



## PERSPECTIVES AND POSSIBILITIES OF INDIAN SPECIES OF GENUS *PHYSALIS* (L.) – A COMPREHENSIVE REVIEW

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Article Received on 13/01/2015

Article Revised on 04/02/2015

Article Accepted on 25/02/2015

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### ABSTRACT

Present review article reveals the importance of different species of genus *Physalis* (L.) distributed in India and this extensive research information on different species is significant for future researchers worldwide. In this article cytomorphological, phytochemical, biological activities and ethnobotanical inputs have been extensively recorded for different species of the genus *Physalis* (L.). As a part of

our investigation on cytomorphological and phytochemical aspects for important medicinal plants from India, the aim of this review article is to provide precise, truthful and detailed information of six Indian species of the genus *Physalis* (L.) viz., (*P. alkekengi* L.; *P. angulata* L.; *P. ixocarpa* Brot. Ex. DC.; *P. longifolia* Nutt.; *P. minima* L.; *P. peruviana* L.). As per our knowledge, there is not even a single, combined, constructive review report available about the different Indian species of genus *Physalis* (L.) evaluated by using cytomorphological, ethnobotanical, phytochemical and biological activities based aspects from India.

**KEYWORDS:** *Physalis* spp., Cytomorphology, Phytochemistry, Ethnobotany, Biological Activities.

### INTRODUCTION

Plants and herbs are used in preparation of medicines and treatment of various diseases from the ancient time. Over the past two decades there is increase in the use of herbal medicine. According to the World Health Organization, 70-80% of world population uses the plant derived traditional methods for the treatment of various health problems.<sup>[1, 2]</sup> The availability of medicines plants and their cheaper cost in comparison to modern therapeutic agents makes them more attractive as therapeutic agents.<sup>[3]</sup> India is crowned with a rich wealth of medicinal plants, which ranked India on the top of the list for the production of herbal medicines.<sup>[4]</sup> It is

clear that, the medicinal value of these herbs and plants is due to the bioactive constituents present in the plants that have physiological effects on the human body. With the help of various phytochemical techniques, it is easy to isolate and introduce valuable drugs in modern medicinal system.<sup>[5]</sup> The present study is therefore, a continuation of on-going labours to explore the traditional knowledge, cultural practices, cytomorphological, biological and biochemical importance in these study areas with the ultimate aim of evaluating medicinal plants for diversity and utilization pattern and also to protect from disappearance of this treasure. Therefore, due to importance of different species of the genus *Physalis* L., it has been taken in to consideration for future exploration and evaluation. As per the literature, genus *Physalis* L. comprises 120 species distributed all over world and out of which six species are distributed in different geographic regions of India. As a part of our investigation on cytomorphological, phytochemical, biological activities and ethnobotanical inputs for important medicinal plants from India, the aim of this review article is to provide precise, truthful and detailed information of six Indian species of the genus *Physalis* L. (*P. alkekengi* L.; *P. angulata* L.; *P. ixocarpa* Brot. Ex. DC.; *P. longifolia* Nutt.; *P. minima* L.; *P. peruviana* L.) to future researchers worldwide. As per our knowledge, there is not even a single, combined, constructive review report available about the different Indian species of genus *Physalis* L. evaluated by using cytomorphological, ethnobotanical, phytochemical and biological activities based aspects from India.

### Botanical Classification

Kingdom: Plantae  
 Order: Solanales  
 Family: Solanaceae  
 Subfamily: Solanoideae  
 Tribe: Physaleae  
 Subtribe: Physalinae  
 Genus: *Physalis* (L.)

### Vernacular Name

*Ben.:* Ban tipariya  
*Guj.:* Parpoti, Popti, Moti popti  
*Hin.:* Rassbhary, Thlati pati, Tipari  
*Kan.:* Gudde hannu  
*Mal.:* Njodi njotta  
*Mar.:* Chirboti, Dhan mori  
*Ori.:* Phutka  
*Tam.:* Tholtakkali  
*Tel.:* Kupanti, Budda budama, Budda basara

**Trade and Common Name:** Winter cherry, Cape goose berry, Hogweed, Balloon cherry, Coqueret, Strawberry tomato, Cutleaf ground cherry, Wild tomato, Winter tomato, Winter cherry, Cow pops, Chinese lantern, Mullaca, Koropo, Camapu.

**Geographic Distribution and Habitat:** There are about 120 species of genus *Physalis* (L.) distributed worldwide, *P. alkekengi* has an unknown center of origin and it is old world species originated from Asia. Other species viz. *P. angulata*, *P. peruviana* and *P. minima* are originated from tropical America.<sup>[6]</sup> *P. peruviana* (L.) found most commonly in Brazil. There are six species of *Physalis* (L.) present in India, viz: *P. alkekengi* (L.); *P. angulata* (L.); *P. ixocarpa* Brot. Ex. DC.; *P. longifolia* Nutt.; *P. peruviana* (L.) as cultivated species and *P. minima* (L.) as common weed.<sup>[7]</sup> The number of species of *Physalis* (L.) occurring in the India does not have the proper distinctions and certainty, this is due to introduction as weeds and cultivated species and the hybridization problems amongst some of these species, a reality outside their native habitats and beyond the experience of those who bred them under captivity. Thus the various species of genus *Physalis* and their hybrids are now well established weeds of disturbed landscapes and crops throughout the tropics, including Asia.<sup>[8]</sup>

**Cytological Status:** Cytological variations among the medicinal plants species caused by environmental stress, genetic recombination and mutation. With the extensive study of meiotic behavior among the populations of medicinal plants species, new cytotypes can be recorded to look for genetic diversity. The genus *Physalis* (L.) is extensively studied by various researchers from India and abroad. Here in this article the cytological data of six Indian species have been extensively compiled and discussed. The cytological analysis of first Indian species viz., *P. alkekengi* (L.) was done by various researchers world-wide and reported  $2n=2x=24$ .<sup>[9-11]</sup> The other variety named *P. alkekengi* var. *franchetii* (Mast.) Makino was also analysed cytologically and reported  $2n=2x=24$ .<sup>[12]</sup> The second Indian species *P. angulata* (L.) was cytologically well studied and reported  $2n=4x=48$ .<sup>[13-17]</sup> The third species of genus *Physalis* L. i.e. *P. longifolia* reported to have chromosome count  $2n=4x=48$ <sup>[18]</sup>, whereas  $2n=2x=24$  was also reported for *P. longifolia* var. *longifolia*.<sup>[19]</sup> The fourth Indian species *P. minima* (L.) was also extensively studied on the basis of cytology and reported to have  $2n=4x=48$  and  $2n=6x=72$  chromosome numbers.<sup>[20-23]</sup> The fifth Indian species *P. peruviana* (L.) was also well studied and reported tetraploid and hexaploid i.e.  $2n=4x=48$  and  $2n=6x=72$ .<sup>[24, 25]</sup> The sixth Indian species i.e. *P. ixocarpa* Brot. Ex. Hornem. was cytologically examined and showed diploid ( $2n=2x=24$ ) chromosome numbers.<sup>[26-28]</sup> From

the cytological data it is clear that the Indian species of the genus *Physalis* (L.) exhibit different (2x, 4x and 6x) ploidy levels. The role of cytological study is to conserve the genetic diversity of medicinal plants especially the germplasm of new cytotypes for future research purposes.

**Morphological Description:** With the help of morphometric characters new morphotypes can be recorded. The morphological aspects of all the six Indian species of the genus *Physalis* have been compiled. *P. angulata* is an annual, erect and branching herb having much branched stems growing to 1m height. Leaves of plant are approximately 9cm long, ovate to elliptic, having 1-2 nodes with pointed tips. Flower of plant is up to 6mm long and pale yellow or white in color, solitary in the leaf axis, produces small, orange edible berries surrounded by an inflated balloon like and ovoid calyx to about 3-5mm long. Seed is 1.0 to 1.5 mm having shape of disc with pale yellow color.<sup>[29, 30]</sup> The second Indian species *P. alkekengi* is also called as winter cherry and it is an herbaceous perennial, erect and ascending herb of height 25 inch approximately. Leaves are green and 3 inch long in size, ovate and elliptic. Flowers are whitish and solitary. Fruit is opposite, globular, berry, tasteless, scarlet when ripe. Seeds are numerous and reniform. *P. peruviana* is a herbaceous, erect, subtropical zone plant and can grow up to 0.6-0.9m, but in some cases it can grow up to the height of 1.8m. Leaves are ovate. Flowers with five large purple spots near the base and pollinated by the insects, wind and by auto-pollination. The fruit is globose berry, ovoid in shape, juicy having diameter 1.25 to 2.50cm, fruit is protected by inflated calyx or fruit basket, protects the plant from insects, birds, diseases and harsh climatic conditions.<sup>[31, 32]</sup> *P. longifolia* is a small herbaceous perennial herb growing 20 to 70cm tall with somewhat oval-shaped leaf blades 5 to 9cm long. Flowers occur in the leaf axis. The bell-shaped corolla is up to 2 cm wide and is yellow with purplish markings around the center.<sup>[33]</sup> *P. minima* herb is commonly called bladder cherry.<sup>[34]</sup> It is an annual herb, 0.5-1.5m in height having dark green dorsal and light green ventral, ovate leaves 9.7cm long and 8.1cm broad. The flowers are solitary and yellow. The fruit is a yellow color berry, enclosed in the calyx, which is 4.1cm long and 2.5cm broad mature in autumn.<sup>[35-40]</sup> *P. ixocarpa* plant is an annual branched herb having weedy appearance. It gets 3-6 feet (0.9-1.8 m) tall and falls over and sprawls on the ground if not given support. The flowers are yellow with purple markings. The fruit develops inside a green and purple bladder-like calyx that looks like a small Chinese lantern hanging from the stem.

**Chemical Constituents:** *Physalis* (L.) species contains various carbohydrates, lipids, minerals, vitamins and phytosterols. They contribute in the withanolide type structures. Withanolides are defined as a group of C<sub>28</sub> ergostane type steroids with a C-22, 26  $\delta$ -lactone group, first isolated from genus *Withania* (L.)<sup>[41]</sup> *P. alkekengi* (L.) sepals contain zeaxanthin and betacytotoxanthin esters or carotenoid esters useful as food additives or nutraceuticals.<sup>[42]</sup> The four steroids, physalin Y, physalin Z, physalin I and physalin II are isolated from the calyces of *P. alkekengi*.<sup>[43]</sup> *P. minima* (L.) contains phenols, alkaloids, steroids, saponins, fatty acids and flavonoids.<sup>[44, 45]</sup> The seeds of *P. minima* contain oil (palmitic, stearic, oleic, linoleic and small amounts of hexadecenoic and hydroxy fatty acid) and protein.<sup>[46]</sup> The leaves, roots stem of the plant contain withanone, withaferin A, withanolide A, stigmasterol and sitosterol, while fruits and flowers contain withanolide A, withanone, withaferin, dihydroxyphysalin B 2-4, physalin A, B and X. The plant also contain physalindicanols, physalinicanol A, withametelins, physalin, withanolide, withanoglutins, vitasteroids, phygrine, withaphysalin A, B, C, D, E and physalin A, C, B, D, I, L, withanone, withaferin A and withanolide A.<sup>[47-53]</sup> There are presence of seven withanolides like physalindicanoles A and B, withamin and withphysalin E and other includes physalin B, D, C and 3-O-glucosides of kaempferol and quercetin. Physalin A, B, C and flavonoids, physalin H, isophysalin B and 5 $\beta$ , 6 $\beta$ -epoxyphysalin B, two new physalins have been isolated from the *P. minima* whole plant.<sup>[54-56]</sup> Physalins are the main steroidal constituents and are characterized by their modified ergostane type framework, being 16, 24-cyclo-13, 14- secosteroids.<sup>[57-66]</sup> It has also been reported to contain withaminimin, phygrine (alkaloid), physalin L, a 13, 14-seco-16, 24 cyclosteroid, other compounds are physalin B, epoxyphysalin B, physalin D and flavonoids.<sup>[67-73]</sup> The fruit of *P. peruviana* contains polyunsaturated fatty acids, carbohydrates, vitamins A, B, C, E, K1, phytosterols, essential minerals (phosphorus, iron, potassium and zinc) and withanolides.<sup>[74-78]</sup> *P. peruviana* contain the pseudo-steroids, physalins with physalin A, B, D, F and glycosides which show the anticancer activity.<sup>[79]</sup> From the aerial parts of *P. peruviana* various withanolide glycosides such as, perulactone, perulactone B, blumenol A, and (*P*)-(*S*)-dehydrovomifoliol have been isolated. Withanolides E and 4 $\beta$ - hydroxywithanolide E have been tested as anti-cancer agents.<sup>[80]</sup> From the whole plant material there is isolation of two withanolides, and characterized as (20R,22R)-5 $\alpha$ ,6 $\beta$ ,14 $\alpha$ ,20,27-pentahydroxy-1-oxowith-24-enolide and (20S,22R)-5 $\beta$ ,6 $\beta$ -epoxy-4 $\beta$ ,14 $\beta$ ,15 $\alpha$ -trihydroxy-1-oxowith-2,24-dienolide.<sup>[81]</sup> The phytochemical study of *P. longifolia* leads to the isolation of three different withanolides such as, withalongolide A, withaferin A, withalongolide B in conjugation with 22 other withanolides. These three

withanolides showed the promising anti-proliferative activity against human head and neck squamous carcinoma (JMAR and MDA, 1986) and melanoma (B16F10 and SKMEL-28) cell lines.<sup>[82-84]</sup> *P. angulata* (L.) contains carbohydrates, lipids, minerals, vitamins and phytosterols. It also have physalins B, E, F, G, H, I and withangulatin A. Withaferin A and withangulatin A are structurally related to each other. Flavonal glycoside named as myricetin 3-*O*-neohesperidoside also present.<sup>[85-87]</sup> Physalin B and F are responsible for the reduction of *Leishmania* infected macrophages and intracellular parasite number *in-vitro* at concentrations non-cytotoxic to macrophages.<sup>[88]</sup> *P. ixocarpa* has slightly acidic flavor and a very good source of vitamins A and C. The chemical present in *P. ixocarpa* is ixocarpalactone A and may have chemoprotective activities.<sup>[89]</sup>

**Pharmacological and Bioactivities of Six Indian Species of Genus *Physalis* (L.):** The genus *Physalis* has great economic importance not only as food supplier, but for its important chemical compounds. Two major groups of chemical compounds are responsible for the various medicinal properties, the tropane alkaloids (mainly tropine and tigoidine) and the physalins (steroid compounds). Tropanes are responsible for an anti-muscarinic activity, they block the activity of neurotransmitter acetylcholine by binding to muscarinic receptors of the parasympathetic nervous system. These chemical compounds are useful in treatment of gastrointestinal and muscular spasms and Parkinsons disease.<sup>[90, 91]</sup> Physalins are under attention because of the anti-tumour and cytotoxic activity.<sup>[92-94]</sup> *Physalis* has a broad spectrum of biological activities such as antibacterial, antiseptic, abortifacient, molluscicidal, antiprotozoal, anticancer, cytotoxic and immune modulatory activities.<sup>[95-100]</sup> But, unfortunately these medicinal properties are not used commercially.

The six species of *Physalis* in India are used for their various medicinal properties viz., *P. alkekengi* (L.) has various activities like, diuretic, used in urinary and skin diseases, can use to cure worm infections and has abortifacient properties. It is also used in kidney and bladder stone, febrile disease, inflammation, constipation, general edema, arthritis and rheumatism. The chemical components present in the extract are physalins, citric acid and vitamin C. *P. alkekengi* has the antineoplastic and cancer static activity, whereas the *P. ixocarpa* fruits are very rich in vitamin C and has antiseptic properties.<sup>[101-105]</sup> *P. minima* is used as a tonic for purgative and diuretic properties and extract shows antifertility and antitumor properties.<sup>[106]</sup> It is also used in the treatment of colic, gastrophy, earache, gonorrhoea and the root paste is used for backache and oedema treatment.<sup>[107-109]</sup> The leaf juice of *P. peruviana* is used for

worm infection treatment and bowel complaints and the plant has diuretic properties (103). *P. longifolia* Nutt and other *Physalis* species are used as food and medicines to treat headache, stomach trouble and to dress wounds.<sup>[110, 111]</sup> *P. peruviana* is a plant with different medicinal uses, the fruit juice of *P. peruviana* is directly used in eye for the treatment of pterygium, which is the common eye disease and it can cause progressive reduction of visual acuity in its more advanced stages and may lead to blindness in Colombia.<sup>[112, 113]</sup> *P. peruviana* has the anti-diabetic activity (114). Finally, *P. angulata* is medicinal plant used in traditional medicine as anti-diuretic and cures the stomach troubles, analgesic, anti-rheumatic. It is also considered as anti-pyretic, anti-nociceptive, anti-inflammatory for hepatitis and cervicitis.<sup>[115, 116]</sup> Few most important and well defined biological activities of the six Indian species of genus *Physalis* (L.) are extensively compiled and discussed.

**Hepato-reno-protective Activity:** Liver is the largest organ of the body and is the main site for the various processes like carbohydrate, protein and fat metabolism, detoxification, storage of bile and storage of vitamins.<sup>[117]</sup> *P. angulata* and *P. peruviana* are the herbs which are widely used in traditional medicine. Ahmed worked on the reno-protective effect of the *P. peruviana* (L.) extract on acute renal injury in rats. *P. peruviana* extract pretreatment improved kidney histology and reduce the level of thiobarbituric acid reactive substances and enhanced other antioxidant enzymes in kidney homogenate compared to cisplatin group.<sup>[118]</sup> In another study the hepatoprotective activity of *P. minima* was checked against paracetamol induced hepatic injury in rats.<sup>[119]</sup> Other activities like antioxidant, antibacterial were also tested against the ethanolic extract. The results from this study indicated that the leaves of *P. minima* were possessing hepatoprotective activity in comparison with standard hepatoprotective drug silymarin. *P. peruviana* roots hepato-renal protective effects were seen against fibrosis in rats. The results were confirmed by liver and kidney histopathological analysis. *P. peruviana* succeeded in protecting the liver and kidney against fibrosis.<sup>[120]</sup> *P. peruviana* was evaluated for its antihepatotoxic, phytochemical analysis and the acute toxicity of the most promising extract in rats. Water, ethanol and hexane extracts of *P. peruviana* showed antihepatotoxic activities against CCl<sub>4</sub> induced hepatotoxicity. The ethanol and hexane extracts showed moderate activity as compared to water extract. The results were analyzed by the serum marker enzymes. Histopathological changes caused by CCl<sub>4</sub> were also significantly reduced by the extract. The extract administration to rats resulted in an increase in hepatic glutathione and decrease in malondialdehyde. Preliminary phytochemical analysis showed the presence of various components in the crude aqueous extract. There was no acute

toxicity in rats.<sup>[121]</sup> In another study, the aqueous and ethanol extracts prepared from the whole plant were evaluated for the anti-hepatoma activity. Three human hepatoma cells, viz. Hep G2, Hep 3B and PLC/PRF/5 were tested using XTT assay.<sup>[122]</sup>

**Anti-inflammatory, Anti-arthritic and Immunomodulatory Activity:** Anti-inflammatory and anti-arthritic activities of aqueous, ethanolic and methanolic extracts of *P. angulata* (L.) leaves were checked by various workers. They checked the anti-inflammatory activity by HRBC membrane stabilization method and *in-vitro* anti-arthritic activity by protein denaturation method in different concentrations and found positive response shown by the all extracts.<sup>[123]</sup> In one of the research work of *P. angulata* (L.), lyophilized aqueous extract from the roots was used to control the inflammatory response induced by the injection of 1% carrageenan into subcutaneous rat's air pouches. The inflammatory mediators action was evaluated by Adenosine deaminase (ADA) activity, nitrite level and prostaglandin E (2) level. Tumor growth factor-beta level was used as a bio indicator of immunomodulatory response. These results indicate that aqueous extracts showed powerful anti-inflammatory and immunomodulatory activities. Juan and co-workers, worked on the fruit juice of *P. peruviana* for treatment of pterygium. In this study the anti-inflammatory and cytosolic activities of the fruit juice in rabbit eye was investigated.<sup>[124]</sup> Anti-inflammatory activity of extracts and fractions obtained from *P. peruviana* calyces were analyzed in mice model of acute inflammation.<sup>[125]</sup> The calyces were extracted using percolation, using different solvents. The anti-inflammatory activity from *P. peruviana* calyces were confirmed and validated its use in folk medicine. Fractions responsible for the anti-inflammatory action were identified and seem promising for phyto-medicinal development. In few experiments, immunomodulatory activities of physalins were tested from *P. angulata* extracts.<sup>[126]</sup> In these experiments, Physalins B, F or G caused a reduction in nitric oxide production by macrophages stimulated with lipopolysaccharide and interferon-g. Physalin B-treated mice had lower levels of serum TNF- $\alpha$  than control mice after lipopolysaccharide challenge. When mice injected with physalins B, F or G survived after a lethal lipopolysaccharide challenge. These results demonstrate that seco-steroids are potent immunomodulatory substances and act through a mechanism distinct from that of dexamethasone. On the basis of Draize test the anti-inflammatory activity and by measuring and comparing growth rates of cultured fibroblasts exposed and not exposed against various fruit juice concentrations were evaluated. The results showed that the *P. peruviana* fruit was mild anti-inflammatory when compared with anti-inflammatory drug methylprednisolone and a dose dependent cytotoxic effect on



cultured fibroblasts was also formed. The different *P. angulata* (L.) extracts fractions (PA-VII, PA-VII-A, PA-VII-B and PA-VII-C) were investigated for immunomodulatory activity.<sup>[127]</sup> The results obtained were, PA-VII and PA-VII-C strongly enhance blastogenesis response, PA-VII-B had moderate activity and PA-VII-A exerted only slight effect on cell proliferation. PA-VII and PA-VII-C possessed stimulatory activity on B cells and have very little effect on T cells. The antibody responses were also showed by PA-VII, PA-VII-B and PA-VII-C, but not by PA-VII-A.

**Aminociceptive Activity:** Bastos and co-workers, identified the aminociceptive activity of the *P. angulata* aqueous extract from the roots. Aqueous extract is given by half or an hour before the acetic acid treatment which causes the abdominal contractions. Aqueous extract inhibit these contractions. Mice treatment with extract or with morphine produced a significant increase of the reaction time in the hot plate test. The results showed the aqueous extract produce marked aminociceptive against the acetic acid induced visceral pain and inflammatory pain responses induced by formalin in mice.<sup>[95]</sup>

**Anti-diabetic Activity and Acute Toxicity:** Sateesh and co-workers, reported the *in-vitro* anti-diabetic activity on the *P. angulata* fruit. The extracts were prepared from powdered material by sequential maceration method by using solvents namely, *n*-hexane, chloroform, ethyl acetate, acetone and methanol. The antidiabetic activity was evaluated using inhibition of alpha amylase and alpha glucosidase enzymes. The study reveals that the methanol extracts of fruits inhibited both of the enzymes *in-vitro*.<sup>[128]</sup> From one of the research work it has been concluded that the aqueous decoction prepared from the dry powder of *P. peruviana* reduces the concentration of glucose in the guinea pigs. So, it has been concluded that the plant have hypoglycemic activity in animal model, but at high doses plant may cause severe intoxication.<sup>[129]</sup> The hypoglycemic effects of different extracts from the *P. minima* in alloxan-induced diabetic albino rats were studied.<sup>[130]</sup> The plant parts were powdered and extracted using boiling water using soxhlet extractor. There was mild reduction in the fasting blood glucose level when seen with the aqueous extracts of roots and stem of *P. minima*. On chronic administration the effect of *P. minima* leaf and flower causes a significant fall in fasting blood sugar of rats. This concludes that the anti-diabetic efficiency leaf and flower extract of plant is almost same and both have a potent anti-diabetic activity than all other root and stem extracts. Abo and Lawal, evaluated the anti-diabetic activity of *P. angulata* aqueous, methanolic extracts and column fraction from whole plant. The extract shows

positive significant lowered blood glucose level in the alloxan diabetic rats. The fraction shows the significant reduction of blood glucose level when compared to crude extracts.<sup>[131]</sup> Antidiabetic potential of ethanolic roots extract of *P. angulata* using alloxan induced diabetes mellitus in rats were also evaluated. The extract was prepared and analyzed their fasting blood glucose and lipid profile. This shows the significant results by reducing the blood glucose, cholesterol, triglycerides and low density lipoproteins, while increases the high density lipoproteins.<sup>[132]</sup> In one of the study it is reported that, *P. alkekengi* has the potential to reduce the serum glucose level in the alloxan-induced diabetic rats, administrated orally. These results in the reduction of glucose level and activity might be due to chemical compounds specially physalins, citric acid and vitamin C.<sup>[114]</sup>

**Anti-cancerous Activity:** Anti-cancer activity of *P. peruviana* was demonstrated by Ngern and co-workers. The methanolic extract of the aerial parts of the whole plant of *P. peruviana* showed inhibition of both the tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )-induced NF-kappa B activity and aberrantly-active Stat3 in human tumor cells. There was isolation of four new compounds in the methanolic extracts of *P. peruviana*. These new isolated compounds showed the inhibition of TNF- $\alpha$ -induced NF-kappa B activation.<sup>[133]</sup> It is concluded in one of the research work, that physalin-F induces cell apoptosis in human renal carcinoma cells by targeting NF-kappa B cells and generating oxygen species in *P. angulata*. It has been resulted that physalin-F appears to be a very promising anti-cancer agent and useful for further clinical development.<sup>[134]</sup> One pure compound 4 $\beta$ -Hydroxywithanolide (4 $\beta$ HWE) was isolated from the plant *P. peruviana* and checked its anti-proliferative effect on human lung cancer cell line (H1299) using survival, cell cycle and apoptosis analyses. DNA damage due to drug is analysed by the alkaline comet nuclear extract assay. The results were analyzed and found that DNA damage induced significantly in a dose dependent manner. The proliferation of cells was inhibited by 4 $\beta$ HWE in both dose and time dependent manner. Half maximal inhibitory concentrations of 4 $\beta$ HWE in HI299 cells, suggests that it could be a potential therapeutic agent against lung cancer.<sup>[135]</sup>

**Anti-microbial Activity:** Nathiya and Dorcus worked on the antimicrobial activity of *P. minima* using different bacterial strains viz., *Bacillus cereus*, *Bacillus subtilis*, *Citrobacter* sp., *Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *P. fluorescens* and *Staphylococcus aureus* using agar well diffusion method. The result revealed that the ethanolic extract of leaf and stem was found to be more effective

against bacterial strains.<sup>[136]</sup> Donker *et al.* compared the antimicrobial activity of zinc oxide ointment and *P. angulata* crude fruit extracts against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The unformulated crude extract of plant fruit exhibited the highest inhibitory activity against *S. aureus*. These results showed that plant fruit extract is useful against the *S. aureus* infections.<sup>[137]</sup> The antifungal activity of *P. alkekengi* (L.) extracts against *Microsporium canis*, *Candida albicans*, *Trichophyton mentagrophytes* and *Nocardia asteroides* were evaluated. The aqueous, ethanol and methanol extracts were used against the fungal strains using agar tube dilution method. Ethanol extracts showed the strongest inhibition effect with minimum inhibition concentration of 15.62mg/mL for all tested fungus. *Nocardia asteroides* was the most sensitive fungus found in this experimental study.<sup>[138]</sup> In other report, the antimicrobial activity of *P. angulata* using essential oils from aerial and root parts on *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Staphylococcus aureus* were tested. The fungal species used in this experiment were *Candida torulopsis*, *Candida albicans* and *Candida stellatoidea*. The results showed the minimum inhibitory concentrations ranging between 3.75mg/mL and 4.0mg/mL for *Bacillus subtilis*, *Klebsiella pneumoniae* by the aerial and root extracts. The fungal strains were susceptible to the essential oils from the aerial and root part of the plant. This study justified the use of plant for treatment of cuts, sores, and some skin diseases often reported in folkloric medicine. Leaf and callus extracts prepared in chloroform were found to be more effective against the pathogenic bacteria and fungi.<sup>[139]</sup> Anti-microbial activity of methanolic extract from the aerial parts and dichloromethane extract from the calyces of *P. alkekengi* was checked. These extracts were tested against five gram-positive and five gram-negative bacteria and five *Candida* species. The extracts were fractionated to isolate physalins using chromatographic techniques, and physalin D was isolated from the extracts. The methods used to check the activity were disk diffusion and broth micro dilution methods. The methanol extract showed moderate activity against fungi at MICs ranging from 128 to 512 µg/mL, the dichloromethane extract and physalin D had low activity against fungi at MICs ranging from 256 to 512 µg/mL.<sup>[140]</sup> Anti-microbial activity of *Physalis minima* leaf and callus extract using solvents absolute alcohol, benzene, chloroform, methanol and petroleum ether against pathogenic bacteria and fungi, following broth dilution assay was evaluated.<sup>[141]</sup>

**Anti-leishmaniasis Activity:** The anti-leishmaniasis activity of physalins purified from *P. angulate* was evaluated. This activity of physalins B, D and F was tested against intracellular amastigotes of *Leishmania amazonensis* (MHOM/BR88/BA-125) and *Leishmania major*

(MHOM/RI/-/WR-173). The *in-vivo* study was done in the BALB/c mice infected with *Leishmania amazonensis* subcutaneously. The results showed that the physalin-F is significantly potent against the leishmania, and suggests these chemical compounds for the development of new therapeutic drugs for cutaneous leishmaniasis. The leishmanicidal activity of *P. minima* was also analyzed by isolating two compounds and these isolated compounds were physalins. The results showed the potent leishmanicidal against the promastigotes of *Leishmania major*.<sup>[142]</sup> *P. minima* shows the anti-leishmaniasis, had been investigated by isolating the different compounds. Three new physalins 1-3 and a new withanolide 7 were isolated. The results showed that the compounds 1-6 were significant *in vitro* leishmanicidal activities against promastigotes of *Leishmania major*.<sup>[143]</sup>

**Anti-asthmatic Activity:** The anti-asthmatic activity of the *P. angulata* roots alcoholic extracts in albino mice was also checked, the asthma was introduced in the rats with ovalbumin. The extract results inhibited ovalbumin induced asthma by decreasing the release of inflammatory mediators. The anti-asthmatic activity is due to the reduction in inflammatory mediator release.<sup>[144]</sup>

**Analgesic and Anti-spasmodic Activity:** The analgesic activity of methanolic extract of *P. alkekengi*, using acetic acid and tail immersion method in rats was also evaluated, the abdominal writhings were reduced when methanolic extract of the plant is given and compared with control and standard drug Aspirin, from this it has been concluded that the methanolic extract of *P. alkekengi* have significant analgesic activity.<sup>[145]</sup> Mohammad *et al.*, studied the effect of hydrochloric extract of *P. alkekengi* ripe fruits on the uterine contraction. The ripened fruit extract prepared by maceration method (70%). The uterus from adult non-pregnant rat was removed and treated by KCl (60mM) or oxytocin (10mU/mL), lead to contraction. The uterus was kept in the organ bath containing De Jalon solution and effect of fruit extract was studied. According to the results KCl and oxytocin induced uterine contractions were inhibited by the extract in the concentration dependent manner. The working mechanism of this extract was mainly via calcium influx blockade, partially through blocking  $\beta$ -adrenoceptors and nitric oxide synthesis.<sup>[146]</sup>

**Molluscicidal Activity:** The molluscicidal activity of *P. angulata* (L.) was studied on different extracts, fractions and also on the physalin modified steroids of this plant species. The results indicated that ethyl acetate and acetone extracts from the whole plant, the

ethanolic extracts of roots, the physalins extracted from stem and leaves were active against *Biomphalaria tenagophila*.<sup>[147]</sup>

**Gastric Inflammation and Gastric Ulcer:** The effect of methanolic extract of *P. minima* (L.) in gastric inflammation and gastric ulcers in rats was also investigated and when compared to the aspirin, the methanolic extract has the lower gastric ulcer formation side effects.<sup>[148]</sup>

**Diuretic Activity:** The methanolic extract of the plant *P. minima* was prepared by soxhlet extractor and its diuretic effect was checked on albino wister rats. Furosemide was used as positive control. The diuretic activity was analyzed by checking the urine volume, sodium and potassium content. The study concluded the methanolic extracts produce a significant diuretic activity.<sup>[149]</sup> The diuretic activity of methanolic extract of *P. angulata* L. were investigated in rats, furosemide was used as the positive control. The diuretic effect of the extract was evaluated by measuring urine volume and excretion of sodium, potassium and chloride ion content. From the results it had been concluded that *P. angulata* shows the significant diuretic activity.<sup>[150]</sup>

**Anti-malarial Activity:** Anti-plasmodial and cytotoxic activity of methanolic and dichloromethane extracts of *P. angulata* *in-vivo* and *in-vitro* against the *Plasmodium berghei* infected mice were checked by various researchers. The extract showed the significant anti-plasmodial and anti-malarial activity.<sup>[151]</sup>

**Anti-oxidant and Cytotoxic Activities:** The anti-oxidant and cytotoxic activities of *P. peruviana* fruit extracts were evaluated by using DPPH and MTT assay. Anti-oxidant potential of crude extract and IC<sub>50</sub> values were calculated as 0.43±0.003mg/mL and the IC<sub>50</sub> values of cytotoxicity for cell lines namely HT-29, Hep3B, SaOS-2 and SH-SY5Y were calculated as 40.79, 24.92, 15.44 and 44.24µg/mL. The plant extract had no cytotoxic effect on MCF-7, LNCap and vero cells. According to these results *P. peruviana* fruit's crude extract was more cytotoxic than the whole plant extract.<sup>[152]</sup> In one of the research investigation, the antioxidant properties of leaves, stem, fruit and root of *P. angulata* using methanol as a solvent for extracts was also evaluated. The DPPH, superoxide, nitric oxide, hydrogen peroxide and hydroxyl radical were used for the investigation. The fruit and leaf extracts were found to be more effective than stem and root extracts. While the total content of phenols and flavonoids were found high in leaves and fruit extracts.<sup>[153]</sup> The aqueous

extract from the leaves of the *P. minima* was evaluated to study the in vitro antioxidant activity. Two methods viz. DPPH radical scavenging assay and nitric oxide scavenging assay were used to check antioxidant activity of the plant leaves. The results indicated that aqueous extract of leaves of *P. minima* is effective in scavenging free radicals and has the potential to be a powerful antioxidant.<sup>[154]</sup> The methanolic extract and chloroform fraction of *P. minima* (L.) were used to investigate the anti-inflammatory, analgesic and anti-pyretic activity in NMRI mice and Wistar rats. Both crude extract and chloroform fraction showed remarkable anti-inflammatory and analgesic activities. The anti-pyretic activity was checked against Brewer's yeast fever model, both extracts were insignificant.<sup>[155]</sup> The work by Chang *et al.* demonstrated the anti-oxidant activity of *P. peruviana* (L.) aqueous extract and its hepatoprotective effects in rats. This study concludes that the water extract possesses anti-oxidant activity and potent hepatoprotective effect against acetaminophen induced liver injury in rats.<sup>[156]</sup> The anti-oxidant, total flavonoid, phenolic anti-inflammatory activities of different extracts of *P. peruviana* were also analyzed. The superficial carbon dioxide (SFCO<sub>2</sub>) method was used to prepare the three extracts (SCEPP-0, SCEPP-4 and SCEPP-5). These extracts were compared against the aqueous and ethanolic extracts of *P. peruviana*. The different extract concentration showed the positive results against the tested activities<sup>[157]</sup> Sue-Jing Wu and co-workers, worked on the anti-oxidant activity of the *P. peruviana*, the hot water and ethanol extracts were prepared in the different concentration of 20, 40, 60, 80 and 95% from the whole plant. Results obtained show that at 100µg/mL, the 95% ethanolic extract exhibit most potent inhibition rate on FeCl<sub>2</sub>-ascorbic acid induced lipid proliferation in rat liver homogenate. The ethanolic extract shows a very significant and stronger anti-oxidant activity than  $\alpha$ -tocopherol and hot water extract. These studies conclude that ethanolic extract have a very potent anti-oxidant activity and the extract with 95% of ethanol possesses highest anti-oxidant activities.<sup>[158]</sup>

**Ethnobotanical Aspects:** Traditional uses of *P. angulata* leaves showed that herb is used to reduce spleen, liver and bladder inflammations. The whole cooked plant is used in baths for inflammatory processes like rheumatism. Its juice is used as a sedative, depurative, anti-rheumatic and for earache in Amazon valley.<sup>[159]</sup> In Taiwan, it is used in the medicine preparation of diabetes, malaria and asthma.<sup>[160]</sup> The rural people of Peruvian Amazon uses the leaves for problems related to malaria, liver and hepatitis.<sup>[161, 162]</sup> The herb is used in Western Africa as a traditional treatment of cancer.<sup>[163]</sup> The fruit and aerial parts of the plant are used in the treatment of boils, sores or wounds, constipation and digestive problems.<sup>[164]</sup>

*P. alkekengi* is distributed and used in Asia (Iran, India, Japan and china) and Europe (Spain, Italy and Turkey) but not much used in modern practices.<sup>[165]</sup> It is also used in Iranian herbal medicine for curing the disease related microbes, urinary tract, kidney and bladder stones.<sup>[166]</sup> This plant possesses multiple traditional uses, in Colombia the fruit juice of the plant used for the treatment of ‘pterygium’. Traditional uses of the herb *P. longifolia* is extensively reported as medicine, the Omaha and Ponca tribes generally using the “crooked medicine” to treat headache, stomach problems and to dress wounds.<sup>[33, 110]</sup> *P. minima* is diuretic, laxative and appetizing bitter tonic used in inflammations, antigonorrhoeic, enlargement of the spleen and abdominal troubles.<sup>[167-169]</sup> The fruits and flowers of the plant used in the stomach pain, constipation and herb paste is used in ear problems.<sup>[170]</sup> Traditionally *P. ixocarpa* fruit juice is used as eyewash and in Guatemala the plant juice is used to cure for the respiratory and gastrointestinal problem.

## CONCLUSION

The species *Physalis* is widely available as weed and is cultivated for different purposes like, medicinal, food, forage, ornamental and other usages. The manifestations can be made on the basis of this comprehensive perusal of literature, that the *Physalis* spp. are being used traditionally, due to their immense therapeutic potential to treat/cure various diseases. The species is a rich source of bioactive compounds like, physalins, secosteroids, and withanolides etc. with wide range of health benefits. Cytomorphological data reveals that there is an immense need to find out new cytomorphotypes for further germplasm maintenance and evaluation, because till today no body is working on these important aspects. As per reported phytochemical data, it is concluded that there is a need to identify few more chemotypes for further herbal and allopathic drugs formations. There is huge need and possibilities to isolate new active components from untouched species of the genus *Physalis* from India. Many studies demonstrated significant anti-inflammatory, anti-cancer, anti-asthmatic, anti-diabetic and anti-bacterial activities etc. which are reported in the extracts of different parts and from its phytoconstituents. As per the recorded data it is cleared that six species have been extensively studied on different parameters but need to do further extensive bioactivities on these species. The various existed therapeutic methods to treat rheumatoid arthritis and other immunological disorders, having lots of future possibilities. Different studies and investigations showed that, these plant species 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 various species. Thus, there remains a very wide scope for further scientific exploration of *Physalis* spp. to establish their therapeutic efficacy and commercial exploitation. Further it is the first constructive, concise and seemed to be more important review article for the genus *Physalis* (L.) from Indian origin, which will definitely help researchers from India and abroad.

#### ACKNOWLEDGEMENT

The authors are grateful to His Holiness Baba Iqbal Singh Ji President, The Kalgidhar Trust & Founder Chancellor of Eternal University (H.P.), Hon'ble Vice Chancellor, Eternal University, Baru Sahib (Himachal Pradesh) India and former Head, Dr. R. C. Gupta, Department of Botany, Punjabi University, Patiala (Punjab) India for providing necessary facilities and logistic support for carrying out the study.

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