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Review Article

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Phytochemical and Pharmacological potential of *Annona cherimola*-A Review

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A B S T R A C T

Several plant remedies have been employed in various medicinal systems for the treatment and management of different diseases. During past several years, there has been growing interest among the usage of various medicinal plants from traditional system of medicine for the treatment of different ailments. Traditional system of medicine consists of large number of plants with various medicinal and pharmacological importances and hence represents a priceless tank of new bioactive molecules. Annona cherimola Miller is a multipurpose tree with edible fruits and is one of the sources of the medicinal products. This review attempts to encompass the available literature on Annona cherimola with respect to its pharmacognostic characters, phytochemical constituents, pharmacological activities and traditional uses.

Keywords: Annona cherimola, phytochemicals, pharmacological activities.

Introduction

Plants are one of the most important sources of medicines. Since the beginning of human civilization, medicinal plants have been used by mankind for its therapeutic value. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Many of these isolations were based on the use of the agents in traditional medicine. According to the WHO, the plant based, traditional medicine systems continues to play an essential role in health care, with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care [1,2]. India has several traditional medicinal systems, such as Ayurveda, Unani and Siddha, which has survived through more than 3000 years, mainly using plant-based drugs. The ancient texts like Rigveda (4500-1600 BC) and Atharva veda mention the use of several plants as medicine. The books on ayurvedic medicine such as Charaka Samhita and Susruta Samhita refer to the use of more than 700 herbs [3]. In India, the ayurvedic system has described a large number of such medicines based on plants or plant product and the determination of their morphological and pharmacological or pharmacognostical characters can provide a better understanding of their active principles and mode of action.

In the present age of pharmaceuticals various chemical has been employed for the effective management of disease. Plants have been always the main principle form of medicine since traditions in India and now-a-days it becomes most popular throughout the world. Herbal medicines are not only providing traditional and ethnic medicine but also promising for highly efficient novel bioactive molecules. Since ages, man has been dependent on nature for curing various diseases. The plants used, as drugs are fairly innocuous and relatively free from toxic effects or were so toxic that lethal effects were well known. The plants are a reservoir of potentially useful chemical compounds which serve as drugs, are provided newer leads and clues for modern drug design by synthesis [4].

In India, it is reported that traditional healers use 2500 plants species and 100 species of plants serve as

regular sources of medicine [5]. During the last few decades there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world [6,7]. Ayurveda, Siddha, Unani and folk (tribal) medicines are the major systems of indigenous medicines. Among these systems, Ayurveda is more developed and widely practised in India. Ayurveda dating back to 1500-800 BC has been an integral part of Indian culture. About 8,000 herbal remedies have been codified in Ayurveda. The Rigveda (5000 BC) has recorded 67 medicinal plants, Yajurveda 81 species, Atharvaveda (4500-2500 BC) 290 species, Charaka Samhita (700 BC) and Sushrut Samhita (200 BC) had described properties and use of 1100 and 1270 species respectively, in compounding of drugs and these are still used in the classical formulations, in the Ayurvedic system of medicine.

Several phytochemical surveys have been published, including the random sampling approach which involved some plant accessions collected from all parts of the world. The major the alkaloids and steroidal saponins, however other diverse group of naturally occurring phytocomponents such as flavonoids, tannins, unsaturated sterols, terpenoids, essential oils etc have also been reported [8,9]. There is currently a large and ever expanding global population base that prefers the use of natural products in treating and preventing medicinal problems because herbal plants have proved to have a rich resource of medicinal properties [10]. In recent years, secondary metabolites, previously with known pharmacological activities, have been extensively investigated as a source of medicinal agents [11]. Among the different plant derivatives, secondary metabolites proved to be the most important group of compounds that showed wide range of antibacterial and antifungal activity [12, 13].

Herbal plants produce a variety of chemical compounds that act upon the body and used to prevent or treat disease or promote health and well-being. Herbal drugs have increasingly been used worldwide during the last few decades as evidenced by rapidly growing global and national markets of herbal drugs [14]. Herbal medicines are in great demand in the developed as well as developing countries for primary health care because of their wide biological and medicinal activities, higher safety margins and lesser costs [15].

This review attempts to include the existing literature on Annona cherimola with respect to its pharmacognostic characters, chemical constituents, synopsis of its various pharmacological activities and traditional uses.

Annona cherimola Miller

The members of the Annonaceae family are mostly perennial small trees comprising about 140 genera and 2500 species within the order of magnoliales [16]. Three genera (Annona, Rollinia and Asimina) produce edible fruits [17]. The genus Annona contains approximately 100 species and can be found in tropical America and Africa [18]. Among these, Annona cherimola is a deciduous or semi-evergreen shrub or small tree reaching 7 m tall. It is also known as cherimoya and is commercially cultivated for its edible fruits and for traditional uses. Anthropological evidence suggests that the cherimoya fruit was an active ingredient in the Incan diet [19].

Table 1. Vernacular names of Annona cherimola [20]

Languages	Common names
English	cherimoya, custard-apple, cherimoya
Spanish	anona poshte, cherimolia, cherimoyer, cherimolla, cherimoya
French	anone, cherimolier, cherimole
German	cherimoya, cherimolia, cherimoyabaum, chirimoya
Portuguese	grabiola, graveola, graviola
Japanese	cherimoa, cherimoya
Italian	cherimolia
Mexico	Pox or poox
Hindi	Hanuman phal, Marytiphal
Telugu	Hanuman phalamu

Origin and geographical distribution

Annona cherimola (Annonaceae), commonly known as cherimoya is a deciduous or semi-evergreen shrub or small tree native to Andean-highland valleys of Ecuador and northern Peru and is distributed widely in the tropical or sub tropical regions, America, Africa and Asia and even in the south of Europe where it is cultivated for its edible fruits [21]. Cherimoya is known to have been cultivated during the time of the Incan Empire, dating back to 1200 BC [22]. Its cultivation must have spread in ancient times to Chile and Brazil for it has become naturalized in highlands throughout these countries.

Many researchers include Peru as centre of origin but others assert that the fruit was unknown in Peru until after seeds were sent by P. Bernabe Cobo from Guatemala in 1629 and those thirteen years after this introduction the cherimoya was observed in cultivation and sold in the market of Lima [23].

In 1757, it was carried to Spain where it remained a dooryard tree until the 1940's and 1950's when it gained importance in the province of Granada, in the Sierra Nevada mountains, as a replacement for the many orange trees that succumbed to disease and had to be taken out.

In 1790, the cherimoya was introduced into Hawaii by Don Francisco de Paulo Marin. In Hawaii, it is still casually grown in the Islands and naturalized in dry highland forests. In 1785, it reached Jamaica, where it is cultivated and occurs as an escape on hill stations between 3,500 and 5,000 ft. It found its way to Haiti sometime later. The first planting in Italy was in 1797 and it became a favoured crop in the Province of Reggio Calabria.

During 1878, the plants has been tried several times in the Botanical gardens, Singapore but has always failed to survive due to climatic conditions. At the same time, in the Philippines, it does well in the hilly areas at an altitude above 2,460 ft.

It was introduced into India and Ceylon in 1880 and there is small scale culture in both countries at elevations between 1500 and 7000 ft. The tree was planted first in Madeira in 1897, then in the Canary Islands, Algiers, Egypt and probably via Italy, in Libya, Eritrea and Somalia. In 1907, the United States department of Agriculture imported a number of lots of cherimoya seeds from Madeira [24].

The edaphoclimatic conditions of the Madeira Islands are favourable for the production of tropical and subtropical fruits. Cherimoya production in Madeira Islands remains from its colonization and nowadays have an important role for the economic development with an annual production around 1000 Ton per year, exporting to the Mainland, France, Spain and England markets. It is also grown on a small scale in the United States, Chile, and Spain [25].

Ecology

Cherimoya is mainly cultivated in the highlands from sea-level up to approximately 1400 m altitude. In Colombia and Ecuador, it grows naturally at elevations between 1400-2000 m where the temperature ranges between 17-20^{0}C [24].

Morphological characteristics

The cherimoya tree is erect but low branched and somewhat shrubby or spreading and ranging from 5 to 9 m [20].

Leaves

Leaves are briefly deciduous to semi-deciduous due to the mitriform petiole concealing the bud. They are alternate, 2-ranked, with minutely hairy petioles; ovate to elliptic, short blunt pointed at the apex; slightly hairy on the upper surface, velvety on the lower surface [26].

Flowers

Fragrant flowers, solitary or in group of 2 or 3, on short hairy stalks, have 3 outer, greenish, fleshy, oblong petal-like tepals and 3 smaller inner tapels [20].

Fruit

The syncarp fruit, formed by amalgation of pistils and receptacle, is conical or somewhat heart-shaped, 10 to 20 cm long and upto 10 cm in width, weighing on average 150-500 g, but extra large specimens of 2.7

kg or more have been reported [27]. The skin may be smooth with finger print-like markings or covered with conical or rounded protuberances. The fruit is easily broken or cut open, exposing the snow-white, juicy flesh of pleasing aroma and delicious, subacid flavour, and is containing numerous hard, brown or black bean like, glossy seeds, 1.25 to 2 cm long [26].

Diseases and Pests

Cherimoya is susceptible to different pests and diseases, which vary according to country of cultivation and probably to cultivar, but is probably resistant to nematodes [26]. The most serious diseases are bacterial wilt (Pseudomonas solanacearum), producing collar rot, tree decline and eventual tree death, Oidium sp and Botrytis cinerea. Important fruit diseases are black canker (Phomapsis annonacearum.), diploidia rot (Botryodiplodia sp), purple blotch (Phytophtora sp.), spot (Cylindrocladium sp), all increasing under moist or wet conditions [28,29]. Anthracnose disease (Colletotrichum gloeosporoides) seems to be a problem in warmer climatic zones such as Florida [30] and Australia [31]. The most serious pest is the fruit fly, belonging to the genus Anastrepha in Southern America [32]. Common pests besides fruit fly are seed borer (Bephratelloides sp.), which damages fruits, and leaf miner (Phyllocnistics sp.) that can destroy considerable amounts of leaves, thus reducing photosynthesis. Minor pests are mealy bugs (Planococcus sp. and Pseudococcus sp.), spotting bugs (Amblypelta sp.) and scales (Parasaissetia sp.) [29].

Nutritional composition

The nutritional composition of cherimoya fruit is that of a typical sweet fruit but with a high content of carbohydrates and low content of acids (Table 2). Its vitamin A content is modest, but it is a good source of thiamine, riboflavin, niacin, iron, calcium and phosphorous [33].

Table 2. Nutritional composition of 100 g of cherimoya pulp [32].

Constituents	Quantity (per 100g edible portion)
Water	77.1 g
Protein	1.9 g
Fat	0.1 g
Carbohydrates	18.2 g
Fibre	2.0 g
Ash	0.7 g
Calcium	32.0 mg
Phosphorous	37.0 mg
Iron	0.5 mg
Vitamin A	0.01 IU
Thiamin (Vitamin B_1)	0.1 mg
Riboflavine (Vitamin B_2)	0.14 mg
Niacine	0.9 mg
Ascorbic acid (Vitamin C)	5 mg
Calories	73 kcal

Phytochemical constituents

The plant is reported to contain alkaloids, flavonoids, glycosides, saponins, tannins, carbohydrates, proteins, phenolic compounds, phytosterols, and amino acids [34]. The antistress activity of cherimoya is mainly attributed to these constituents with established antioxidant activity [34]. The various chemical constituents isolated from stem and seeds of the plant including annocherine A, B, cherianoine, aromin-A, N-cis-caffeoyltyramine, dihydro-feruloyltyramine, N-trans-feruloylmethoxytyramine and N-cis-feruloyltylmethoxytyramine [35,36,37]. Specimens of cherimoya from Taiwan contained cherimoline [38]. Seeds contain cyclooctapeptieds, cherimolacyclopeptide A, and cherimolacyclopeptide B [21].

The volatile constituents of cherimoya bark were identified from the essential oil obtained by the steam distillation and studied by Gas chromatography and Mass spectrometry. The bark contains annonaine, an alkaloid which is found to posses many of the properties. The major compounds were identified as methyl butanoate (69.08%), butyl butanoate (56.56%), 3-methylbutyl butanoate (15.36%), 3-methyl butyl 3-

methyl butanoate (56.69%) and 5-hydroxymethyl-2-furfural (71.82%) [39].

Traditional uses

Cherimoya is essentially a dessert fruit that is eaten fresh. It can also be used for making ice-cream, milkshakes or sorbets and is processed into yoghurt, flan fruit juice and wine [40, 41]. Occasionally it is seeded and added to fruit salads or used for making sherbet or ice-cream. Due to its enzymatic characteristics, cherimoya fruits cannot be submitted to thermal processes and its processing should utilize refrigerating or freezing, with addition of antioxidants to avoid enzymatic oxidation and subsequent colouring [42]. Traditionally, cherimoya seeds are crushed and used as insecticide, mostly to kill lice and cure parasitic skin disorders [43].

Biochemically, cherimoya seeds are an important source for acetogenins [44], a type of alkaloid, all of which show antiparasitic and cytotoxic activities that are used in pharmaceuticals [45]. The annonaceous acetogenins are a new group of powerful bioactive agents and more than 300 of these compounds have been found. Properties attributed have been antimicrobial, antitumor, cardiotonic and insecticidal [28].

The fruit is very low in cholesterol and sodium. It is a good source of dietary fibre, vitamin B_6 and potassium, and a very good source of vitamin C. The cherimoya fruit is known for its exceptional taste, its use in traditional medicine as an antimicrobial and insecticide, and as an effective treatment for digestive disorders such as stomach-ache and pancreatic ulcers [46]. In Jamaica, the dried flowers have been used as flavouring for snuff. Cherimoya is an immature fruits are used in vegetable curries. The entire immature fruit is used as a cooked vegetable. A decoction of the bark is used both as a tonic and a remedy for diarrhoea. The root is chewed to relieve toothache and a decoction from the root is used to treat fevers. A decoction of the leaves is used to treat worms. The leaves are used to tan leather.

Pharmacological activities

Antioxidant activity

The free radical scavenging potential of the different extracts of fruits of Annona cherimola was evaluated in-vitro by employing diphenyl-picryl-hydrazy (DPPH) assay method. In this investigation, the antioxidant which present in the fruit extracts reacted with DPPH, which is a stable free radical and converted into 1,1-diphenyl-2-picryl hydrazine which has measured at 517 nm. The ethanolic, methanolic and dimethyl formammide (DMF) extracts at 1000 µg/ml showed good radical scavenging activity towards DPPH, although the DMF extract showed maximum of quenching DPPH free radicals, observed upto 69% followed by methanolic extract (52.7%) and ethanolic extract (50.5%). In this investigation different extract of A. cherimola fruits possess concentration dependent free radical scavenging activity [47].

Antidiabetic activity

The present work has detected the antidiabetic activity of A. cherimola leaf extract in streptozotocin (STZ) induced hyperglycemia in rats. STZ induced diabetes mellitus and insulin deficiency lead to increased blood glucose level. When A. cherimola leaf extract was administered to normal and diabetic rats, hypoglycaemia was observed after 2 h, with the maximum effect being seen at 6 h. It is assumed that the leaf extract could be responsible for stimulation of insulin release and observed restoration of blood glucose level [48].

The antihyperglycemic activity of the methanolic extract of leaves of A. cherimola was comparable with glibenclamide, a standard hypoglycaemic drug [49]. The methanolic extract of A. cherimola leaves posses considerable hypoglycaemic activity in normal rats [49].

Antimicrobial activity

The chemical composition of the essential oils of leaves, flowers and fruits of A. cherimola were studied for its antimicrobial activity. Five Gram-Positive (Staphylococcus aureus, Enterococcus faecalis, E. coli, Shigella sonei and Proteus mirabilis) and one fungus (Candida albicans) were selected for screening.

The screening results showed that highest zone of inhibition were observed in leaf extract against E.coli [50]. Volatile compound (cherimolacyclopeptide E) of this plant was also studied for its antimicrobial activity [51]. The methanolic extracts of the leaves and a pure compound isolated from A. cherimola plant exhibit antiviral activity against herpes simplex type 2 (HSV-2) viruses [52].

Antitumor activity

The plant annona cherimola is a well known source of cytotoxic compounds and previously acetogenins have been reported. Annomolin and annocherimolin were isolated from the seeds of A. cherimola, collected in Peru [53]. Annomolin was selectively cytotoxic against the human prostate tumour cell line (PC-3), with a potency of over 10,000 times that of adriamycin [54]. Annocherimolin possessed cytotoxic potencies about 10,000 times those of adriamycin in the breast (MCF-7) and colon (HT-29) cancer cell lines [55].

The effect of ethanolic extracts from leaf of A. cherimola was studied on bovine kidney cells (MDBK) and human larynx epidermoid carcinoma cells (Hep-2). The ethanol extract from leaves possessed significant antitumor activity in vitro against MDBK and Hep-2 cells [52].

Antianxiety activity

Hexane extract of leaves of A. cherimola produced anxiolytic-like actions in mice when tested in avoidance exploratory behaviour, burying behaviour and open field tests. The effect is antagonized by picrotoxin, a GABA-gated chloride ion channel blocker, suggesting the involvement of $GABA_A$ receptor complex. β-cariophyllene, β-selinene, β-cubebene and linalool could explain anxiolytic effect of the extract [56].

Antiparasitic activity

Methanolic extracts of A. cherimola seeds were tested for antiparasitic activity against Entamoeba histolytica, Nippostrongylus brasiliensis, Molinema dessetae and Artemia salina. The acetogenins isolated from these extracts are inhibited the larvae of Molinema dessetae [57].

Conclusion

The above collected information regarding the Annona cherimola Miller is reviewed to congregate the ethano-botanical, phytochemical and pharmacological information. Few novel chemical constituent isolated from the A. cherimola showed antimicrobial, antioxidant, anti-diabetic and antiparasitic properties too. Further evaluation needs to be carried out on Annona cherimola in order to investigate the obscured areas and their practical clinical applications, which can be used for the welfare of the mankind.

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