A COMPREHENSIVE REVIEW OF PHYSALIS ANGULATA

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ABSTRACT

Medicinal herbs are the local heritage with global importance. World is endowed with a rich wealth of medicinal herbs. Medicinal plants have curative properties due to the presence of various complex chemical substances of different composition, which are found as secondary plant metabolites in one or more parts of these plants. Mullaca is the dried whole plant of Physalis angulata (Solanaceae). It is a multipurpose plant with many attributes and considerable potential. The plant has traditional uses such as anticancer, immunomodulatory, antimicrobial, anti-inflammatory, anti-allergic and cardiovascular activity. It is reported to possess a wide range of phytochemical constituents including flavonoids, alkaloids, and many different types of plant steroids, some of which have never before been seen in science. The present review aims to update information on its phytochemistry and pharmacological activities.

KEYWORDS: Solanaceae, Physalis angulata, Phytochemical constituents, Pharmacological activities.

INTRODUCTION

Plants have been used by the human society to combat diseases, from the dawn of civilization. Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs. The plant kingdom is vast and the antique use of...
plants to treat various diseases in human beings is not well known. There are a considerable number of natural products used in the traditional medical systems in many countries as alternative medicine for the treatment of various diseases. Many of these medicinal plants provide relief of symptoms comparable to that obtained from allopathic medicines.

One of these plants, *Physalis angulata* is a branched annual shrub that belongs to the Solanaceae family. It is the dried whole plant of *Physalis angulata* L. (Solanaceae). The genus name *Physalis*, a Greek word, means bladder and refers to the inflated calyx, while the Latin species name *angulata* means angled and refers to the stems. It is also known as *Phyasalis capsicifolia, Phyasalis lanceifolia, Physalis ramosissima*. It is known by various common names like Mullaca, camapu, bolsa mullaca, cape gooseberry, wild tomato, winter cherry, juá-de-capote, capulí cimarrón, battre-autour, k’u chih, ‘urmoa batoto bita, cecendet, dumadu harachan, hog weed, nvovo, polopa, saca-buche, thongheng, tino-tino, topatop, wapotok. This plant is widely distributed throughout tropical and subtropical regions of the world and its extracts or infusions have been used in many countries in popular medicine in the treatment of a variety of diseases such as malaria, asthma, hepatitis, dermatitis and rheumatism. The traditional use of mullaca has been recorded in herbal medicine systems in the following countries: Bougainville Brazil, Colombia, Guatemala, Guinea, Ivory Coast, Jamaica, Mozambique, Nicaragua, Nigeria, Peru, Philippines, Rotuma, Solomon Islands, Surinam, Taiwan, Tonga, West Indies.

**Taxonomic Classification**

Kingdom: *Plantae*
Subkingdom: *Tracheobionta*
Division: *Magnoliophyta*
Class: *Magnoliopsida*
Subclass: *Asteridae*
Order: *Solanales*
Family: *Solanaceae*
Genus: *Physalis* L.
Species: *Physalis angulata* L.

**Parts Used:** Whole plant, leaves, roots.
Occurrence and Distribution
Mainly found in the tropics, including the Amazon. It can be found on most continents in the tropics, including Africa, Asia, and the Americas. This weed occurs in fields, pastures, roadsides and open woodlands throughout Florida to eastern Texas and northward to Pennsylvania. It prefers disturbed sites. Maximum germination occurred at 21°C with 10 hours of alternating temperatures and 30°C with 14 hours of alternating temperatures. Planting depth directly affected emergence with a decrease from 89 percent to 0 percent with a corresponding increase of depth from 0.0 cm to 10.0 cm. The many-seeded fruit is edible when ripe.

Morphology
It is an annual herb growing to 1 m in height. It is usually hairless; however, occasional plants have short appressed hairs especially on the younger parts. It grows up to 1 m high. The leaves are dark green and roughly oval, often with tooth shapes around the edge. They are ovate to lanceolate, 4-10 cm long and 3-6 cm wide. The petioles are up to 4 cm long or longer. The leaf margin is usually irregularly toothed but may be smooth. The leaf bases are unequal. The flowers are five sided and pale yellow. They are borne on stalks from 5-40 mm in length. The corolla is yellow, usually without spots or occasionally with distinct spots, and is from 4-12 mm long and 6-12 mm wide. The anthers are bluish or violet, up to 2.5 mm long and are borne on stalks up to 5 mm long. The green outer layer is 4-7 mm long with triangular lobes about as long as the tube. The yellow-orange fruits are borne inside a balloon-like calix, and sided and pale yellow.

The fruit is enclosed in the outer layer. This outer layer (calyx) grows around and encloses the fruit and becomes 10-angled or ribbed, 20-35 mm long and from 15-25 mm wide; it is borne on a stalk 1-4 cm long. The cotyledons are ovate with reddish petioles and without a distinct midvein. The first leaves are similar in shape to the cotyledons, but with an acute apex and evident venation.

Chemical Constituents
Phytochemical studies on mullaca reveal that it contains many types of biologically active, naturally occurring chemicals including flavonoids, alkaloids, and many different types of plant steroids, some of which have never before been seen in science. Mullaca has been the subject of recent clinical research (which is still ongoing), based on the preliminary studies showing that it is an effective immune stimulant, is toxic to numerous types of cancer and
leukemia cells, and that it has antimicrobial properties. The new steroids found in mullaca have received the most attention, and many of the documented anti-cancerous, anti-tumorous and anti-leukemic actions are attributed to these steroids. The main plant chemicals isolated in mullaca thus far include: ayanin, chlorogenic acid, choline, ixocarpanolide, myricetin, phygrine, physagulin A thru G, physalin A thru K, physangulide, sitosterol, vamonolide, withaminimin, withangulatin A, withanolide D, withanolide T, and withaphysanolide.

**Traditional Uses**

Indigenous tribes in the Amazon use a leaf infusion as a diuretic. Some Colombian tribes believe the fruits and leaves have narcotic properties and also decoct them as an anti-inflammatory and disinfectant for skin diseases; others use a leaf tea for asthma. Indigenous peoples in the Peruvian Amazon use the leaf juice internally and externally for worms and the leaves and/or roots for earache, liver problems, malaria, hepatitis, and rheumatism. Indigenous tribes in the Brazilian Amazon use the sap of the plant for earaches and the roots for jaundice. Mullaca has also been used by indigenous peoples for female disorders. In the Solomon Islands, the fruit of mullaca is decocted and taken internally to promote fertility. A tea is made of the entire plant and/or the leaves in the West Indies and Jamaica to prevent miscarriages. In Peru the leaf is infused and used to treat postpartum infections. Brazilian herbal medicine the plant is employed for chronic rheumatism, for skin diseases and dermatitis, as a sedative and diuretic, for fever and vomiting, and for many types of kidney, liver, and gallbladder problems.\[^{24}\]

**Pharmacological Activity**

**Anticancerous activity**

The extract of mulecca have been used for many years to treat cancerous growths. A methanol leaf extract in cats was active against human lung carcinoma (CA-A549), with an IC50=3.93 mcg/ml. A water and methanol extract of aerial parts at 4 mcg/ml demonstrated *in vitro* activity towards M\(T^-4\) (metallothionein-4) cells.\[^{1}\]

Ethanol extracts of the entire plant at 10 mcg/ml were active *in vitro* against the following cell lines: human oral epidermoid carcinoma (Ca-9KB); human colon cancer; human lung cancer (Lu-1), human cervical adenocarcinoma (HeLa), hepatoma-2 and hepatoma-HA22T.\[^{2}\]

In an *in vitro* study a methanol extract of the leaf was found to be active against the human cell line KB-16, with an IC50=3.15 mcg/ml. An ethanol extract of the entire plant given intraperitoneally to mice at 75 mg/kg was active against leuk-P388.\[^{2}\] In an *in vitro* study a
methanol extract from the leaf showed activity towards leuk-P388 cells at IC50=2.5 mcg/ml. The P388 cell line is a general predictor of antitumor activity. *In vitro* ethanol extracts of the entire plant at 0.39-20 mcg stimulated T-lymphocyte blastogenesis. At 10 mcg antibody formation was enhanced in mice.\(^3\)

**Immunomodulatory Activity**

Extract of mullaca has shown significant immunomodulatory potential. In a *in vivo* study extracts of mullaca enhanced antibody response, similarly in a *in vitro* study extracts stimulated T-lymphocyte blastogenesis. Immunomodulatory activity is considered to be due to the physalin chemicals.\(^4\) The propose mechanism of action for its immunomodulatory activity is reduction in nitric oxide production by macrophages stimulated with lipopolysaccaride and interferon-gamma. Physalin-B lowered serum TNF-alpha significantly after lipopolysaccaride challenge. Mice injected with physalins survived after a lethal lipopolysaccaride challenge.\(^5\)

**Central Nervous System Effect**

The extract of plant has shown serotonin receptor binding activity.

**Anti-inflammatory Activity**

The aqueous extract of the flower were reported to possess anti-inflammatory activity. Various parts of mullaca were also screened for anti-inflammatory activity. Flower extracts at 200 mg/kg orally in mice inhibited acute and subacute carrageenan-induced paw oedema, arachidonic acid-induced ear edema and formaldehyde-induced arthritis.

**Anti-allergic Activity**

Flower extracts at 200 mg/kg orally, administered for 1 week, inhibited 2,4-dinitrofluorobenzene-induced contact hypersensitivity type IV allergic reaction in mice. Flower extracts at 200 mg/kg orally in mice inhibited acute and subacute carrageenan-induced paw edema, arachidonic acid-induced ear edema and formaldehyde-induced arthritis.\(^6\)

**Antibacterial**

Crude extract of plant shows significant antimicrobial activity and support folkloric use in the treatment of some diseases as broad-spectrum anti-microbial agents. The methanol extracts of the entire plant at 2 mg/ml showed *in vitro* activity against Corynebacterium diphtheriae,
Klebsiella sp., Neisseria sp., Pseudomonas aeruginosa, Staphylococcus aureus, and Streptococcus sp.\cite{7-8} No activity was seen against Salmonella sp. and Streptobacillus sp. A leaf methanol extract in a broth culture inhibited Bacillus subtilis. The leaf extract was tested against Escherichia coli, Proteus sp., Pseudomonas aeruginosa, Staphylococcus albus and Staphylococcus aureus. But found to be inactive. An ethanol-water leaf extract at 50 ul/agar plate was inactive against Neisseria gonorrhea.\cite{9}

Antimycobacterial
Ethanol, chloroform, hydroalcoholic and chemical fractions of the leaf and aerial parts of mullaca demonstrated antimycobacterial activity \textit{in vitro} at 32-625 mcg/ml. Activity was against the following mycobacterium: \textit{M. tuberculosis}, \textit{M. intracellulare}, \textit{M. malmoense}, \textit{M. avium} and \textit{M. kansasii}.\cite{10} A leaf ethanol extract showed the greatest activity at 32 mcg/ml towards \textit{M. tuberculosis}.\cite{11} Chloroform extracts were active towards a greater number of organisms at a lower dose than the hydroalcoholic extracts.

Antiviral
A hot water extract of the aerial parts of the plant at 0.1 mg/ml showed \textit{in vitro} activity against poliovirus I.\cite{12} At 340 mcg/ml a methanol extract showed protease inhibition \textit{in vitro}; a water extract was inactive.\cite{13}

Antimalarial
A plant decoction using mullaca (\textit{Physalis angulata}) along with \textit{Jatropha curcas}, \textit{Gossypium hirsutum} and \textit{Delonix regia}, was administered to human patients with malaria. The complex eliminated malaria parasites (\textit{Plasmodium falciparum} and \textit{Plasmodium malarie}) from the peripheral blood of patients with malaria. No undesired effects were seen. In rats the herbal complex affected select cytochrome p450 isozymes in relation to the sex of the rat, indicating it may precipitate interactions with other drugs via liver transformation and elimination.\cite{14}

Antitrypanosomal
Various extracts of the aerial parts, leaf, root and fruit showed \textit{in vitro} antitrypanosomal activity against \textit{Trypanosoma brucei rhodesiense} between the concentrations of 19-56 mcg/ml.\cite{15}
Molluscicidal
Ethyl acetate and acetone extracts from the whole plant and ethanol extracts of the roots between 0.1-500 mg/l had *in vitro* molluscicide activity against *Biomphalaria tenagophila*. An aqueous slurry of the fruit, roots and leaves was inactive against *Lymnaea columella* and *Lymnaea cubensis in vitro*.\(^{16}\)

Hypotensive Activity
A water extract of the fruit had a hypotensive effect in cats. Activity was blocked by gallamine or atropine.\(^{18}\)

Anticoagulant Activity
In an *in vitro* study a leaf extract at 50% concentration had an anticoagulant effect on whole human blood.\(^{19}\)

Central Nervous System Effect
A chloroform extract of the entire plant at 100 mcg/ml had weak serotonin receptor binding activity in calves.\(^{20}\)

Antihyperglycemic Activity
Mild hypoglycaemic action of *mullaca* also has been reported. A study reported that water extract of the root mice had weak hypoglycemic activity.\(^{21}\)

Antispasmodic Activity
The entire plant extract have been reported to possess antispasmodic activity. In the guinea pig ileum 2 mg/ml of an entire plant extract inhibited muscle spasms induced with electrical stimulation.\(^{22}\) Moreover, spasmolytic activity exhibited by different constituents provides pharmacological basis for the traditional uses of this plant in gastrointestinal motility disorder.

CONCLUSION
Mullaca has long held a place in natural medicine in the tropical countries where it grows. It's use by rainforest Indians in the Amazon is well documented and it's edible sweet-tart fruits are enjoyed by many rainforest inhabitants, animal and human alike. Phytochemical screening on mullaca reveal that it contains many types of biologically active, naturally occurring chemicals including flavonoids, alkaloids, and many different types of plant steroids, some of which have never before been seen in science. Mullaca has been the subject
of recent clinical research (which is still ongoing), based on the preliminary studies showing that it is an effective immune stimulant, is toxic to numerous types of cancer and leukemia cells, and that it has antimicrobial properties. The new steroids found in mullaca have received the most attention, and many of the documented anti-cancerous, anti-tumorous and anti-leukemic actions are attributed to these steroids.

Interestingly enough, much of the clinical research has ignored the local and indigenous uses of the plant thus many of its effective uses in herbal medicine remain unexplained. It's tested antibacterial properties could validate its uses in as a antiseptic and disinfectant for skin diseases and affections and its use for gonorrhea. Its antiviral properties could well explain its long history of use for hepatitis although scientists have not tested it specifically against hepatitis. Possibly the antispasmodic and muscle contractive properties documented on Mullaca might explain its wide spread use for asthma as well. Yet its use throughout the rainforests for malaria and diabetes are still unexplained by science. In view of its multiple uses, the plant Mullaca needs to be widely cultivated in most of the areas where climatic conditions favor its optimum growth. In this way, a maximum yield of its different usable parts could be achieved to derive the maximum benefit for the welfare of mankind.

REFERENCE


