

Plants of Annonaceae Family A Potential Source of Various Pharmacological Activity: A Brief Review

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Abstract

Herbs are the oldest form of health care known to mankind. All cultures throughout history have used herbs. Medicinal plants have provided the basis of health systems worldwide since the dawn of man and plant products remain a major source of medicine/ preparations for a variety of diseases. The Annonaceae family is a family of flowering plants made up of trees, shrubs, or more or rarely lianas, with 2106 recognized species and more than 130 genera. Several genera produce edible fruit including Annona, Annonidium, Asimina, Rollinia, and Ovaria. The family is concentrated in the tropics, with about 900 species in the neotropics, 450 species in the African tropics, and the rest in India- Malaysia. Some species of this family are used as food ingredients with medicinal properties. Herbs and phytoconstituents appear safe and effective and produce fewer or no side effects than synthetic drugs. The use of plants in religious rituals as well as for magic and medicinal purposes is well-known and widespread. In the modern era most people believe that plants and plant phytoconstituents are better options for treating diseases than allopathic medicines, even though most of the drugs used in primitive medicine are derived from plants. In this review, various plants of the Annonaceae family have been described and detailed information on their pharmacological activities have been reported.

Keywords: Annonaceae, Traditional uses, Phytoconstituents, Pharmacological activity, Herbs.

Introduction

Herbs have been used by all cultures throughout history. Medicinal plants have created the foundation of health care systems throughout the world since the initial stage of humanity and still, plant products are the major source of drug/formulation in the treatment of various diseases. Herbal drugs and phytoconstituents resemble safety and efficacy, they produce less/no side effects when compared to synthetic drugs. The use of plants in religious rituals as well as for magic and medicinal purposes is well-known and widespread.

In the modern era, most people believe that plants and plant phytoconstituents are better options for treating diseases than allopathic medicines, even though most of the drugs used in primitive medicine are derived from plants [1-3]. According to the World Health Organization, 80% of people living in developing countries depend almost exclusively on traditional medicine for their primary healthcare needs. Exploration and pharmacological screening of phytochemicals can provide us with a basis for developing new lead compounds for drug development. World Health Organization (WHO) defines medicinal plants as herbal preparations produced by introducing plant materials into various processes, including extraction, fractionation, purification, concentration, or other physical or biological processes that may be produced as the basis for an herbal product or for immediate consumption. The Annonaceae are a very large botanical family made up of about 120 genera and more than 2000 species. It is a very homogeneous family, based on morphology and habitat, as a source of edible fruits and oil. Compared to its large size, the Annonaceae appear as one of the least known families chemically and pharmacologically [4,5]. This family is widely distributed across the continents such as Asia, South and Central America Australia, and Africa. Annonaceae has been listed as a diverse family of aromatic trees, bushes or shrubs, and climbers or lianas, which are predominantly found in tropical and subtropical regions, with a limited number growing in temperate zones. As this family is widely distributed in tropical and subtropical regions, it is traditionally used. The various parts of the species are used including leaves, seeds bark, fruit, and roots used traditionally. A wide range of chemical compounds from various parts of Annonaceae plants have been discovered isolated and characterized for their phytoconstituents and various biological activities [6].

Various plants from this family have recently attracted the attention of researchers due to their medicinal value. *Annona squamosa* is a medicinal plant with edible fruits and has been used as a traditional medicine for many years with benefits for patients with various diseases. Various chemical compounds, such as alkaloids, carbohydrates, tannins, phenolic compounds, isomeric hydroxyl ketones, cyclopeptides, and acetogenins can be found in different parts of the *A. squamosa* plant [7]. Studies report that the purified fruit pod extracts and seed oil of *A. squamosa* exhibit broad-spectrum antibacterial properties. Many studies reported the therapeutic effects of *A. muricata*, such as anti-tumor, anti-helminth, anti-fungal, anti-bacterial, hypotensive, anti-viral, and anti-inflammatory effects [8]. Various parts of *A. cherimola* were phytochemically screened and found to contain various polyphenols and alkaloids. The leaves were found to contain bioactive compounds that potentially be used as treatment for skin and eye diseases, and gastric, cardiovascular intestinal disorders [9]. *A. reticulata* is commonly known as Bullock's heart or Ramphal and is widely distributed all over India. Its leaves, bark, roots, and stem possess isoquinoline alkaloids. Its leaves are used as anthelmintic, insecticides, and sypitics [10]. *A. reticulata* has been used to treat epilepsy, dysentery, cardiac problems, constipation, hemorrhage, bacterial infection, parasite and worm infestations, fever, ulcers, and as an insecticide. *Annona crassiflor* is known as the araticum of cerrado. In folk medicine, the seeds are used to treat scalp infections, and infusions of the leaves and seeds are utilized for their antidiarrheal and antitumor properties [6].

The genus *Artabotrys* consists of 2200 species and it belongs to the family Annonaceae. Geographically it is distributed in tropical and subtropical regions of East Asia and Africa. *Artabotrys suaveolens* is traditionally used to treat menstruation and cholera [11].

Artabotrys Hexapetalus wildy grown in China, Phillipines, Indochina, and Java. This species is reported to be an indigenous shrub to southern India and Shri Lanka. *A. hexapetalus* is considered a folk drug having various medicinal uses. As Chinese traditional folk medicines, its roots and fruit are used to treat malaria and scrofula. The flowers of *A. hexapetalus* are tonic and stimulant. The fruits and the bark are used to treat fever, diarrhea, skin diseases, wounds, ulcers, inflammation, cough, asthma, and bronchitis. The decoction of leaves is used as an antimicrobial, antifertility, muscle relaxant, and cardiac stimulant. Flowers are used as a flavoring in tea in Southern India; in Sri Lanka Used in perfumery as the source of essential oils [12].

Plants from the Family Annonaceae

Annona Squamosa Linn

Annona squamosa Linn is a small ever green tree is cultivated throughout India for its fruits, and different parts [13]. This plant is extensively cultivated in various states of India, including Maharashtra, Gujrat, Madhya Pradesh, Assam, Bihar, Andhra Pradesh, and Tamil Nadu. *Annona squamosa* is a medicinal plant with edible fruits and is commonly known as the sugar apple or custard apple. This plant belongs to the Annonaceae family and has been used as a traditional medicine for many years with benefits for patients with various diseases [14,15]. The plant is traditionally used for the treatment of epilepsy, dysentery, cardiac problems, worm infestation, constipation, hemorrhage, antibacterial infection, dysuria, fever, and ulcers. It also has antifertility, antitumor, and abortifacient properties [16-22]. Custard apple fruit are numerous and it appears to possess potent bioactive principles in most of its plant parts (fruit, seed, and leaves). The various chemical constituents isolated from leaves, stems, and roots of the plant include anonaine, aporphine, coryeline, isocorydine, norcorydine, and glaucine. Essential oils, pinenes have also been described and extracted from custard apple [23]. The phytochemical screening demonstrated the presence of different types of compounds like alkaloids, coumarins, flavonoids and steroids which could be responsible for the antidiabetic activities [24]. 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 -Dxylopyranosyl- β -D-glucopyranosyl)-oxy)benzene, Anonaine, Benzyltetrahydroisoquinoline, Borneol, Camphene, Camphor, car-3-ene, Carvone, β Caryphyllene, Eugenol, Farnesol, Geraniol, 16- Hetriacontanone, Hexacantanol, Higemamine, Isocorydine, Limonine, Linalool acetate, 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 nTriacontanol. Alkaloids, proteins & amino acids are absent in the leaf extract [25]. antidiabetic activity of hydroalcoholic extract of *Annona Squamosa* Linn. in experimentally induced diabetic rat model. Treatment with *Annona Squamosa* extract and Glibenclamide at a dose of 350mg/kg and 5mg/kg respectively for 28 days, after induction of diabetes by Streptozotocin, caused significant reduction in blood serum glucose, lipid profiles like serum cholesterol and triglycerides but significant increase in HDL and body weight in diabetic rats compared to untreated group. And leaves of *Annona Squamosa* Linn. can be used as potential antidiabetic drug. [26].

Annona Montana

Annona montana contains monotetrahydrofuranic acetogenins which have toxicity to liver cancer in Hep G2 cells [27]. A novel Annonaceous acetogenin, montanacin F, with a new type of terminal lactone unit, was isolated from the leaves of *Annona montana*. In addition, the cytotoxicity of montanacin F was evaluated in vitro against Lewis lung carcinoma (LLC) tumor cell lines. Furthermore, the previously isolated cytotoxic acetogenin annonacin against LLC was examined for in vivo antitumor activity with LLC tumor cells [28].

Annona Muricata

Annona muricata is the most widely used species worldwide in traditional medicine, as foodstuff, and in the cosmetic industry. Most commonly this plant is used to treat malaria, fevers, liver ailments, and headache. *Annona muricata* L. commonly known as graviola or soursop, belongs to the family of Annonaceae. It is a typical tropical tree with heart-shaped edible fruits and widely distributed in most of tropical countries. Various parts of *A. muricata*, such as leaves and bark, have been used for medicinal purposes. Over 200 chemical compounds have been discovered and extracted, including phenolics, acetogenins, and alkaloids. The leaves of it are lanceolate with glossy and dark green in color had been traditionally used to treat headaches, hypertension, cough, and asthma, and are used as antispasmodic, sedative, and nervine for heart conditions. Previous reports over the years have demonstrated that the leaf, bark, root, stem, and fruit seed extracts of *Annona muricata* are antibacterial. *Annona muricata* (soursop) is a potent anticancer plant of the Annonaceae family. The therapeutic potentials of the n-butanolic extract of *Annona muricata* were studied on WRL-68, MDA-MB-435S, and HaCaT cell lines. Since most of the chemotherapeutic drugs also affect normal cells, WRL- 68 cells were analysed for the relative cytotoxic response in comparison that was quantified in MDA-MB-435S and HaCaT cell lines. nButanolic leaf extract of *A. muricata* possesses significant anticancer potentials in human cancerous cells. Plant phenolics are a major group of compounds that act as primary antioxidants or free radical scavengers [29].

Annona Reticulata

Phytochemicals are secondary metabolic compounds found in plants. Many of these are known to provide protection against insect attacks and plant diseases, stimulation of the immune system, modulation of hormone metabolism, and antibacterial and antiviral effects [30, 31]. The most important of these bioactive constituents of *Annona reticulata* are Alkaloids, Tannins, Flavonoids, Cardiac glycosides, Steroids, and Saponins [31]. The Ethyl acetate extract of leaves showed 19 mm of zone of clearance in both *Pseudomonas putida* and *Lactobacillus acidophilus*. The Butanol extract of the leaf showed the highest zone of inhibition in *Streptococcus mutans* with 18mm. The Methanol extract showed a high zone (19.5mm), which is approximately equal to the commercially available synthetic antibiotic (22 mm). Thus, the *Annona reticulata* leaf extract showed antibacterial activity against both gram-positive and gram-negative bacterial strains [32].

Annon Crass flora

The traditional use of this plant includes the treatment of wounds, venereal diseases, snake bites, louses and as antimicrobial, antidiarrheal, and antirheumatic [33, 34, 35]. The seeds of *Annona crassiflora* have high antioxidant activity. Annonaceous acetogenins, aporphine alkaloids, and steroids were isolated from the ethanolic extract of wood.

The extract and some fractions presented antimalarial and antimicrobial activities. The ethanolic extract of *Annona crassiflora* seeds exhibited in vitro significant cytotoxicity to human lung carcinoma (A-549) and melanoma (RPMI 7951) cells. From this extract, an acetogenin (ACG – acetogenin) named araticulin was isolated. The biological effects of many annonaceous have been related to the ability of ACGs to inhibit the NADH: ubiquinone oxidoreductase (complex 1) of the mitochondrial electron transport chain. This class of molecules has been suggested to be a group of potential anti-neoplastic agents. However, cytotoxicity could be associated with genotoxicity, as observed in many anti-tumoral substances of natural or synthetic origin. The presence of genotoxic action in anti-tumoral compounds does not benefit the organism in the long term [36].

Anon Cherimoya

The plant contains alkaloids, flavonoids, glycosides, saponins, tannins, carbohydrates, proteins, phenolic compounds, phytosterols, and amino acids. The anti-stress activity of cherimoya is mainly attributed to these constituents with established antioxidant activity [37].

Artabotrys Hexapetalus

The genus artabotrys is one of the big genera of the family Annonaceae which is composed of more than 100 species and distributed in tropical and subtropical regions of the world specifically Asia, Africa, and Indomalayan regions. Plants of Artabotrys genus are climbing herbs bearing recurved hooks borne on lateral branches and scandent shrubs are one of the largest genera of the family. *A. hexapetalus* is considered a folk drug having medicinal value [12,38]. The flowers of *A. hexapetalus* are tonic and stimulant. The fruits and the bark are used to treat fever, diarrhea, flatulence, colic constipation, skin disorders, wound healing, cough, and bronchial asthma. The decoction of leaves is used as an antimicrobial, antifertility, muscle relaxant, and cardiac stimulant [39]. Studies show that Artabotrys hexapetalus leaves ethanolic extract contain various phytochemicals like carbohydrates, proteins, alkaloids, flavonoids, terpenoids, glycoside, saponins, and phytosterol and studies revealed the presence of compounds the presence of reducing sugars, fatty acids, phenolic compounds, alkaloids, flavonoids, tannins, saponins, emodins, anthroquinones, anthocyanin, steroids, coumarins and leucoanthocyanins in hydro-ethanolic extract of leaves of *A. hexapetalus* [40,41].

Artabotrys Suave lens

Artabotrys Suaveolens is an evergreen shrub belonging to the family Annonaceae. Traditionally this plant is used to regulate menstruation and treat cholera. *A. suaveolens* has a unique aroma and is very fragrant, classifying it as an aromatic plant. This plant is widely distributed in Southeast Asian countries. Local people in Indonesia, especially the Batak tribe, use *A. suaveolens* leaf as one of the ingredients in their local food to cure digestive disturbance. Other traditional usages are as emmenagogues, as well as a remedy against cholera and inflammation related to enlarged spleen [42].

Conclusion:

The Annonaceae family is rich in potential as a source of chemical entities for the development of novel drugs. Several species belonging to this family have been well studied and have provided active biochemical substances. A large number of species traditionally used to treat various ailments from this family have not been studied so far, thus ample chemical or pharmacological data are available. Thus, the finding of chemical entities along with screening for various pharmacological activities could provide the lead compounds necessary for new drug development.

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