

THERAPEUTIC POTENTIAL OF PHYSALIS PERUVIANA (CAPE GOOSEBERRY) IN MITIGATING RISK FACTORS AND PATHOPHYSIOLOGY OF NON-COMMUNICABLE DISEASES

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ABSTRACT

A significant global health concern, non-communicable diseases (NCDs) include metabolic syndrome, type 2 diabetes mellitus, cancer, renal disorders, and inflammatory conditions. Their multifactorial pathophysiology involves chronic inflammation, oxidative stress, and metabolic dysfunction. A nutrient-dense fruit bearing plant with a long history of traditional medicinal use, *Physalis peruviana* (Cape Gooseberry) has recently drawn scientific attention for its diverse therapeutic potential against several NCDs. The botany, phytochemical profile, and preclinical data demonstrating *P. peruviana*'s effectiveness in modifying important pathological pathways associated with the onset and progression of NCDs are all thoroughly examined in this review. *P. peruviana* is a plant rich in phenolics, flavonoids, withanolides, and phytosterols. It has strong anti-inflammatory, anti-diabetic, anti-obesity, anti-cancer, nephro-, hepato-, and anti-arthritic properties. *P. peruviana* therapy is consistently associated with improved glycaemic management, lipid modification, tumor suppression, renal protection, and a reduction in joint inflammation in both rodent and in vitro models. Clinical translation still faces obstacles despite encouraging preclinical results, such as the requirement for carefully planned human studies, standardized extract formulation, and enhanced bioavailability of important phyto-constituents. Furthermore, cautious processing and dose considerations are required due to safety concerns regarding solanine in unripe fruits. To fully realize the therapeutic promise of this adaptable plant, future studies should concentrate on thorough molecular analyses, sophisticated delivery methods, and rigorous clinical evaluation. All things considered, *Physalis peruviana* is a powerful multi-target functional food that has great potential for reducing the intricate pathophysiology of NCDs.

KEYWORDS-*Physalis peruviana*, Cape gooseberry, non-communicable diseases, Anti-oxidant, Anti-inflammatory

1. INTRODUCTION

An estimated 74% of all fatalities worldwide are caused by non-communicable diseases (NCDs), of which the majority are caused by diabetes, cancer, cardiovascular disease, and chronic respiratory conditions. NCDs represent a serious global health concern. Poor eating habits, sedentary lifestyles, alcohol and tobacco use, and other environmental and lifestyle variables are major contributors to these illnesses. However, complicated biological factors that contribute to the genesis and progression of disease, including oxidative stress, metabolic dysregulation, and chronic inflammation, lurk underlying these behavioral reasons. Reactive oxygen species (ROS) and antioxidant defenses are out of balance during oxidative stress, which damages cellular components and throws off physiological equilibrium. Parallel to this, chronic low-grade inflammation accelerates tissue damage and encourages insulin resistance, endothelial dysfunction, and atherogenesis. It is frequently brought on by adipose tissue malfunction or an imbalance in the gut microbiota [Chew *et al.*, 2023]. The pathogenesis of NCDs is further complicated by metabolic dysfunction, which includes hypertension, dyslipidemia, and poor glucose metabolism. Since these illnesses have a complex etiology, integrative preventative approaches that focus on these molecular pathways are becoming more and more popular [Zhang *et al.*, 2024].

Physalis peruviana, commonly known as Cape Gooseberry, goldenberry, or Peruvian groundcherry, is a small, orange-yellow fruit encased in a delicate, papery husk. Native to the Andean regions of South America, particularly Peru and Colombia, this plant has garnered global attention for both its nutritional and medicinal attributes. Traditionally, it has been employed in folk medicine for treating ailments such as asthma, hepatitis, dermatitis, and urinary tract infections [El-Beltagi *et al.*, 2019]. With increasing scientific interest, modern studies have begun to validate these ethnopharmacological claims, attributing them to the rich phytochemical profile of the fruit, which includes withanolides, polyphenols, carotenoids, and vitamins particularly vitamin C and provitamin A. The unique bioactive compounds found in *P. peruviana* exhibit antioxidant, anti-inflammatory, hepatoprotective, and antidiabetic properties, making the fruit a promising candidate for nutraceutical and

functional food development. Its relevance in combating risk factors associated with NCDs is thus becoming an area of growing research focus. In recent years, there has been a paradigm shift toward exploring plant-based therapeutics as complementary or alternative approaches for managing chronic diseases [de Freitas *et al.*, 2024]. *Physalis peruviana* is unique among the botanicals being studied because of its wide range of pharmacological potential, which is backed by preclinical and new clinical data. As a functional meal, it offers pharmacologically active components that can alter important biological pathways linked to NCDs in addition to vital micronutrients. While its anti-inflammatory and lipid-lowering properties imply benefits in metabolic syndrome, cardiovascular dysfunction, and type 2 diabetes mellitus, its antioxidant-rich composition helps scavenge free radicals. These diverse effects are in line with the current scientific search for food-derived bioactives that can address metabolic, inflammatory, and oxidative abnormalities all at once. Thus, there is great potential for public health nutrition and integrative medicine to comprehend the therapeutic significance of *P. peruviana* in the context of managing and preventing non-communicable diseases [Añibarro-Ortega *et al.*, 2025].

Physalis peruviana's rich and varied phytochemical makeup, which includes withanolides, phenolic acids, flavonoids, carotenoids, phytosterols, and vital vitamins, is a major factor in the plant's rising scientific attention. It has been demonstrated that these substances have strong biological effects, especially when it comes to controlling oxidative stress and inflammatory cascades, two key processes in the pathophysiology of NCDs. *P. peruviana* extracts have been shown in preclinical research in both in vitro and animal models to attenuate inflammatory markers, modify lipid profiles, enhance glycemic management, and lessen hepatic steatosis. These results imply that it has therapeutic potential in contemporary clinical settings in addition to supporting its traditional use in ethnomedicine [Tiwari *et al.*, 2023]. Despite the encouraging outcomes, a thorough assessment and synthesis of the available data are required to close the gap between clinical application and laboratory research. Therefore, a targeted examination of its therapeutic applicability in relation to non-communicable diseases is both necessary and timely.

2. Botany and Phytochemical Profile

Physalis peruviana L. is a perennial herbaceous plant that belongs to the Solanaceae family. It is indigenous to South America's tropical and subtropical climates, especially the Andes of Ecuador, Colombia, and Peru. According to taxonomy, it is a member of the *Physalis* genus, which includes more than 90 species, many of which are distinguished by the inflated calyx, or "husk," that envelops the fruit. In terms of morphology, the plant has oval leaves and soft, pubescent stems that reach a height of 0.5 to 1.5 meters. The dark brown or purple cores of its bright yellow flowers eventually turn into round, smooth, orange-yellow berries that are encased in a papery, lantern-like calyx. This calyx protects *P. peruviana* and acts as a visual cue to set it apart from other closely related species. Rich in nutrients and bioactives, the fruit's edible part is the calyx, which is typically not eaten because it contains some bitter alkaloids [Bazalar Pereda *et al.*, 2020]. The plant has expanded to parts of Africa, Asia, and Europe thanks to its resilience to a variety of agroclimatic conditions and its comparatively short culture cycle. It is now being grown more often for both commercial and therapeutic uses in these locations. A nutrient-dense food with a well-balanced composition of macronutrients and micronutrients is *P. peruviana* fruit. It is rich in physiologically active chemicals but relatively low in energy, with roughly 11–16% carbs, 0.3–1.5% proteins, and 0.1–0.6% lipids. Vitamin C, also known as ascorbic acid, is abundant in it and is essential for immune system and antioxidant defense. Provitamin A (β -carotene), a number of B-complex vitamins (including niacin and riboflavin), and trace minerals including potassium, phosphorus, and iron are also present. Beneficial fatty acids from the seeds, especially oleic and linoleic acids, are known to have cardiovascular advantages. Additionally, there is moderate levels of dietary fiber, which promotes glycemic control and digestive health. Due to its extensive nutritional profile, *P. peruviana* is a functional food that has potential for both prevention and treatment [Ye *et al.*, 2019].

In addition to its basic nutritional value, *Physalis peruviana* has a variety of phytochemicals with pharmacological activity that enhance its potential for medicinal use. It has been determined that polyphenolic chemicals, such as caffeic acid, gallic acid, and chlorogenic acid, are strong antioxidants that can scavenge free radicals and prevent lipid peroxidation. Quercetin and kaempferol are two flavonoids that have extra anti-inflammatory and Vaso protective properties [Mishra *et al.*, 2024]. The feature that sets *P. peruviana* apart is the high concentration of withanolides, which are naturally occurring steroidal lactones that share structural similarities with withanone and ginsenosides. Among these, withanolides with anti-inflammatory, anti-cancer, and immunomodulatory qualities have been investigated, including magnoflorine, withanolide D, and withaperuvin A and B. Moreover, β -sitosterol, one of the fruit's noteworthy phytosterols, lowers cholesterol by fighting with dietary cholesterol for intestine absorption [Tiwari *et al.*, 2023]. The wide spectrum of biological activities seen in preclinical research, particularly in relation to oxidative stress, inflammation, and metabolic dysfunction linked to non-communicable illnesses, is supported by the synergy between these bioactive substances [Guiné *et al.*, 2024].

Table – 1: Cape Gooseberry and a Number of other High-Value Fruits: A Comparison of Their Nutritional Content (Per 100g FW)

Fruits	Vitamin (mg)	C	Dietary fiber (g)	Potassium (mg)	Total polyphenols (mg GAE)	References
Cape Gooseberry	47.2- 52.2		4.69	306.5-327.6	68.2-83.4	[Obregón-La Rosa et al., 2023; Muñoz et al., 2021]
Amla	193-720 (commonly-478)		5	198	274.59	[Gul et al., 2022; Halim et al., 2022]
Apple	19.38		51.1	144	270.97	[Kumar et al., 2018; Sudha et al., 2007; Kschonsek et al., 2018]
Strawberry	58.8		0.9-1.2	170	954.33	[Nishu et al., 2021; Ganhão et al., 2019; Mondal et al., 2017]
Blueberry	3.4 – 9.5		2.4	66.2 – 98.0	393	[Krishna et al., 2023; Mondal et al., 2017]

3. Mechanisms of Action in NCD Risk Reduction

3.1 Antioxidant Activity

Physalis peruviana's strong antioxidant activity is one of the main ways it helps prevent and treat non-communicable diseases. An excess of reactive oxygen species (ROS) causes oxidative stress, which is a key pathogenic element in the development of cancer, diabetes, cardiovascular disease, and neurodegeneration. In a number of in vitro antioxidant tests, such as ferric reducing antioxidant power (FRAP) assays, DPPH (2,2-diphenyl-1-picrylhydrazyl), and ABTS (2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid), the ethanol extracts of *P. peruviana* have continuously shown notable radical-scavenging activity. Interestingly, research has shown that *P. peruviana* extracts' antioxidant capacity not only equals but in certain tests exceeds that of α -tocopherol (vitamin E), a recognized antioxidant benchmark [Abou Baker & Ramadan, 2024]. Flavonoids and phenolic acids, which are abundant in the fruit and function as electron donors to neutralize free radicals and stop oxidative chain reactions, are primarily responsible for this increased activity. Certain chemicals in *P. peruviana* enhance endogenous antioxidant defense pathways, including the overexpression of enzymes including glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD), in addition to directly scavenging radicals. When these antioxidant pathways work together, they lessen oxidative damage to proteins, lipids, and DNA, which is a key factor in the pathophysiology of noncommunicable diseases [Luis *et al.*, 2024].

3.2 Anti-Inflammatory Effects

The onset and progression of many non-communicable diseases, including as cardiovascular problems, metabolic syndrome, type 2 diabetes, and several types of cancer, are significantly influenced by chronic, low-grade inflammation. Because of the abundance of withanolides, polyphenols, and other bioactives in its fruit and calyces, *Physalis peruviana* has shown considerable anti-inflammatory potential. *P. peruviana* ethanol and methanol extracts have been demonstrated in a number of preclinical investigations to inhibit pro-inflammatory mediators, including cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2), which are enzymes involved in prostaglandin formation and inflammatory signaling. Together with these effects, there is a noticeable reduction in pro-inflammatory cytokines, such as interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α), which are important causes of tissue damage and systemic inflammation in NCDs [Mohammed *et al.*, 2024].

Animal models for experimental validation support these results even further. Specifically, topical administration of *P. peruviana* extracts in the mouse ear edema model a commonly used technique to evaluate anti-inflammatory activity led to a notable decrease in the infiltration of inflammatory cells and the development

of edema. These results are similar to and sometimes better than those of conventional anti-inflammatory medications. This anti-inflammatory response is thought to be mechanistically mediated by downregulating NF- κ B signaling pathways, which are essential for the transcriptional activation of several inflammatory mediators. Additionally, withanolides like physalins and withaperuvin may have immunomodulatory effects by regulating macrophage activation and preventing the generation of reactive species like nitric oxide. These findings suggest that *P. peruviana* holds promise not only as a natural anti-inflammatory agent but also as a potential adjuvant in managing inflammation-linked chronic diseases [Moya *et al.*, 2024].

3.3 Antidiabetic Potential

The increasing number of people with type 2 diabetes mellitus (T2DM) and the difficulties that come with it has highlighted the need for complementary and alternative medicines that can control glucose homeostasis and stop metabolic decline. *Physalis peruviana* has strong antidiabetic potential via a number of pathways, most notably the suppression of enzymes that break down carbohydrates. Research conducted in vitro has demonstrated that fruit extracts can inhibit α -amylase and α -glucosidase, two important enzymes involved in the breakdown and absorption of dietary starch, at levels similar to those of the widely used antidiabetic medication acarbose. Postprandial hyperglycemia, a primary cause of glucotoxicity and insulin resistance, is lessened by *P. peruviana* by postponing the breakdown of carbohydrates and the absorption of glucose [González-Buenrostro *et al.*, 2024]. Additionally, the inhibition of advanced glycation end-product (AGE) formation further contributes to its protective effect, as AGEs play a critical role in the development of diabetic complications, including nephropathy, retinopathy, and vascular dysfunction.

These antidiabetic benefits have been further confirmed by in vivo studies employing diabetic mouse models. It has been demonstrated that taking *P. peruviana* extracts orally improve glycemic management by raising insulin sensitivity, improving glucose tolerance, and lowering fasting blood glucose levels. Increased insulin secretion and histological investigations show that pancreatic β -cell architecture and function are frequently preserved along with these metabolic benefits. Additionally, decreases in inflammatory markers and systemic oxidative stress imply that *P. peruviana*'s antidiabetic effects go beyond glucose control to include reducing the chronic oxidative-inflammatory environment that fuels the development of diabetes [Tshibangu *et al.*, 2025]. These findings indicate that *P. peruviana* holds promise as a natural therapeutic agent for diabetes prevention and management, particularly as part of a functional food or nutraceutical strategy.

Central adiposity, insulin resistance, dyslipidemia, and low-grade chronic inflammation are some of the complex conditions that make up obesity and metabolic syndrome. These conditions raise the risk of type 2 diabetes, cardiovascular disease, and hepatic steatosis. *Physalis peruviana* may have preventive effects against the onset and progression of several related illnesses, according to emerging preclinical research. Daily treatment of *P. peruviana* extracts has been demonstrated to dramatically lower body weight growth, visceral fat accumulation, and serum triglyceride levels in obese rodent models produced by a high-fat diet. Modification of lipid metabolism, enhanced insulin signaling, and reduction of adipose tissue inflammation seem to be the mechanisms underlying these effects [Abdelmottaleb Moussa *et al.*, 2024].

Furthermore, rats given *P. peruviana* supplements showed reduced homeostatic model assessment for insulin resistance (HOMA-IR) scores and increased insulin sensitivity, suggesting a halt or reversal of the progression of insulin resistance. Fat profiles and indicators of hepatic function also improved, indicating a decrease in oxidative damage and hepatic fat infiltration. It is believed that the bioactive substances, especially withanolides, phytosterols, and polyphenols, control important metabolic processes including AMPK activation and PPAR- γ regulation, which are both connected to lipid use and energy homeostasis. Additionally, by lowering TNF- α and IL-6 levels in adipose and hepatic tissues, *P. peruviana*'s anti-inflammatory properties may lessen cytokine-mediated insulin resistance. These results highlight the plant's potential as a natural treatment for metabolic diseases linked to obesity and for enhancing metabolic resistance [Yang *et al.*, 2025].

3.5 Anticancer & Antiproliferative Effects

Chronic inflammation, oxidative stress, and dysregulated cell signaling pathways are increasingly being associated with cancer, a significant subset of non-communicable disorders. In a number of in vitro and in vivo studies, *Physalis peruviana* has shown encouraging anticancer and antiproliferative qualities. One of its most researched bioactive components is 4 β -hydroxywithanolide E, a withanolide that has been demonstrated to disrupt the Wnt/ β -catenin signaling pathway, which is a major factor in colorectal cancer development. *P. peruviana* inhibits the transcription of oncogenes that encourage cell invasion, proliferation, and metastasis and triggers apoptosis via altering this route. Because aberrant Wnt signaling is linked to both the early and late stages of colorectal carcinogenesis, this pathway is very pertinent [Cevik *et al.*, 2024].

Magnolin, a lignan contained in *P. peruviana*, is another noteworthy molecule. It has been shown to have substantial antiproliferative and anti-migratory actions on pancreatic cancer cells, with an IC₅₀ value of roughly 0.51 μ M, indicating great cytotoxic activity at low concentrations. It has been documented that magnesium inhibits important cell cycle regulators and suppresses pathways including PI3K/Akt and ERK1/2, which are frequently overactivated in cancerous cells. Additionally, administration of *P. peruviana* extracts has been linked to improved production of pro-apoptotic proteins (like Bax) and decreased expression of anti-apoptotic markers (like Bcl-2), which promotes intrinsic apoptotic signaling. These antiproliferative properties, along with its

comparatively low toxicity in healthy cells, demonstrate *P. peruviana*'s potential as a source of new phytotherapeutics or as an adjuvant to traditional cancer treatment [Aneja *et al.*, 2025].

3.6 Nephroprotective & Hepatoprotective Activity

Since the liver and kidneys are essential organs involved in metabolic regulation and detoxification, they are particularly vulnerable to harm from oxidative stress, environmental pollutants, and chronic inflammation all of which are strongly associated with the development of non-communicable illnesses. In experimental models of heavy metal toxicity, especially cadmium-induced nephrotoxicity, calyx extracts from *Physalis peruviana* have shown notable nephroprotective benefits. Excessive reactive oxygen species (ROS) production brought on by cadmium exposure damages DNA, causes lipid peroxidation, and causes inflammation in renal tissues. When *P. peruviana* calyx extract is administered, these negative effects are lessened by strengthening endogenous antioxidant defenses like glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD). This reduces oxidative damage and restores renal function indicators like blood urea nitrogen and serum creatinine [Prabhu *et al.*, 2024].

Additionally, parallel hepatoprotective qualities have been discovered, with extracts of *P. peruviana* shielding liver cells from oxidative stress and chemically induced toxicity. TNF- α and IL-1 β are pro-inflammatory cytokines that are downregulated, which has anti-inflammatory effects that help preserve liver tissue. Mechanistically, it is believed that these effects result from the combined action of the calyx's withanolides, phenolic chemicals, and flavonoids, which together prevent NF- κ B activation and block apoptotic pathways in renal and hepatocyte cells. These results suggest that *Physalis peruviana* may be useful as a natural defense against hepatic and renal damage, with consequences for avoiding organ failure linked to long-term NCDs and exposure to environmental toxins [Gangawat *et al.*, 2025].

3.7 Anti-arthritis Effects

Chronic non-communicable diseases like rheumatoid arthritis (RA) and other inflammatory arthritic syndromes are typified by systemic immune dysregulation, cartilage deterioration, and ongoing joint inflammation. In several *in vivo* models of adjuvant-induced arthritis, *Physalis peruviana* has shown great promise in reducing arthritic symptoms. In these animals, oral treatment of *P. peruviana* extracts results in significant decreases in histological joint damage, inflammatory cell infiltration, and paw edema, suggesting efficient control of the inflammatory process. Withanolides, a family of steroidal lactones that are prevalent in *P. peruviana*, are primarily responsible for the anti-arthritis actions mechanistically [Mohammed *et al.*, 2024]. Tumor necrosis factor- α (TNF- α), a master regulator cytokine in RA pathogenesis that promotes synovial inflammation and cartilage degradation, is strongly inhibited by these bioactive substances. Pro-inflammatory cytokines including TNF- α , interleukin-1 beta (IL-1 β), and interleukin-6 (IL-6) have been shown to be significantly downregulated in treated mice, and NF- κ B signaling pathways have also been suppressed. This immunomodulatory action highlights the therapeutic potential of *Physalis peruviana* as a natural anti-arthritis drug by lowering acute inflammation and preventing progressive joint degradation [Gupta *et al.*, 2025].

4. Preclinical Evidence across NCD Categories

A growing body of preclinical research has rigorously evaluated the efficacy of *Physalis peruviana* in mitigating risk factors and pathophysiological features across multiple non-communicable disease (NCD) categories. These studies employ a variety of biochemical assays, cell culture systems, and animal models to elucidate the plant's multifaceted pharmacological actions.

4.1. Metabolic Syndrome and Type 2 Diabetes Mellitus (T2DM):

P. peruviana extracts have shown strong α -amylase and α -glucosidase inhibitory activity in the field of metabolic diseases, which is similar to those of drugs like acarbose [1]. An important aspect of managing diabetes is postprandial glycemic control, which is improved by this enzymatic inhibition, which slows the digestion of carbohydrates and the absorption of glucose. By using conventional indices like HOMA-IR, rodent models of type 2 diabetes supplemented with *P. peruviana* show greater insulin sensitivity, decreased insulin resistance, and improved fasting blood glucose. These models also show positive modulation of the lipid profile, with increases in HDL-C and decreases in triglycerides and low-density lipoprotein cholesterol (LDL-C). Additionally, histopathological analyses show that the integrity of the pancreatic β -cells has been preserved, indicating a protective effect against diabetic damage [Pino-de la Fuente *et al.*, 2020].

4.2. Obesity

The ability of *P. peruviana* to effectively prevent or attenuate weight gain and adipose tissue expansion is demonstrated by the use of high-fat diet-induced obesity models in animals. Alongside this anti-obesity action, there are improvements in metabolic markers such lower levels of inflammatory cytokines (TNF- α , IL-6), improved insulin signaling pathways, and lowered blood triglycerides. Mechanistically, the bioactive substances in the plant, such as phytosterols and withanolides, seem to stimulate AMP-activated protein kinase (AMPK), a crucial modulator of lipid metabolism and energy balance, which in turn promotes fatty acid oxidation and suppresses lipogenesis. Restoring metabolic balance and lowering inflammation linked to obesity are two benefits of these metabolic changes [Abdelmottaleb *et al.*, 2022].

4.3. Cancer

The anticancer properties of *P. peruviana* have been thoroughly investigated in models of pancreatic, hepatoma, and colorectal cancer. Withanolides, such as 4 β -hydroxywithanolide E and magnolin, dramatically inhibit the growth, migration, and invasion of cancer cells in both in vitro cell lines and in vivo xenograft models. By disrupting carcinogenic signaling pathways such as Wnt/ β -catenin, ERK1/2, and PI3K/Akt, these substances cause apoptosis by altering pro- and anti-apoptotic proteins (e.g., overexpression of Bax and downregulation of Bcl-2). Genes necessary for tumor growth and metastasis are less frequently transcriptionally active in colorectal cancer models when the Wnt pathway is inhibited. Magnolin has high antiproliferative activity in pancreatic cancer, as evidenced by its low IC₅₀ values and strong cytotoxicity. According to these results, *P. peruviana* is a potentially useful source of chemopreventive drugs [Chang *et al* 2016].

4.4. Kidney Disease

The nephroprotective characteristics of *P. peruviana* have been shown in animal models of toxicity caused by toxins including cadmium and cisplatin. Through the enhancement of natural antioxidant enzyme activity (SOD, CAT, GPx) and the reduction of malondialdehyde (MDA), a sign of lipid peroxidation, calyx extract treatment decreases oxidative stress. At the same time, tissue damage and renal inflammation are reduced due to the suppression of inflammatory markers such as TNF- α and IL-1 β . Serum creatinine and blood urea nitrogen, two functional indicators that indicate intact renal function, exhibit a noticeable improvement. The extract's preventive function is further supported by histological investigations that show decreased tubular necrosis and inflammatory infiltration [Aljadani *et al.*, 2024].

4.5. Rheumatoid Arthritis

In adjuvant-induced arthritis models, *P. peruviana* demonstrates significant anti-arthritic effects through the inhibition of cyclooxygenase enzymes (COX-1 and COX-2) and pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6. These bioactivities result in decreased joint swelling, reduced synovial inflammation, and mitigation of cartilage degradation. Withanolides are the primary bioactive constituents implicated in these effects, acting as potent TNF- α inhibitors and modulating NF- κ B signaling to suppress the inflammatory cascade. Histopathological improvements include reduced pannus formation and preservation of joint architecture, suggesting the potential of *P. peruviana* as a complementary therapy for inflammatory arthritis [Mohammed *et al.*, 2024].

5. Safety, Toxicology & Bioavailability

5.1. Toxicity Concerns

While *Physalis peruviana* is usually thought to be safe when taken in normal dietary proportions, the presence of solanine and other glycoalkaloids in its unripe fruits and other components raises safety concerns. At high quantities, solanine, a naturally occurring toxin present in some members of the Solanaceae family, can have gastrointestinal and neurotoxic effects. It is crucial to properly harvest and ripen *P. peruviana* fruits before consuming them because eating unripe fruits might cause symptoms including nausea, vomiting, and abdominal pain. Ripe fruit extracts have been shown to have low acute toxicity, high median lethal dosage (LD50) values, and no negative effects on critical organs in toxicological tests conducted in animal models [Perk *et al.*, 2013].

However, as incorrectly handled or immature fruits may have high levels of solanine, care should be used when processing and eating them. Although they are scarce, genotoxicity evaluations and chronic toxicity studies are essential to fully define long-term safety profiles, particularly for concentrated extracts used for medicinal application. Other areas that require more research include possible allergenicity and interactions with medications, which have not been fully examined. For the most part, toxicological concerns are limited to unripe or badly processed materials, and current research generally supports the safe use of *P. peruviana* fruit in food and supplement form when picked at full ripeness [Ayşe, 2024].

5.2. Bioavailability Issues

Physalis peruviana's high polyphenolic and withanolide content is largely responsible for its medicinal efficacy; yet, bioavailability is a major problem for these bioactive chemicals. Because of their low water solubility, instability in the gastrointestinal tract, and substantial degradation by intestinal enzymes and gut microbes, polyphenols including flavonoids and phenolic acids generally have poor oral bioavailability. Methylation, glucuronidation, and sulfation are examples of phase I and phase II metabolic changes that these substances go through after consumption that can change their biological activity and lower systemic exposure [Guiné *et al.*, 2020].

As a consequence, intact polyphenols frequently have low plasma concentrations, which restricts their direct therapeutic potential. Moreover, withanolide absorption and bioefficacy are not entirely understood, although they might encounter comparable metabolic obstacles. Various approaches have been suggested to increase bioavailability, including co-administration with probiotics, formulation with absorption enhancers, and nanoencapsulation. Furthermore, the complicated pharmacokinetics of *P. peruviana* substances may be highlighted by the production of bioactive metabolites that contribute to systemic effects through their interaction with the gut flora. To maximize the clinical translation of phytochemicals produced from *P. peruviana* as potent

medicines against non-communicable diseases, these bioavailability concerns must be resolved [Puentes *et al.*, 2019].

6. Future Perspectives and Challenges

Despite promising preclinical evidence demonstrating the therapeutic potential of *Physalis peruviana* against various non-communicable diseases, its clinical translation remains limited. Rigorous randomized controlled trials (RCTs) in human populations are urgently needed to validate efficacy, determine optimal dosing regimens, and assess long-term safety. Such trials should incorporate well-defined endpoints related to metabolic, inflammatory, and oncological outcomes, with adequate sample sizes and standardized intervention protocols. Moreover, population diversity in terms of genetics, diet, and comorbidities must be considered to ensure the generalizability of findings [Mishra *et al.*, 2024]. Filling up these gaps will assist in transforming *P. peruviana* from a phytotherapeutic candidate with promise to a clinically recognized adjuvant. Creating effective formulations is essential to optimizing *Physalis peruviana*'s medicinal advantages. However, stability, bioavailability, and palatability issues must be resolved before these can be transformed into consumer-friendly forms like functional foods, dietary supplements, or nutraceuticals. Currently, most research uses crude extracts or isolated molecules [Prat & Sáenz, 2024].

The bioefficacy of bioactive components, particularly polyphenols and withanolides, may be improved by novel delivery methods such as encapsulation, liposomal formulations, or nanoemulsions. Furthermore, including *P. peruviana* extracts into functional foods can offer a workable strategy for preventive healthcare, utilizing dietary practices to fight noncommunicable diseases [Bazana *et al.*, 2019]. Future research should concentrate on chemical stability, extraction process optimization, and efficacy validation in these innovative delivery systems. The absence of standardized extracts with consistent phytochemical profiles is a significant obstacle to the widespread therapeutic use of *Physalis peruviana*. Significant variations in the amount and potency of bioactive compounds can result from variations in plant growing circumstances, harvest timing, extraction methods, and storage. Creating standardized procedures and quality assurance methods is crucial to guaranteeing efficacy, safety, and reproducibility [Peng *et al.*, 2019].

To precisely categorize *P. peruviana* products, specify acceptable bioactive levels, and require thorough safety evaluations, regulatory frameworks must be created or modified. This will make it easier for consumers and healthcare professionals to accept it and open the door for the commercial manufacture of high-quality, standardized *Physalis peruviana* products [Añibarro-Ortega *et al.*, 2025]. Even though recent research shows that *Physalis peruviana* has a wide range of pharmacological properties, more in-depth molecular and cellular mechanistic studies are still desperately needed. Clarifying the precise pathways that its bioactive chemicals activate will help to find potential synergistic interactions and clarify their therapeutic processes. Pharmacokinetic studies and thorough dose-response profiling can assist maximize therapeutic windows and reduce side effects. Furthermore, studies examining changes in gene expression, epigenetic alterations, and signaling cascades in pertinent disease models will yield important information. Such fundamental information will support the scientific justification for therapeutic uses and guide the logical development of next-generation treatments based on *P. peruviana* [Bazana *et al.*, 2019].

7. CONCLUSION

Cape Gooseberry, or *Physalis peruviana*, is a promising multipurpose plant with significant medicinal potential against non-communicable diseases (NCDs). Its ability to influence a variety of pathogenic pathways, including oxidative stress, chronic inflammation, metabolic dysregulation, and aberrant cellular proliferation, is shown by the abundance of preclinical data reviewed. Its complex phytochemical composition, which includes strong antioxidants, anti-inflammatory compounds, withanolides, and bioactive sterols, is largely responsible for these multi-target benefits. Considering its complexity, *P. peruviana* is a desirable option for integrative techniques meant to lessen the multifactorial aspect of NCDs. The effectiveness of *P. peruviana* in enhancing glycemic control, preventing obesity, slowing the evolution of tumors, preserving renal and hepatic function, and minimizing inflammatory joint damage is supported by strong data from in vitro research and animal models. Its promise as a comprehensive functional food or nutraceutical is highlighted by its capacity to simultaneously address several risk factors that underlie metabolic syndrome, cancer, kidney disorders, and rheumatoid arthritis. These results not only support the plant's traditional use but also offer a solid scientific basis for its application in therapeutic and preventative measures. The benefits of *P. peruviana* are still being translated from the bench to the bedside, despite these promising results. Well-designed human clinical trials are essential for defining therapeutic dosages, assessing long-term safety, and validating preclinical results. To get around restrictions on bioavailability and guarantee reliable distribution of bioactive substances, such research needs to be supported by developments in formulation technologies. Furthermore, strict frameworks for standardization and quality control are necessary to ensure product dependability and promote regulatory approval. Clarifying the precise chemical pathways by which *P. peruviana* produces its therapeutic properties should be another area of future investigation.

Its phytochemicals' synergistic interactions, dose-response analyses, and comprehensive pharmacokinetic investigations will expand our knowledge and improve clinical application. This process may be accelerated by combining systems biology techniques with contemporary omics technology, providing fresh insights into its

complex effects against intricate NCD networks. As a multi-target functional food, *Physalis peruviana* has great potential to alleviate the worldwide burden of non-communicable diseases. Its rich phytochemistry and proven preclinical effectiveness offer a solid basis for further translational studies. *P. peruviana* may be positioned as a useful natural remedy in the worldwide battle against cancer, metabolic disorders, renal diseases, and inflammatory conditions if present difficulties with clinical validation, formulation, and standardization are resolved.

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Author Contributions

Shreya: Collected relevant references, wrote the manuscript, and prepared the figures and tables.

Dr. Amarjeet Kaur: Reviewed the manuscript, provided critical feedback, and contributed to the interpretation of data.

Dr. Monika Gupta: Supervised the overall work, revised the manuscript for intellectual content, and approved the final version for submission.

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Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

DECLARATIONS

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