Physalis Angulata Leaves Act as An Anti-Cancer Potential: A Review

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***Abstract*—Physalis angulata L. (Solanaceae) is a traditionally valuable medicinal herb widely distributed across tropical regions and extensively used in ethnomedicine for treating fever, inflammation, parasitic infections, diabetes, liver disorders, and tumor-like conditions. Phytochemical investigations have identified several bioactive constituents including physalins, withanolides, alkaloids, flavonoids, tannins, and phenolic compounds, which contribute to its diverse therapeutic profile. Recent preclinical evaluations reveal strong anticancer potential of P. angulata through mechanisms such as induction of mitochondrial-mediated apoptosis, modulation of caspase activity, G0/G1 and G2/M cell-cycle arrest, suppression of NF-κB and PI3K/Akt signalling pathways, and inhibition of metastasis and angiogenesis. Additionally, the plant demonstrates significant antioxidant, anti-inflammatory, antiparasitic, antibacterial, antifibrotic, and antidiabetic effects, supporting its role as a multi-target pharmacological candidate. Although experimental data are promising, the absence of standardized dosing, toxicity studies, pharmacokinetic profiling, and clinical validation currently limits therapeutic translation. Therefore, Physalis angulata presents strong research potential for future development in phytomedicine, oncology, and integrative drug discovery.**

Physalis angulata L. shows strong anticancer potential by inducing cancer cell death and blocking tumor growth pathways.Its rich phytochemical profile—especially physalins, withanolides, flavonoids, and phenolic compounds—enables it to target cancer cells through multiple mechanisms, including induction of apoptosis,Along with this, the plant also exhibits important antibacterial, anti-inflammatory, antidiabetic, and antiparasitic properties due to its rich phytochemicals. These combined activities make it a promising medicinal plant, but further studies and clinical trials are needed to confirm its safety and effectiveness for medical use.

***Keywords*—Physalis angulata anticancer activity; apoptosis; antioxidant; anti-inflammatory; antiparasitic; antifibrotic;**

I. INTRODUCTION

Physalis angulata L. belonging to nightshade plant family Solanaceae accredited with medicinal properties and contains different classes of secondary metabolites of pharmacological importance. In Andhra Pradesh and Telangana Physalis angulata L. commonly called as budda kodisha and budda gochi respectively.

Use in Traditional Medicine Recent ethnopharmacological studies show that Physalis angulata is used in many parts of the world to treat several diseases, as anticancer, antibacterial, for diabetes, treatment of malaria, anemia and reducing fever. Since the dawn of civilization, people have relied heavily on the therapeutic qualities of medicinal plants. The World Health Organization estimates that even now, almost 80% of the world's population, particularly in less developed countries uses traditional medicine as their major source of healthcare. There are roughly 2000 different ethnic groups in the world, and nearly all of them have unique traditional medicinal practices. Physalis angulata commonly referred to as the cut-leaf ground cherry or bladder cherry, is an herbaceous shrub that is native to tropical America but is currently found as a weed around the world. This erect herb boasts smooth leaves with deeply cut edges. Physalis angulata, is a bit of a bully in the garden. It spreads easily, handles most weather conditions, and shrugs off weed killers. This bushy annual herb stands roughly 50 cm tall and has smooth or slightly hairy stems. Beyond its well-known ability to strengthen the immune system, this plant surprisingly finds a role in the kitchen, particularly when making sauces . Standardised medicinal plant extracts are used in a variety of traditional and mainstream medications across the globe. Natural remedies have been shown to regulate the aberrant cell division process and have a very good therapeutic index against various tumour cell. Physalis angulata boasts a rich history of medicinal use in Japan, particularly for fevers. This plant's extracts or infusions are used as dermatitis,

asthma, and anti-malarial remedies in many parts of the world.

In other countries physalis angulata is called as "totototo". The juice of physalis angulata is used in the treatment of earache, jaundice, fever, bladder disease to mention a few. The fruit and other aerial parts are used in the treatment of boils, sores or wounds, constipation and digestive problems. It has been shown to have therapeutic application in treating a variety of skin conditions in products such as baby powder, barrier creams to treat diaper rashes, calamine cream, anti-dandruff shampoos, and antiseptic ointments Application of physalis angulata as a vehicle in the formulation of zinc oxide for medicinal purpose may be worthwhile. This study was conducted to validate the scientific basis of using P. angulata in the treatment of wounds and to verify if zinc oxide ointment in combination with the extract of P. angulata will result in enhancement of inhibitory activity of the extract. Phenolic compounds are plant secondary metabolites with a wide spectrum of biological activities. The antioxidant activity is one the most relevant because oxidation is related to the development of neurodegenerative diseases and cancer . Plant phenolic composition is the result of the interaction of genetic and environmental factors and has been reported as species-specific. However, changes associated with growth stages, seasons of growing and eco-geographical growth conditions have been reported for some species, like Rosmarinus officinales.

These changes can modify the flavor and biological properties of edible and medicinal plants and reveal that neither the concentration nor the relevance of different phenolic compounds in plants are always .The characterization of those variations may contribute to ensure the reliability and quality of edible and medicinal plant species to make more efficient use of their phytochemicals for nutraceutical and pharmaceutical purposes. Besides, chemical characterization may support the development of quality control tools of plant-based medicinal preparations, as adulteration is a global latent risk for traditional herbal preparations . who compared the phenolic profiles of five species of Physalis, included P. angulata. To the best of our knowledge, except for the fruits of P. peruviana studies on the changes of phenolic composition during development of Physalis species have not been carried out. The growth-related variation of phenolic composition and antioxidant properties of above- and under-ground parts of P. angulata, during four growth stages to evaluate their potential as chemical quality indicators for herbal preparations of this edible and medicinal plant. Plants with medicinal properties serve as the basic treatment for many ailments in cultural diversities worldwide. These medicinal plants exhibit various activities against many major diseases and their active constituents. In recent years, phytoscience has made significant contributions to modern medicine. As a result, medicinal plants are the primary source of treatment for a wide range of health issues. Another reason is that herbal treatments are readily available and accessible and are very inexpensive. In several nations, people in rural areas still rely on herbal medicines to treat all of their health problems. Phytomedicine is widely used in modern medicine to treat various disorders, including diabetes and cancer. Many studies have been published on the use of phytomedicine in cancer treatment. According to the World Health Organization (WHO), herbal medicine is used by 60% of the world's population, and about 80% of the people in emerging nations rely on it nearly entirely for their basic health care requirements.

Cancer is the term used for diseases when abnormal cells multiply without any control in any body organ or tissue and attack the nearby body parts. If the spread is uncontrollable, it can cause death. It is considered the second foremost reason for death around the world. The common types of cancer found mostly in men are lung, liver, colorectal, prostate, and stomach. In women, breast, lung, colorectal, cervical, and thyroid cancers are mostly found Much recent research has focused on plant-derived chemoprotective constituents. These active constituents can act as target specific for malignant cells or can prevent cancerous cell multiplication . The current cancer treatment is associated with severe side effects, including the damage of normal body cells and many others. Therefore, the need for safe drugs or methods for cancer treatment is in high demand. The current study on the leaves and fruit of Physalis angulata includes the cytotoxic activity on the breast cancer, colorectal and cervical cancer cell lines.

II. BACKGROUND HISTORY OF PHYSALIS ANGULATA

Physalis angulata L., commonly known as cut-leaf groundcherry or wild gooseberry, has a long history

that spans traditional medicine, indigenous cultures, and later modern scientific interest. Its origins trace back to tropical regions of the Americas, where native communities first recognized the value of its distinctive lantern-like fruit and medicinal properties. From these early centers of use, the plant gradually spread across continents through natural dispersal, human migration, and agricultural exchanges.

Over time, Physalis angulata became widely naturalized throughout tropical and subtropical regions, including Asia, Africa, and Oceania. Its hardy nature allowed it to thrive in disturbed soils, fields, village outskirts, and forest margins. By the early modern era, the plant was already integrated into local ethnomedicinal practices across several cultures. Traditional healers used the leaves, stems, roots, and fruit to treat fever, inflammation, stomach ailments, skin infections, and respiratory disorders. Such widespread use led to numerous vernacular names and diverse methods of preparation. As botanical exploration expanded during the 18th and 19th centuries, P. angulata was formally described and included in global plant classifications. Its characteristic inflated calyx and berry-like fruit made it easily recognizable to botanists who began documenting its distribution across newly surveyed regions. With the development of pharmacognosy, researchers also began isolating its bioactive components, uncovering steroidal lactones later known as physalins and withanolides. These findings sparked significant scientific interest, especially in the 20th and 21st centuries, as laboratory studies revealed notable antimicrobial, anti-inflammatory, antioxidant, and cytotoxic activities. In India, Physalis angulata gradually integrated into local healing traditions, especially in rural and tribal communities. Although often overlooked in classical Ayurvedic texts, it became well known in folk medicine for managing conditions such as asthma, abdominal discomfort, body pain, and general inflammation. Its availability as a common weed allowed communities to use it easily and regularly. The ripe fruits were sometimes consumed as food, adding nutritional and cultural importance to the plant. By the modern era, Physalis angulata had transformed from a traditional folk remedy into a plant of global scientific relevance. Researchers began exploring its therapeutic potential, particularly in immunomodulation, metabolic disorders, and cancer-related mechanisms. Although still under study and not yet mainstream in clinical medicine, the plant continues to hold significance as both a traditional resource and a promising subject in phytochemical and pharmacological research.

III. HERBAL OVERVIEW OF PHYSALIS ANGULATA

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 name like Mullaca, camapu, bolsa mullaca, cape gooseberry, wild tomato, winter cherry, hog weed, 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.

Taxonomic Classification :

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

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.

IV. CHARACTERISTICS OF PHYSALIS ANGULATA

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.

Image No. 01:

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 antiinflammatory 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.

V. MECHANISM OF ACTION OF CANCER

1.Induction of Apoptosis (Programmed Cell Death)

Cancer cells avoid apoptosis. Leaf extracts of P. angulata can re-activate cell death pathways.

Mechanism:

Activation of caspase-3, caspase-8, caspase-9
Upregulation of pro-apoptotic proteins
Downregulation of anti-apoptotic proteins (Bcl-2)
Nuclear condensation and DNA fragmentation

2. Inhibition of Cancer Cell Proliferation
Leaf extracts interfere with pathways responsible for uncontrolled cancer growth:
Inhibition of NF-κB, a transcription factor that supports cancer survival
Blocking the MAPK/ERK signaling pathway
Arresting cancer cells at G2/M phase of the cell cycle
This prevents cancer cells from multiplying.

3. Anti-metastatic Activity
Metastasis is the spread of cancer cells. Leaf extracts can inhibit:
MMP-2 and MMP-9 enzymes, which help cancer cells invade tissue
Cell migration and adhesion molecules (ICAM, VCAM)
Signaling pathways that promote spreading (JAK-STAT, PI3K-Akt)
Studies show reduced metastasis in breast, lung, and colon cancer cell models.

4. Antioxidant Activity
Oxidative stress contributes to cancer development. Leaf extracts contain flavonoids and phenolics that:
Neutralize free radical
Lower oxidative DNA damage
Reduce lipid peroxidation
This provides protective effects against carcinogenesis.

5. Anti-inflammatory Effects
Chronic inflammation supports cancer progression.
P. angulata leaves suppress: COX-2 and iNOS expressionTNF-α, IL-1β, IL-6, and other cytokines
Physalin B and D significantly inhibit inflammatory pathways.

6. Immunomodulatory Activity
The immune system plays a role in killing cancer cells. Leaf extracts have been shown to:
Increase macrophage activity
Activate T-lymphocytes
Enhance natural killer (NK) cell function
These effects may help the body identify and destroy abnormal cancer cells.

7. Anti-angiogenic Effect (Prevents New Blood Vessels to Tumor)
Cancer cells need blood supply. Research shows that Physalis angulata leaf extracts can:Inhibit VEGF signalling Block formation of new blood vessels

VI. TRADITONAL TREATMENT ON CANCER

The leaves of Physalis angulata contain several active phytochemical groups such as physalins, withanolides, flavonoids, and phenolic compounds. Modern research suggests that these constituents may influence cancer cells through multiple biological pathways. One of the most important mechanisms is the ability of leaf extracts to induce apoptosis, a natural programmed cell-death process that is often defective in cancer cells. Studies have demonstrated that ethanol and methanol extracts of Physalis angulata leaves activate caspase enzymes, disrupt mitochondrial membrane potential, and cause the release of cytochrome-c, ultimately leading to the death of tumor cells. These apoptosis-inducing effects have been observed in breast cancer, melanoma, leukemia, and colorectal cancer cell lines. Another essential pathway through which the leaves exert anticancer activity is inhibition of cell cycle progression. Experiments conducted on human breast cancer cells (MDA-MB-231 and MCF-7) have shown that leaf extracts cause G2/M cell cycle arrest. This means the cancer cells are prevented from dividing and multiplying. The mechanism involves downregulation of cyclin B1 and CDK1, proteins required for mitosis, along with increased expression of p21, a natural cell cycle regulator. Inflammation plays a major role in tumor growth and metastasis, and Physalis angulata leaf compounds appear to interfere with these pathways as well. Physalin B and physalin F, which are abundant in the leaves, have been shown to suppress NF-κB, a transcription factor that controls genes responsible for inflammation, cell survival, and metastasis. By blocking NF-κB and COX-2 expression, the extracts reduce the ability of cancer cells to grow, invade tissues, or resist cell death.

In addition to affecting inflammation and apoptosis, the leaves also possess strong antioxidant capabilities due to high levels of flavonoids and phenolic compounds. These antioxidants help protect cells

from oxidative stress and DNA damage, which are key contributors to cancer formation. By neutralizing free radicals, the leaves may help prevent mutations that lead to malignancy. This antioxidant activity has been documented using DPPH and ABTS assays, where leaf extracts showed strong free-radical scavenging ability. Some studies have also highlighted the anti-metastatic potential of Physalis angulata leaves. The extracts may reduce the expression of matrix metalloproteinases (MMP-2 and MMP-9), enzymes that cancer cells use to break down surrounding tissues and spread to new organs. Reduction of these enzymes has been observed in cultured cancer cells treated with purified physalins. Animal studies provide additional support but remain preliminary. In vivo experiments using purified leaf-derived physalins have shown reduction in tumor size in mouse models of leukemia and sarcoma. These studies demonstrated slower tumor progression and improved survival rates; however, temporary liver and kidney strain was noted, indicating that safety evaluation and dose standardization are necessary before any therapeutic application in humans. Although traditional medicine systems in India, South America, and Southeast Asia have used Physalis angulata leaves for swelling, infections, and tumor-like growths, these uses do not equal clinical cancer treatment. Modern research shows encouraging results, but there are no approved clinical trials in humans. Therefore, the leaves cannot be considered a cancer treatment; rather, they represent a promising source for future anticancer drug discovery.

1. Breast Cancer :

Human breast cancer of human has a poor prognosis on the basis of present-day therapeutic measures. Therapeutic approaches for human breast cancer include surgery, radiation treatment, hyperthermia and chemotherapy. However, conventional strategies for the treatment of human breast cancer are not yet satisfactory. Some of the wellknown anticancer drugs are known to induce apoptosis via the inhibition of topoisomerase II.

Cell apoptosis is characterized by a series of typical morphological events, for example, shrinkage of the cell, DNAfragmentation, fragmentation into membrane-bound apoptotic bodies and rapid phagocytosis by neighboring cells . Many epidemiological studies have shown that protective effects of vegetables and fruits against cancer reduced risks of cardiovascular disease associated with high intakes of dietary antioxidants. Physalis angulata (PA) is a annual herb indigenous to many parts of the tropics and sub-tropics, including Tai wan. Each fruit of PA is like a yellow pearl in the small lantern shape pod is very delicious to eat. The herbal medicine, PA has long held a place in natural medicine in the sub-tropical countries where it grows. People in Taiwan use PA for ear ache, liver problems, malaria, hepatitis, and rheumatism . PA has been the subject of recent clinical research that is still ongoing. Based upon the preliminary studies, it is an effective immune stimulant, is cytotoxic to numerous types of cancer cells and has anti -viral properties, including against HIV. In several in vivo animal tests and in vitro lab tests, an extract of the entire plant of PA and/or its steroidal fractions demonstrated immune stimulant properties by strongly enhancing blastogenesis, antibody responses and increased T and B lymphocyte production . Various water, alcohol and ethanol extracts of PA and its plant steroids have shown to behave strong in vitro and in vivo cytotoxic activity against numerous types of cancer cells including; leukemia, lung, colon, cervix, hepatoma and melanomas.

The pathogenesis of retinoblastoma is initiated with a disruption of cell cycle regulation leading to abnormal retinal cell growth. In retinoblastoma, mutations or inactivation of tumor suppression proteins include the retinoblastoma protein (pRB) and the transcription factor Both of the pRB and p53 allow the two main pathways of tumor suppression controlling cellular responses to oncogenic stimuli such as errors in cell division, DNA damage and incompatible mitogenic signals. Each of these pathways has certain regulators and effectors to stop the cell cycle or even induce apoptosis Inactivation of pRB prohibits cells to enter the proliferation phase resulting in uncontrolled DNA replication and imperfect replication results A mere pRB pathway is insufficient to induce tumor formation. Dysregulation in p53 pathway will also induce anti-apoptosis and excessive cell growth.

Physalis angulata is a plant, evidenced to have photochemical attributes addressing the anti-cancer potential. One of the anticancer active substances successfully isolated from Physalis angulata leaf extract is physalin, which is a derivative of flavonoid glycosides. In addition, other ingredients were found, such as luteolin, carotenoids, and withanolides. In addition to anticancer effect, Physalis angulata leaf extract is also believed to have antiparasitic, anti-inflammatory, antimicrobial, anti-inflammatory, and

immunosuppressive potential. Several concerned studies have proven the anticancer potential of Physalis angulate However, there has not been any study that proves its benefits in retinoblastoma cancer cells.

2. Liver Cancer :

Physalin A (PA) is a bioactive withanolide with multiple pharmacological properties and has been indicated to be cytotoxic to hepatocellular carcinoma (HCC) cell line HepG2. This study aims to explore the mechanisms underlying PA antitumor activity in HCC. HepG2 cells were exposed to various concentrations of PA. Cell counting kit-8 assay and flow cytometry were implemented for evaluating cell viability and apoptosis, respectively. Immunofluorescence staining was utilized for detecting autophagic protein LC3. Western blotting was employed for measuring levels of autophagy-, apoptosis- and phosphatidylinositol-3-kinase/protein kinase B (PI3K/Akt) signaling-related proteins. A xenograft mouse model was established to verify the antitumor activity of PA in vivo. PA impaired HepG2 cell viability, and triggered apoptosis as well as autophagy. Inhibiting autophagy augmented PA-evoked HepG2 cell apoptosis. PA repressed PI3K/Akt signaling in HCC cells and activating PI3K/Akt reversed PA-triggered apoptosis and autophagy. PA treatment inhibited tumor growth in tumor-bearing mice. PA triggers HCC cell apoptosis and autophagy by inactivating PI3K/Akt signaling.

Scientists study Physalis angulata (PA) for its anticancer potential through a series of laboratory-based research steps. First, the plant materials such as leaves and fruits are collected and extracted using solvents like methanol, ethanol, or water to isolate bioactive compounds such as physalins, withanolides, flavonoids, and phenols. These extracts are then tested in vitro on different cancer cell lines, including breast, liver, lung, and colon cancer cells, to evaluate their ability to reduce cell growth, induce apoptosis (programmed cell death), arrest the cell cycle, and prevent cell migration or metastasis. Molecular studies are carried out to understand the underlying mechanisms, and results often show that PA regulates important cancer-related pathways such as NF-κB, PI3K/Akt, p53, caspase activation, and ROS generation. After successful cell studies, in vivo experiments on animals are performed to determine whether PA reduces tumor size and is safe at certain doses. Researchers also isolate specific compounds like Physalin B and Physalin F to test their individual anticancer effects. In addition, computer-based in-silico studies help predict how PA compounds bind to cancer-related proteins. Overall, PA is studied scientifically through extraction, cell testing, molecular mechanism analysis, animal experiments, and computational evaluation to explore its potential as an anticancer agent.

The mechanism of liver cancer

(hepatocellular carcinoma) begins with chronic liver injury caused by factors such as hepatitis B or C infection, alcohol abuse, fatty liver disease, or toxins. Continuous liver damage leads to inflammation and oxidative stress, which cause DNA mutations in liver cells (hepatocytes). These mutations affect important regulatory genes such as p53, Rb, Wnt/β-catenin, and TERT, resulting in loss of normal cell-cycle control. As a result, hepatocytes start dividing rapidly and uncontrollably. Chronic inflammation also activates signaling pathways like NF-κB, PI3K/Akt, MAPK, and JAK/STAT, which promote survival, proliferation, angiogenesis (formation of new blood vessels), and resistance to cell death. Fibrosis gradually develops into cirrhosis, creating a microenvironment that further supports tumor growth. Over time, these abnormal cells transform into malignant hepatocellular carcinoma, capable of invading nearby tissues and spreading to other organs. Overall, liver cancer develops through a combination of DNA damage, disrupted signaling pathways, chronic inflammation, and uncontrolled cell proliferation.

3. Leukemia Cancer :

Researchers have studied Physalis angulata (PA) for its anticancer potential, including effects on leukemia cells. Many of these studies focus on its bioactive compounds, especially physalins and withanolides, which show strong activity in laboratory experiments.

1. Active Compounds Showing Anti-leukemic Activity The compounds from PA that are most studied against leukemia include: Physalin Physalin F Physalin G Physalin D Withangulatin A .These compounds belong to the steroidal lactone family, known for strong cytotoxic effects on cancer cells.

2. How PA Affects Leukemia Cells (In-Vitro Studies) :Researchers have tested PA extracts on leukemia cell lines like:K562 (Chronic Myeloid Leukemia) HL-60 (Acute Promyelocytic Leukemia) Jurkat (T-cell leukemia)

Major findings include:

a) Induction of Apoptosis (Programmed Cell Death) PA compounds trigger cancer cell death by: Activating caspase-3 and caspase-9 Causing mitochondrial membrane damage Increasing ROS (Reactive Oxygen Species) Causing DNA fragmentation .This is one of the strongest effects seen in leukemia research.

b) Cell Cycle Arrest: PA extracts stop leukemia cells from dividing by arresting them in: G0/G1 phase,G2/M phase.This slows down cancer cell proliferation.

c) Inhibition of Leukemia Cell Proliferation: Physalins reduce leukemia cell growth by:Decreasing ATP production,lowering metabolic activity,Blocking growth signals.This results in strong cytotoxicity toward leukemia cells.

3 Molecular Mechanisms Identified:Research shows that PA compounds affect key cancer-related pathways: NF-κB Inhibition Leads to reduced inflammation Lowers cancer cell survival signals PI3K/Akt Pathway Downregulation. Causes reduced cell growth Increases apoptosis JAK/STAT Pathway Modulation Slows proliferation of leukemia cells Increased Oxidative Stress.Cancer cells become more sensitive to apoptosis Downregulation of anti-apoptotic proteins (Bcl-2, Bcl-XL)Makes cancer cells easier to kill.These mechanisms explain why leukemia cells respond strongly to PA in lab studies.

4. In-Vivo (Animal) Studies:Some studies tested physalins in leukemia animal models and found:Reduced leukemia cell count Improved survival in mice.Decreased spleen and liver enlargement (common in leukemia)However, this research is early-stage.

5. Safety and Toxicity Studies :Before testing in humans, scientists evaluate:Liver and kidney toxicity,Blood cell counts.So far, controlled doses of PA extracts appear safe in animal models, but not validated for human treatment.

4. Lung Cancer :

Physalis angulata shows strong anticancer potential against lung cancer through several molecular mechanisms demonstrated in laboratory studies. Its major bioactive compounds—especially physalins and withanolides—act by reducing the growth of lung cancer cells such as A549 and H1299. The extract induces apoptosis, or programmed cell death, by increasing reactive oxygen species (ROS), disrupting mitochondrial membrane potential, and activating caspase-3 and caspase-9. PA also causes cell cycle arrest, usually in the G0/G1 or G2/M phase, preventing lung cancer cells from dividing. Another important mechanism is the inhibition of cancer-promoting pathways like NF-κB, PI3K/Akt, and MAPK/ERK, which decreases cell survival, inflammation, and resistance to therapy. PA further reduces metastasis by lowering MMP-2 and MMP-9 expression, preventing migration and invasion of lung cancer cells. Overall, Physalis angulata acts through apoptosis induction, oxidative stress, cell cycle arrest, pathway inhibition, and anti-metastatic effects, making it a promising natural compound for lung cancer research.

Mechanism of Action of Physalis angulata Against Lung Cancer :

Research on Physalis angulata demonstrates that its anticancer activity against lung cancer is driven by multiple, interconnected molecular mechanisms. The plant contains powerful bioactive compounds—including physalin B, physalin F, physalin G, withangulatin A, and various withanolides—which show strong cytotoxic effects on lung cancer cell lines like A549, H1299, and H358. These compounds initiate apoptosis by generating high levels of reactive oxygen species (ROS), leading to mitochondrial dysfunction, cytochrome-c release, and activation of intrinsic apoptotic pathways involving caspase-9 and caspase-3. PA also increases the expression of pro-apoptotic proteins (Bax) while reducing anti-apoptotic proteins (Bcl-2), making cancer cells more prone to death.

In addition, Physalis angulata causes cell cycle arrest, often at G0/G1 or G2/M, by downregulating cyclins and CDKs that drive cell division. Its compounds significantly suppress tumor growth signals by inhibiting major pathways such as PI3K/Akt, NF-κB, and

MAPK/ERK, which are central to lung cancer cell survival, proliferation, and inflammation. PA also interferes with metastasis by reducing the activity of MMP-2 and MMP-9 enzymes, which are responsible for cancer cell invasion and tissue breakdown. Furthermore, studies suggest PA has anti-angiogenic activity, meaning it can prevent the formation of new blood vessels that tumors need for growth. physalins also exhibit strong anti-inflammatory effects, decreasing cytokines like TNF-α and IL-6, which contribute to tumor progression. Through

these combined effects—pro-apoptotic action, redox imbalance, suppression of growth pathways, anti-metastatic behavior, and anti-inflammatory activity—Physalis angulata demonstrates significant

potential as a natural anti-lung-cancer agent in scientific and preclinical research.

5. Colon Cancer :

Physalis angulata has shown promising anticancer potential against colon cancer in laboratory and preclinical studies. Its major active compounds—especially physalin B, physalin F, withangulatin A, and several withanolides—demonstrate strong cytotoxic effects on colon cancer cell lines such as HT-29, HCT-116, SW620, and Caco-2. Research shows that PA induces apoptosis (programmed cell death) in colon cancer cells by increasing reactive oxygen species (ROS), disrupting mitochondrial membrane potential, releasing cytochrome-c, and activating caspase-3 and caspase-9. PA also causes cell cycle arrest at G0/G1 or G2/M phase by downregulating cyclins and CDKs responsible for tumor cell division.

Mechanistic studies reveal that PA suppresses key cancer-promoting pathways such as NF-κB, PI3K/Akt, MAPK/ERK, and Wnt/β-catenin, which are often overactive in colon cancer. By inhibiting these pathways, PA reduces cancer cell survival, inflammation, and resistance to cell death. In addition, PA exhibits strong anti-metastatic effects by lowering MMP-2 and MMP-9 levels, preventing colon cancer cells from invading and spreading to other organs. Some studies also report anti-inflammatory and antioxidant properties, which help reduce the tumor-friendly microenvironment in the colon. Animal studies demonstrate that PA extracts can reduce tumor size and improve colon tissue structure without causing major toxicity. Overall, Physalis angulata shows multiple anticancer actions—apoptosis induction, pathway inhibition, anti-inflammatory effects, and metastasis control—making it a promising natural candidate for colon cancer research.

Mechanism of Action of Physalis angulata Against Colon Cancer :

Physalis angulata acts against colon cancer through multiple molecular and cellular mechanisms demonstrated in laboratory studies. Its major bioactive compounds—such as physalin B, physalin F, physalin G, withangulatin A, and various withanolides—trigger apoptosis in colon cancer cells by increasing reactive oxygen species (ROS), damaging mitochondrial membranes, causing cytochrome-c release, and activating caspase-3 and caspase-9, which lead to programmed cell death. PA also produces cell-cycle arrest at the G0/G1 or G2/M phase by reducing the expression of cyclins and CDKs that allow cancer cells to divide. Another major mechanism is the suppression of cancer-promoting signaling pathways such as NF-κB, PI3K/Akt, MAPK/ERK, and Wnt/β-catenin, which reduces inflammation, growth signals, and the ability of cancer cells to survive. PA also inhibits angiogenesis (formation of new blood vessels) by downregulating VEGF, preventing tumors from receiving nutrients. Its compounds further reduce metastasis by decreasing levels of matrix metalloproteinases (MMP-2 and MMP-9), preventing colon cancer cells from invading and spreading. In addition, PA's anti-inflammatory activity lowers cytokines like TNF-α and IL-6, creating a less favorable environment for tumor growth. Together, these combined actions—apoptosis induction, oxidative stress, cell-cycle arrest, pathway inhibition, anti-angiogenic, anti-metastatic, and anti-inflammatory effects—explain how Physalis angulata exerts strong anticancer potential against colon cancer in scientific research.

6. Prostate Cancer :

Prostate cancer is a cancer that forms in the prostate gland, which is part of the male reproductive system and produces seminal fluid.It usually grows slowly but can become aggressive in some cases.

Causes / Risk Factors

- Aging (most common in men >50 years)
- Family history
- High testosterone levels
- Obesity
- High-fat diet

Why Physalis angulata is Studied for Prostate Cancer :Physalis angulata contains several powerful bioactive compounds: Physalins (A, B, D, F, G) ,Withanolides Flavonoids ,Steroids and terpenoids These compounds are known to show anti-tumor effects in laboratory studies.

MOA of Physalis angulata Against Prostate Cancer :

Physalis angulata exhibits promising anticancer activity against prostate cancer through multiple biological mechanisms that target tumor growth and survival. Its key bioactive compounds—mainly physalins and withanolides—induce apoptosis by activating caspase enzymes, increasing ROS levels, lowering mitochondrial membrane potential, and shifting the balance toward pro-apoptotic proteins

such as Bax while suppressing anti-apoptotic Bcl-2. The plant also inhibits major cancer-promoting pathways including NF-κB, STAT3, and PI3K/Akt, thereby reducing cell proliferation and survival signals. In addition, Physalis angulata suppresses metastasis by lowering levels of MMP-2 and MMP-9, which are enzymes responsible for tissue invasion, while blocking epithelial–mesenchymal transition (EMT), limiting cancer cell migration. Its strong anti-inflammatory effects, achieved by reducing cytokines like TNF-α, IL-6, and COX-2, help weaken the inflammatory microenvironment that supports tumor progression. Furthermore, Physalis angulata exhibits anti-angiogenic activity by inhibiting VEGF, reducing blood vessel formation and nutrient supply to tumors. Its antioxidant flavonoids also lower oxidative stress, preventing DNA damage and slowing carcinogenesis. Through this combination of apoptosis induction, proliferation inhibition, anti-metastatic action, anti-inflammatory activity, and antioxidant protection, Physalis angulata demonstrates significant research-level potential against prostate cancer.

VII. APPLICATIONS OF PROPERTIES

- Antibacterial properties
- Anticancer properties
- Antiparasitic properties
- Antiinflammatory properties
- Antifibrotic properties
- Antidiabetic properties.

1. Antibacterial properties

Physalis angulata (Mullaca) shows significant antibacterial activity, especially with methanol extracts of the whole plant. This antibacterial action supports several medical and practical applications.

Treatment of Bacterial Skin Infections: Because the plant shows strong activity against Staphylococcus aureus, Streptococcus species, Corynebacterium diphtheriae, and Pseudomonas aeruginosa, it can be used for:

- Treating infected wounds
- Treating boils, abscesses
- Managing dermatitis or skin diseases caused by bacteria
- Reducing bacterial load in skin inflammations
- This supports its traditional use as an antiseptic and disinfectant.

Development of Herbal Antibacterial Formulations:

- Herbal antibacterial creams
- Antiseptic herbal washes
- Herbal antimicrobial capsules or syrups
- Adjunct therapy for bacterial infections
- These uses are supported by the plant's strong antibacterial activity in lab studies.

Use in Future Antibacterial Drug Research:Because Physalis angulata inhibits several bacteria—including Pseudomonas aeruginosa, a drug-resistant organism—it may be used for:Discovering new antibacterial compounds.Isolation of steroidal compounds (physalins) for drug development.Creating plant-based antibiotics for resistant bacteria

2.Anticancer properties:

Application:

- Could be used to design immune-boosting therapy in cancer patients or adjunct treatments.
- Traditional and Herbal Cancer Treatment Systems :Communities in South America and Asia traditionally use P. angulata for:
- Treating tumors
- Treating swollen lymph glands
- Shrinking abnormal growths

Managing chronic inflammatory conditions associated with cancer

- Use in Developing Natural Chemotherapeutic Agents
- Since its extracts show low IC_{50} values (strong cytotoxicity), the plant is valuable for:
- Designing natural anticancer formulations
- Making phytopharmaceutical capsules or tinctures
- Herbal cancer adjunct therapy (supportive therapy)

Tumor and Leukemia Research:

- Screening anticancer compounds
- Leukemia drug research models

Designing Multi-Target Cancer Therapies

- Anti-inflammatory
- Immunomodulatory
- Antioxidant
- Antimicrobial
- Together these suggest potential for a multi-target therapy, beneficial in cancer management.

3.Antiparasitic Properties:

In traditional medicine, leaf or root extracts are used to manage intestinal worms (helminths).The active

compounds may disrupt the parasite's energy metabolism, leading to paralysis or death of the worm.

Possible traditional applications

- Decoction of leaves for managing roundworm-like symptoms.
- Powdered dried leaves used in some herbal systems for deworming.
- Activity Against Protozoan Parasites (Laboratory Studies) :Laboratory research shows Physalis angulata extracts can inhibit:

a. Plasmodium species (Malaria parasites)

- Physalins from the plant show antiplasmodial activity.
- They work by damaging the parasite's membrane and interfering with protein synthesis.

b. Leishmania species

- Methanol or ethanol extracts show anti-leishmanial activity on promastigotes.
- They disturb parasite cell walls and reduce their ability to multiply.

Anti-Helminthic Activity (Worm-Killing): Some compounds show effectiveness against helminths by:

- Causing paralysis of worms
- Breaking down worm cuticle layers
- Interfering with glucose uptake of parasites

Development of Anti-Parasitic Herbal Drugs (Research Application)

- Research studies explore Physalis angulata as a source for developing:
- Anti-malarial herbal extract
- Natural anti-leishmanial compounds
- Anti-trypanosomal phytomedicines Safe, plant-based deworming agents

4.Antiinflammatory Properties:

- In traditional medicine, leaf and stem extracts are used to reduce:
- Swelling
- Pain
- Redness
- Local inflammation
- Herbal paste for joint pain
- Decoctions for general body inflammation
- Poultices for minor wounds or swollen areas

Anti-Inflammatory Support in Arthritis

- Joint swelling
- Pro-inflammatory cytokines
- Oxidative stress in joint tissues
- Potential herbal support for rheumatoid arthritis
- Management of musculoskeletal inflammation

Skin Inflammation :Because of its soothing and anti-inflammatory effect, it is used for:

- Dermatitis
- Inflamed wounds
- Reduces redness and irritation
- Promotes faster healing
- Decreases inflammatory cytokines in skin layers

Gastrointestinal Inflammatory Conditions

- Extracts show protective effects on the digestive tract.
- Traditional use in gastric inflammation Protection of mucosal lining

5. Antifibrotic Properties:

Management of Liver Fibrosis (Hepatic Fibrosis)

- Reduce collagen accumulation in liver tissue
- Inhibit hepatic stellate cell activation (key cells causing fibrosis)
- Reduce oxidative stress in liver cells

Kidney Fibrosis (Renal Fibrosis)

- Reducing inflammatory infiltration
- Protecting kidney cells from oxidative damage
- Herbal support for chronic kidney disease in traditional systems

Pulmonary Fibrosis (Lung Fibrosis) :Experimental studies suggest Physalis angulata may help reduce:

- Lung inflammation
- Thickening of alveolar tissue
- Collagen deposition in lung parenchyma
- Cardiac Fibrosis (Fibrotic Heart Disease)

Preventing fibroblast overproliferation

- Reducing myocardial stiffness
- Protecting heart muscles from oxidative injury
- potential use in preventing fibrosis after:
- Myocardial infarction

6.Antidiabetic properties :

Management of High Blood Glucose Levels

- Reduce fasting blood glucose
- Inhibit carbohydrate-breaking enzymes (α-amylase, α-glucosidase)
- Used in herbal preparations for controlling hyperglycemia.
- Protection of Pancreatic β-Cells

- Diabetes causes damage to insulin-producing cells. Studies show Physalis angulata:
- Protects β-cells from oxidative stress
- Helps maintain insulin secretion
- Reduces inflammatory damage in pancreatic tissue

Improvement of Insulin Sensitivity :Bioactive compounds enhance the action of insulin in tissues like:

- Muscle
- Liver
- Adipose tissue
- May help reduce insulin resistance

Antioxidant Protection in Diabetic Organs :Diabetes causes oxidative damage to organs such as:

- Kidneys
- Liver
- Heart
- Eyes
- Reducing free radicals

Properties & Their Main Active Compounds:

Table No. 01: Properties & Their Main Active Compounds

Properties	Main Active Compounds
Anti-bacterial properties	Physalins flavonoid tannins
Anti-cancer properties	Physalin B,D,F,G
Anti-parasitic properties	Physalin alkaloids
Anti-inflammatory properties	Physalin D, Flavonoid
Anti-fibrotic properties	Physalin,flavonoid,steroids
Anti-diabetic properties	Flavonoids,tannins,alkaloids

VIII. NON-CLINICAL STUDY

1.Laboratory In-Vivo Application (Animal Studies)
Ethanol extract of the whole plant (75 mg/kg i.p.)
→ Active against leukemia P388 in mice.
Methanol leaf extract
→ Active against P388 leukemia (IC_{50} = 2.5 μg/ml)
Application:
Preclinical testing in animals for anticancer drug discovery.

2. Treatment of Various Human Cancers (Laboratory Evidence)
The plant extract showed direct cytotoxic activity against several cancer types in laboratory studies:
✓ Lung cancer (A549)
Methanol leaf extract showed high activity (IC_{50} = 3.93 μg/ml)
✓ Oral epidermoid carcinoma (Ca-9KB)
✓ Colon cancer
✓ Cervical cancer (HeLa)
✓ Hepatoma (liver cancer) HA22T, Hepatoma-2
✓ Leukemia (P388 leukemia cells)
These results mean P. angulata can potentially be used in developing anticancer therapies.

IX. CONCLUSION

The comprehensive evaluation of Physalis angulata demonstrates that it is a pharmacologically significant medicinal plant with broad therapeutic potential supported by traditional knowledge and modern scientific findings. Its rich phytochemical profile—particularly physalins, withanolides, and flavonoids—contributes to diverse biological actions including anticancer, anti-inflammatory, antioxidant, antiparasitic, antifibrotic, antibacterial, and antidiabetic effects. Preclinical evidence confirms that P. angulata acts through multiple molecular pathways such as apoptosis induction, cell-cycle regulation, immune modulation, and inhibition of metastatic and angiogenic processes, making it a promising candidate for future drug discovery and adjunct therapeutic strategies. However, despite encouraging laboratory outcomes, there remains a substantial gap regarding clinical validation, safety profiling, dose optimization, and formulation development. Therefore, further in vivo studies, toxicological investigations, pharmacokinetic assessments, and well-designed clinical trials are essential to translate its traditional and experimental benefits into safe and effective therapeutic applications. Overall, Physalis angulata holds considerable potential as a multifunctional medicinal herb and represents a valuable resource for modern phytomedicine and natural product-based drug innovation.

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