**PHYSALIS ANGULATA L.: AN ETHANOPHARMACOLOGICAL REVIEW**

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**ABSTRACT**

Physalis species are annual or perennial, erect or decumbent, sometimes rhizomatous, glabrous or pubescent, and with variously toothed or lobed leaves. Physalis angulata L. (P. angulata L.) belongs to Solanaceae family and it includes about 120 species with herbal characteristics and perennial habits. It is widely used in traditional medicine to cure several disorders such as malaria, asthma, kidney and bladder diseases, jaundice, gout, cancer, inflammatory disorders mainly rheumatism, constipation, digestive problems and others; and used in other manifestations like fever, boils, sore or wounds. A variety of phytoconstituents are isolated from the P. angulata L. which includes carbohydrates, lipids, minerals and vitamins; and secondary metabolites include, physalins B, E, F, G, H and I, phytosterols, withangulatin A, flavonol glycoside and others. The plant having potential pharmacological values screened for its various pharmacological activities namely, antiinflammatory, immunomodulating, anticancer, and antibacterial activities which are reported in the extracts of different parts and its phytoconstituents of this plant. An overview of the ethanopharmacological investigations of the P. angulata L. is presented in this review.

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INTRODUCTION

Plants are indispensable sources of medicine since time immemorial. Studies on natural product are aimed to determine medicinal values of plants by exploration of existing scientific knowledge, traditional uses and discovery of potential therapeutic agents. Phytochemicals are used as templates for lead optimization programs, which are intended to make safe and effective drugs [1,2]. A number of modern drugs like aspirin, atropine, ephedrine, digoxin, morphine, quinine, reserpine, tubocurarine and artimisinin are examples, which were originally discovered through observations of traditional cure methods of indigenous people [3].

![Image](physalis_angulata_l.png)

**Figure 1: Different parts of Physalis angulata L.**

The name *Physalis* in Greek for ‘a bladder’ reference to the inflated calyx [4]. The genus *Physalis* is a member of the Nightshade family, Solanaceae. *Physalis* species are annual or perennial, erect or decumbent, sometimes rhizomatous, glabrous or pubescent, and with variously toothed or lobed leaves. *Physalis* is believed to have originated in Mexico, and there is only one species (*P. alkekengi*) whose origin is not of the New World, although many cultivated and weedy. This species have been introduced, both intentionally and inadvertently, to warm areas worldwide. Whitson has proposed separating *P. alkekengi* into a new genus, Alkekengi, and conserving the name *Physalis* for the rest of the species. This is based on recent molecular studies that separate Alkekengi, in addition to its distinctive red inflated calyx, lobed white flowers, and its unique Eurasian geographic distribution [5]. Historically, *Physalis* species have been taxonomically classified based on characters such as habit, hair type, and number of calyx angles [6]. The typical *Physalis* species is an herb with axillary yellow flowers that are solitary and bee pollinated [7].

The genus *Physalis* contains several species grown for their ornamental or edible fruits, which are eaten raw or cooked. The most commonly cultivated species in North America is the tomatillo (*P. philadelphica*), which is often cultivated for food and used in salsa verde. Many other species, such as the Cape gooseberry (*P. peruviana L.*) and the husk tomato or muyaca in South America (*P. pubescens L.*) have been cultivated and eaten for their acidulous fruit [8]. The Chinese lantern plant (*P. alkenkengi*) is an ornamental species that is cultivated for its brightly colored orange-red husk [4].

DESCRIPTION AND DISTRIBUTION

*Physalis angulata* L. (*P. angulata* L.) is popularly known as Camapu [9], Cutleaf groundcherry, Wild tomato, Winter cherry, Cow pops, Chinese lantern, Mullaca, Koropo (in Western Africa) and Wild gooseberry [10]. *P. angulata* L. belongs to Solanaceae family and it includes about 120 species with herbal characteristics and perennial habits [11,12]. Its other scientific names are *Physalis capsicifolia*, *Physalis lancefolia*, and *Physalis ramossissima*. It is bushy annual herb grows to about 50 cm height, glabrous or with minute simple hairs [13]. The details of taxonomy and morphological features are discussed in Table 1 and 2 respectively [14]. This plant is generally considered native to Australia although it is a widespread indigenous herb distributed throughout the tropical and subtropical regions of the world of Africa, Asia, and America, including the Amazon [12,15-18].

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>Plantae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Super division</td>
<td>Angiosperms</td>
</tr>
<tr>
<td>Division</td>
<td>Eudicots</td>
</tr>
<tr>
<td>Class</td>
<td>Asterids</td>
</tr>
<tr>
<td>Order</td>
<td>Solanales</td>
</tr>
<tr>
<td>Family</td>
<td>Solanaceae</td>
</tr>
<tr>
<td>Genus</td>
<td>Physalis</td>
</tr>
<tr>
<td>Species</td>
<td>Angulata</td>
</tr>
</tbody>
</table>
The leaves are sometimes used against inflammations of the bladder, spleen and liver. The whole plant cooked is recommended in baths for inflammatory processes, such as rheumatism [19]. In Amazon valley, its juice is used as sedative, depurative, anti-rheumatic, and for the relief of earache [9]. In Taiwan, it was used as traditional medicine preparation for diabetes, hepatitis, asthma and malaria [20]. In Western Africa this herb used as a traditional medicine for the treatment of cancer [21]. It is also considered as some of its extracts showed antipyretic, analgesic/ antinociceptive, anti-diuretic, anti-inflammatory, and anti-rheumatic; and to treat for hepatitis, sore throat, abdominal pain and cervicitis [16, 18]. Number of lines evidenced that this plant is considered as some of its extracts showed antipyretic, analgesic, anti-inflammatory, and anti-rheumatic; and to treat for hepatitis, sore throat, abdominal pain and cervicitis [16, 18]. Number of lines evidenced that this plant is traditionally used for the treatment of malaria, asthma, kidney and bladder diseases, jaundice, gout and fever [17, 22, 23]. The fruit and other aerial parts are used in the treatment of boils, sores or wounds, constipation and digestive problems [24]. Rural inhabitants in the Peruvian Amazon use the leaf for liver problems, malaria, and hepatitis [25, 26].

PHYTOCHEMICAL CONSTITUENTS

*P. angulata* L. contain carbohydrates, lipids, minerals, vitamins, and phytosterols. It also having major contributor of withanolide-type structures. Withanolides are classically defined as a group of C28 ergostane-type steroids with a C-22, 26 δ-lactone group [4]. It is also having physalins B, E, F, G, H and I and Withangulatin A, Withaferin A, a compound structurally related to Withangulatin A [31]. It also contains flavonol glycoside named as myricetin 3-O-neohesperidoside [32].

PHARMACOLOGICAL ACTIVITIES

In the recent years, the use of herbal products has been increasing in developing countries. Plants have always been an attractive source of drugs. On the other hand, intricate ways of molecular interactions and bioactivity mechanisms of the extracts or their bioactive constituents provide a challenge to the scientists [33]. The *P. angulata* L. displays a wide range of pharmacological activities with correlate to mechanistic possibilities over respective disorders and ephemeral overview of its pharmacological activities, has been presented in Table 3.

Table 2: The morphological features of *P. angulata* L.

<table>
<thead>
<tr>
<th>Part</th>
<th>Macroscopic features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herb</td>
<td>An erect and branching herb with angled and much branched stems, growing to 1m height.</td>
</tr>
<tr>
<td>Leaves</td>
<td>Alternate, oblong-ovate, up to 9 cm long, 1 or sometimes 2 per node with pointed tips; acute and unequal base with margins that are more or less entire dark green; lamina ovate-lanceolate, often with tooth shapes around the edge.</td>
</tr>
<tr>
<td>Flowers</td>
<td>Five-sided, solitary, campanulate, pale yellow-cream colored; up to 6 mm long.</td>
</tr>
<tr>
<td>Fruits</td>
<td>Produces small, orange edible fruits (berries), 1.5 to 2 cm diameter surrounded by an inflated, balloon-like and ovoid calyx; to about 3-5 mm long.</td>
</tr>
<tr>
<td>Seeds</td>
<td>Disc-shaped to broadly reniform, 1.0 to 1.5 mm long, pale yellow.</td>
</tr>
</tbody>
</table>

Table 3: Summary of Pharmacological activities of *P. angulata* L.

<table>
<thead>
<tr>
<th>Pharmacological activity</th>
<th>Parts</th>
<th>Extract/Possible chemical constituents</th>
<th>Screening method employed</th>
<th>Possible mechanistic action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxicity activity</td>
<td>Leaves</td>
<td>Methanol extract and flavonol glycoside, myricetin 3-O-neohesperidoside</td>
<td>in-vitro model against murine leukemia cell line P-388, epidermoid carcinoma of the nasopharynx KB-16 cells, and lung adenocarcinoma A-549 Changes in Nuclear morphological, membrane blebbing and activation of caspase-9 against human oral cancer cell line HSC-3 v-raf murine sarcoma viral oncogene homolog B1 (BRAF)-mutated melanoma A375 and A2058 cell line model</td>
<td>The extract and active molecule showed strong cytotoxicity against three tested cell lines [32] Extract inhibits glutathione or N-acetylcyesteine, mediated by the production of ROS [34].</td>
</tr>
<tr>
<td></td>
<td>Whole plant</td>
<td>Ethyl acetate extract</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole plant</td>
<td>Physalin B</td>
<td>v-raf murine sarcoma viral oncogene homolog B1 (BRAF)-mutated melanoma A375 and A2058 cell line model</td>
<td>Physalin B has the potential and effective chemotherapeutic lead compound for the treatment of malignant melanoma [35].</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Activity Type</th>
<th>Organ Part</th>
<th>Extract Type</th>
<th>Assay/Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxic activity</td>
<td>Aerial parts</td>
<td>Methanol extract and Physalin B</td>
<td>4-ubiquitiluciferase (DLD-1 4Ub-Luc) reporter protein assay against Human DLD-1 colon cancer cells</td>
<td>Physalin B interferes with proteasome functions might be different from those of reference proteasome inhibitors. It also induced an increase of the level of the pro-apoptotic protein NOXA, identified as a component of the overall cell killing mechanisms of proteasome inhibitors [37].</td>
</tr>
<tr>
<td>Antihepatoma activity</td>
<td>Whole plant</td>
<td>Aqueous and ethanol extracts</td>
<td>Using XTT assay, three human hepatoma cells, namely Hep G2, Hep 3B and PLC/PRF/5</td>
<td>Extracts possess potent antihepatoma activity and its effect on apoptosis is associated with mitochondrial dysfunction [38]. Strongly an anti-metastatic and anti-angiogenic activity [39].</td>
</tr>
<tr>
<td>Anti-metastatic and anti-angiogenic activity</td>
<td>Whole plant</td>
<td>Ethyl acetate extract</td>
<td><em>In-vitro</em> and <em>in-vivo</em> by Wound-healing migration, trans-well invasion, Western blotting and chick chorioallantoic membrane assay.</td>
<td>Seco-steroids are potent immune-modulatory substances and act through mechanism distinct from that of dexamethasone [40]. The phytosteroids have lower toxic effects when compared to conventional steroidal immunosuppressive drugs [41].</td>
</tr>
<tr>
<td>Immuno-modulatory activity</td>
<td>Stem</td>
<td>Ethanolic extract; Physalins B, D, F &amp; G; seco-steroids</td>
<td>Mitogen-induced lymphoproliferation, Mixed lymphocyte reaction, Lymphoproliferative and cytokine production assays in allogeneic transplantation model</td>
<td>The phytosteroids have lower toxic effects when compared to conventional steroidal immunosuppressive drugs [41]. The phytosteroids have lower toxic effects when compared to conventional steroidal immunosuppressive drugs [41].</td>
</tr>
<tr>
<td>Immuno-suppression activity</td>
<td>Aerial parts</td>
<td>Withangulatin A</td>
<td>Determination of HO-1 activity by ELISA assay</td>
<td>Withangulatin A shows low cytotoxicity and compelling immune-suppressive activity and directly induces HO-1 expression to restrict the T lymphocytes from over-expression and modulates Th1/Th2-type balance [31]. Attributed to suppression of T cell activation and proliferation, modulation of Th1/Th2 cytokine balance and the induction of HO-1 in T cells [42]. Aqueous extract produces antinociception still remains unclear [18].</td>
</tr>
<tr>
<td></td>
<td>Whole plant</td>
<td>Physalin H</td>
<td>Physalin H on T cells both in vitro and in vivo</td>
<td>Aqueous extract produces antinociception still remains unclear [18]. Plant antioxidants inhibit arachidonic acid metabolism during the stage of the enzymatic peroxidation reaction [43]. Possible constituents may interfering with the COX pathway, lymphocyte proliferation, and production of NO and TGF-α [9].</td>
</tr>
<tr>
<td>Antinociceptive activity</td>
<td>Roots</td>
<td>Aqueous extract</td>
<td>Acetic acid induced writhing, Formalin induced licking and hot-plate methods</td>
<td></td>
</tr>
<tr>
<td>Activity</td>
<td>Part</td>
<td>Extract</td>
<td>Description</td>
<td></td>
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</tr>
<tr>
<td><strong>Anti-asthmatic activity</strong></td>
<td>Roots</td>
<td>Ethanol extract</td>
<td>Ovalbumin induced experimental mice model</td>
<td></td>
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<tr>
<td><strong>Anti-allergic activity</strong></td>
<td>Flower</td>
<td>Methanol extract</td>
<td>DNFNB induced contact hypersensitivity reaction (type IV) in mice</td>
<td></td>
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<tr>
<td><strong>Anti-proliferative activity</strong></td>
<td>Whole plant</td>
<td>Ethyl acetate</td>
<td>Anti-proliferative activity against HSC-3 and HUVECs by trypan blue exclusion method</td>
<td></td>
</tr>
<tr>
<td><strong>Antibacterial activity</strong></td>
<td>Fruits</td>
<td>Ethanol extract</td>
<td>Clinical wound model of extract-ointment formulation and unformulated crude extract against isolates of <em>S. aureus</em> and <em>P. aeruginosa</em></td>
<td></td>
</tr>
<tr>
<td><strong>Antimycobacterial activity</strong></td>
<td>Aerial parts</td>
<td>Chloroform extract; Physalin-containing fraction</td>
<td>Antimycobacterial activity against <em>M. tuberculosis</em>, <em>M. avium</em>, <em>M. kansasii</em>, <em>M. malmoense</em>, and <em>M. intracellulare</em> against <em>M. tuberculosis</em></td>
<td></td>
</tr>
<tr>
<td><strong>Anti-leishmanial activity</strong></td>
<td>Aerial parts</td>
<td>Physalins B, D &amp; F</td>
<td>Against intracellular amastigotes of <em>L. amazonensis</em> and <em>L. major</em>, and <em>in-vivo</em> in a model of cutaneous leishmaniasis in BALB/c mice infected with <em>L. amazonensis</em></td>
<td></td>
</tr>
<tr>
<td><strong>Antimalarial activity</strong></td>
<td>Whole plant</td>
<td>Methanol and dichloromethane Extracts</td>
<td><em>In-vivo</em> and <em>in-vitro</em> antimalarial against rodent parasite <em>P. berghei</em> activity</td>
<td></td>
</tr>
</tbody>
</table>

Physalin E may be a potent and topically effective anti-inflammatory agent useful to treat the acute and chronic skin inflammatory conditions [44]. Significant reduction of production of NO, iNOS, COX-2, TNF-α, and IL-6 by *in-vitro* and *in-vivo* model. The possible various plant antioxidants inhibit arachidonic acid metabolism during the stage of the enzymatic peroxidation reaction [43]. Shows significant anti-asthmatic property [46]. The possible various plant antioxidants inhibit arachidonic acid metabolism during the stage of the enzymatic peroxidation reaction [43]. Unclear [39]. Comparatively high activities shown by both the crude extract ointment formulation and the unformulated crude extract [47]. Further chemical work on isolation of bioactive constituents is required [48]. Unclear [49]. The physalins, especially physalin F shows potent anti-leishmanial activity, and suggest these molecules as the basis for the development of new therapeutic options for cutaneous leishmaniasis [50]. The extracts showed promising Antiplasmodial and antimalarial activity [51].

XTT, ; PLC/PRF/5, ; Cdc2, cyclin-dependent kinases; p21waf1/cip1 and P27Kip1, cyclin-dependent kinase inhibitors; Cdc25C, Chk2 and Wee1 kinase, cyclin-dependent kinase relative factors; ROS, reactive oxygen species; NO, nitric oxide; TPA, 12-O-tetradecanoyl phorbol-13- acetate; iNOS, intracellular nitric oxide synthase; COX-2, cyclooxygenase-2; TNF-alpha, tumor necrosis factor-alpha; IL-1 beta, interleukin-1 beta; NO, nitric oxide; IFN-gamma, gamma interferon; Th1, T-helper cell 1; DPPH, 1,1-diphenyl-2-picrylhydrazyl; MIC, minimum inhibitory concentration; PGE2, Prostaglandin E2; *M. tuberculosis*, *Mycobacterium tuberculosis*; *M. avium*, *Mycobacterium avium*; *M. kansasii*, *Mycobacterium kansasii*; *M. malmoense*, *Mycobacterium malmoense*; *M. intracellulare*, *Mycobacterium intracellulare*; COX, cyclooxygenase; DNF, 2,4-dinitrofluorobenzene; HSC-3, human oral squamous carcinoma-3; HUVECs, human umbilical vein endothelial cells; *S. aureus*, *Staphylococcus aureus*; *P. aeruginosa*, *Pseudomonas aeruginosa*; *L. amazonensis*, *Leishmania amazonensis*; *L. major*, *Leishmania major*; *L. amazonensis*, *Leishmania amazonensis*; and *P. berghei*, *Plasmodium berghei*.

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CONCLUSION

The plant *P. angulata* L., is widely available as weed and also it is cultivated for various purposes including, medicinal, food, forage, ornamental and other usages. The manifestations can be made on the basis of this comprehensive perusal of literature, that the plant *P. angulata* L. is being used traditionally, due to their immense therapeutic potential to treat/cure various diseases. It is a rich source of bioactive compounds like, physalins and secosteroids are present in plant and exhibit with wide range of health benefits. Many studies demonstrated significant anti-inflammatory, immunomodulating, anticancer, and antibacterial activities which are reported in the extracts of different parts and its phytoconstituents of this plant. The various existed therapeutic methods to treat rheumatoid arthritis and other immunological disorders, having lots of drawbacks [52]. Many studies and investigations showed that, this plant mainly involved in the immunological effects. Thus, evidences promising drug therapy for immunological disorders. These pharmacological activities and identified compounds provide solid scientific evidence for some of the traditional therapeutically claims. A variety of phytoconstituents has been isolated from the different parts of it. Thus, there remains a tremendous scope for further scientific exploration of *P. angulata* L. to establish their therapeutic efficacy and commercial exploitation.

Authors’ Statements
The authors declare no conflict of interest

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