the medicinal properties which makes them to be a potential species in the family of *Annonaceae.* Research works done on this plant reveals its beneficial aspect in the field of pharmacy. Ayurvedic preparation in the form of fruit would be the target of the present technology. This could be achieved in case of the above plant.

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