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Essay

Goldenberry L.: phytochemicals and applications in human health

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Abstract

Goldenberry is a species of great socioeconomic importance in different countries of Latin America and Africa. At the phytochemical level, this species presents a variety of biologically important phytochemicals. Therefore, this paper aims to provide an exhaustive summary of *Physalis peruviana* goldenberry, focusing on its phytochemicals and applications in human health. This work was conducted in 2024; it indicates that, at the level of its fruits, there are terpenes, phenolic compounds, alcohols, steroids, withanolides, highlighting carotenoids and flavonoids, reduced levels of fat, high water content and vitamins A, B3, B6, C and E, as well as the minerals calcium, potassium, phosphorus and magnesium. This richness in phytochemicals and nutrients of goldenberry translates into significant health benefits thanks to its antioxidant, antibacterial and antiproliferative properties. In particular, goldenberry calyxes and leaf extracts have demonstrated antihepatotoxic, antifibrotic and antidiabetic activity. In summary, the goldenberry has an optimal nutritional content and it is necessary to optimize the bioavailability of its components to fully take advantage of its benefits. Due to its potential as a promising component in functional foods and phytomedicine, there is a need for more in-depth evaluations of its impact on the well-being of humanity.

Keywords:

Physalis peruviana, health benefits, nutrition, phytomedicine.

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The species *Physalis peruviana* L., known as *aguaymanto* in Peru, *uchuva* in Colombia, *uvilla* in Ecuador and goldenberry or cape gooseberry in the United States of America, is native to the Andes in South America (Kasali *et al*., 2021), where it grows wild at altitudes of 1 500 to 3 000 m (Y#ld#z *et al*., 2015; Ramos *et al*., 2022). Currently, Colombia and South Africa are the world's leading producers, with Zimbabwe, Ecuador and Peru standing out (Majcher *et al*., 2020).

The properties of the active compounds present in *P. peruviana* have been recognized and used over the centuries for the benefit of health. More recently, various nutritional and bioactive properties have been demonstrated, including anti-asthmatic, diuretic, antiseptic, anti-inflammatory, antiproliferative, sedative, analgesic and antidiabetic effects (Yıldız *et al*., 2015; Singh *et al*., 2019), which are linked to its phytochemical content (Muñoz *et al*., 2021). These compounds include physalins, alkaloids, flavonoids, carotenoids, vitamins and polysaccharides, which are present in optimal amounts in various organs (Bazalar *et al*., 2019), which has generated a growing interest in knowing the mechanisms of action of these and other bioactive metabolites present in *P. peruviana*. For this reason, it is essential to provide an exhaustive summary of *Physalis peruviana* goldenberry, focusing on its phytochemicals and its applications in human health.

Phytochemicals identified in different parts of *Physalis peruviana* L.

Figure 1 presents a summary of the phytochemicals identified and characterized in the different organs of *P. peruviana*. The search carried out demonstrated the presence of various classes of phytochemicals, including terpenes (monoterpenes, sesquiterpenes, diterpenes, triterpenes and carotenoids), phenolic compounds (phenolic acids, phenolic esters, phenolic aldehydes, chalcones, coumarins, cinnamic acid derivatives, flavonoids and glycosides), alcohols, aldehydes, ketones, carboxylic acids, lactones, steroids and withanolides, alkaloids, sucrose esters, glycosides, siloxanes, vitamins, phytoprostanes, derivatives of phytol and enols.

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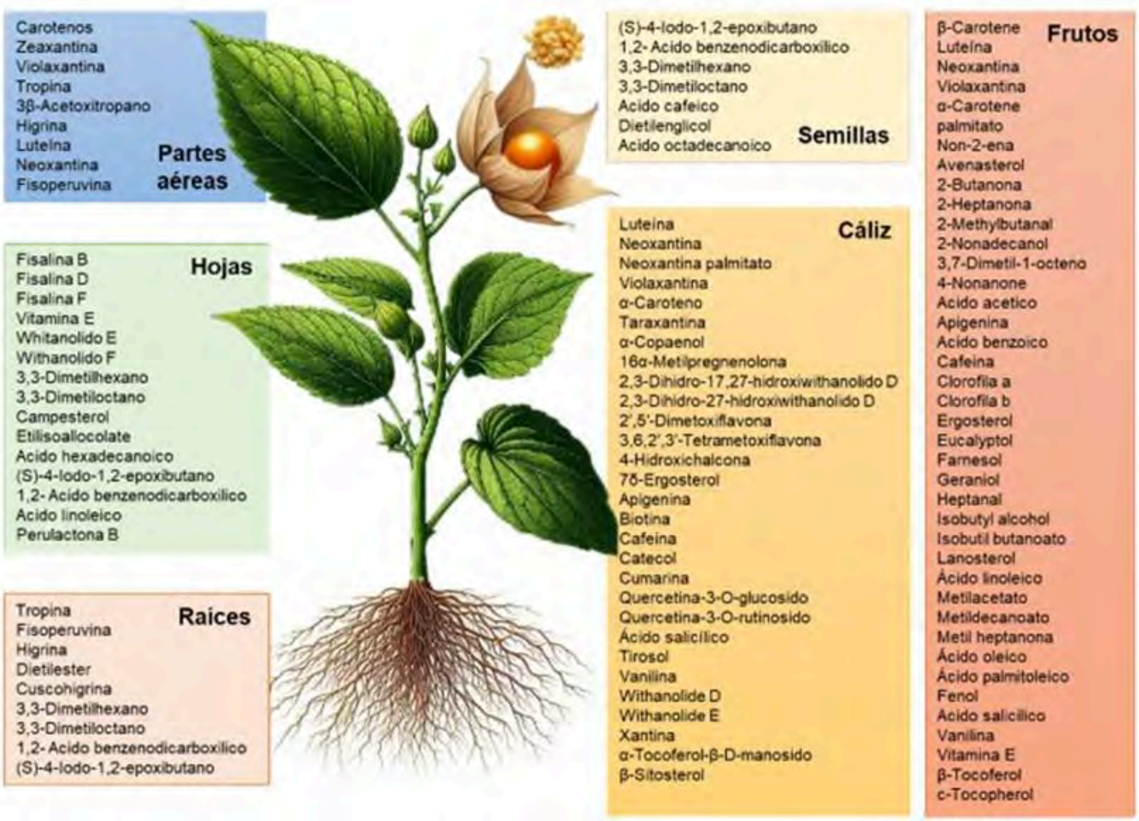
Figure 1. Phytochemicals identified in different parts of *Physalis peruviana* L.



Various parts of *P. peruviana* contain a rich variety of phytochemicals, among which terpenes and polyphenols stand out, which account for 26.09% and 14.94%, respectively. In the terpene category, carotenoids stand out as the most representative (11.15%), followed by monoterpenes (8.76%), sesquiterpenes (5.57%), and diterpenes (3.18%).

Regarding phenolic compounds, flavonoids are the most prevalent (5.17%), followed by cinnamic acid derivatives (3.98%), monophenolic compounds (1.79%), phenolic acids (1.39%), coumarins (0.79%), phenolic esters (0.79%), chalcones (0.39%), phenolic aldehydes (0.39%), and stilbenes (0.19%) (Medina *et al*., 2019). These compounds are synthesized and accumulated in all plant tissue; however, their concentration varies between different parts. Phenolic acids and flavonoids are the subject of extensive research due to their pharmacological properties and medical applications related to cellular detoxification (Zhang *et al*., 2005).

The results also indicate the finding of phytol at the level of the calyx and leaves of *P. peruviana*. In addition, phytoene is a 40-carbon alkene that acts as an intermediary in the synthesis of carotenoids, compounds abundant in the genus *Physalis*, used in the food industry as dyes for fats, oils and that act as precursors of violaxanthin (Yu *et al*., 2019). At the level of its seeds, *P. peruviana* can contain up to 30% fatty acids, with hexadecanoic acid (palmitic acid), decanoic acid, linoleic acid, and octadecanoic acid standing out (Asilbekova *et al*., 2016). Hexadecanoic acid is the most common saturated fatty acid, whereas linoleic acid is essential in plant lipids and crucial in human and animal diets (Rustan *et al*., 2005).

The family Solanaceae is the main producer of withanolides, with more than 350 withanolides having been identified in the genus *Physalis*, with *P. peruviana* and *P. angulata* standing out as the main sources (Huang *et al*., 2020). In particular, in *P. peruviana*, the presence of dihydrowithaferins,

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perulactones, withaferins, and hydroxywithanolides stands out (Kasali *et al*., 2021). Among other steroids, physalins stand out for their biological activity (Ballesteros-Vivas *et al*., 2019).

Therefore, *P. peruviana* is a species of great phytochemical interest due to its richness in bioactive compounds, including terpenes (monoterpenes, sesquiterpenes, diterpenes, triterpenes, and carotenoids), phenolic compounds (phenolic acids, phenolic esters, phenolic aldehydes, chalcones, coumarins, and flavonoids), fatty acids, steroids, withanolides, vitamins, phytol derivatives and enols. These compounds, identified and characterized in different parts of the plant, hold promise for the development of pharmaceuticals and functional foods.

Nutritional value of *Physalis peruviana* L.

Table 1 presents the approximate composition of the nutritional value of *P. peruviana*. The low content of fat in the fruit stands out, which does not exceed 1% of the total weight on average, a situation that contrasts with the high content of water of the fruit (77.3% to 85.5%). The high level of water and high concentration of carbohydrates provide the fruit with greater protection in structural terms (Cortés-Díaz *et al*., 2015; Bazalar *et al*., 2019). In contrast, the protein content is relatively low (1.4-1.7%), with an acidic pH (3.9-6.1) that ensures vitamin C activity. Regarding the amount of ash, there are differences (0.8-3%), probably due to variations between different growing regions since climatic conditions, soil characteristics, and other multiple factors directly intervene in the qualities of the fruit (Cortés-Díaz *et al*., 2015).

Table 1. Composition of the fruit of *Physalis peruviana* L.

Component	Y#ld#z *et al*. (2015)	Cortés-Díaz *et al*. (2015)	Bazalar *et al*. (2019)
Water (%)	-	85.5	79.1
Ash (%)	3	0.8	0.8
Protein (%)	1.7	1.5	1.4
Fat (%)	0.2	0.5	0.4
Carbohydrates (%)	13.9	11.9	14.2
pH	6.1	-	3.9
Total energy (kcal 100 g^{-1})	-	58	-

The fatty acid content of *P. peruviana* comes mainly from its seeds and is mainly composed of saturated and polyunsaturated fatty acids, among which palmitic acid and linoleic acid stand out, these being the most prominent as shown in Table 2 (Chasquibol *et al*., 2015; Morillo *et al*., 2017). In addition, linolenic acid is a bioactive compound capable of affecting proliferation and invasion by inhibiting the enzyme Fatty Acid Synthase and promoting apoptosis of cancer cells (Fan *et al*., 2022). Other compounds detected were hexadecene epoxide and phytol, which could be used as precursors for the manufacture of synthetic forms of vitamins E and K (Morillo *et al*., 2017).

Table 2. Fatty acid composition in leaves and seeds of *Physalis peruviana* L.

Fatty acid (g kg^{-1})	Leaves (Morillo *et al*., 2017)	Seeds (Chasquibol *et al*., 2015)
Myristic acid (C14:0)	4	10
Palmitic acid (C16:0)	428	72.9
Palmitoleic acid (C16:1 #-7)	-	5.2
Stearic acid (C18:0)	7	31
Oleic acid (C18:1 #-9)	20	117
Linoleic acid (C18:2 #-6)	10	767
Linolenic acid (C18:3 #-3)	-	3

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Fatty acid (g kg-1)	Leaves (Morillo *et al*., 2017)	Seeds (Chasquibol *et al*., 2015)
Arachidic acid (C20:0)	-	4
Total saturated fatty acids	-	113
Total unsaturated fatty acids	-	890

The fruit of *P. peruviana* is a significant source of vitamins, such as vitamin A (retinol), provitamin A (β-carotenes), vitamins B3, B6, and vitamin C (ascorbic acid) according to Table 3. Vitamin A, fat-soluble and antioxidant, plays crucial roles in vision, reproduction, embryogenesis and integrity of membranous structures. At the fruit level, β-carotene acts as a precursor of vitamin A, which provides antioxidant properties and the characteristic orange coloration to *P. peruviana* (Carazo *et al*., 2021). In the lipid fraction of different goldenberry organs, vitamin E (#-tocopherol) is also found. This compound plays a crucial role as a lipid antioxidant, breaking chain reactions by interacting with peroxide radical in polyunsaturated fatty acids (Table 3), thus exerting a protective role against oxidation and reducing the production of reactive oxygen and nitrogen species (Xiong *et al*., 2023).

Table 3. Vitamin content in the fruit of *Physalis peruviana* L.

Vitamins (mg per 100 g of fruit)	Cortés-Díaz *et al*. (2015)	Vega-Gálvez *et al*. (2016)	Llano *et al*. (2018)
Carotenes	-	1.2	0.7
Thiamine B1	0.01	-	-
Riboflavin B2	0.17	-	-
Niacin B3	0.8	26.6	-
Pyridoxine B6	-	24.8	-
Retinol A	0.52		103.3
Ascorbic acid C	20	16.5	33.3
Tocopherol	-	-	21

As for the vitamin B complex, present in notable quantities, B3 participates in the production of cellular energy and acts as an immune modulator and antioxidant, whereas B6 is essential in the synthesis of neurotransmitters, influencing immune function and gene expression. Vitamin C, essential in the synthesis of collagen and neurotransmitters, also stands out for its immunomodulatory and antioxidant properties (Cortés-Díaz *et al*., 2015; Vega-Gálvez *et al*., 2016; Llano *et al*., 2018).

The minerals present in the fruit of *P. peruviana* are shown in Table 4. At the pulp level, the high contents of potassium, magnesium, calcium, sodium and phosphorus stands out, which are essential for proper metabolism. Potassium is a vital element for maintaining cellular function at the level of muscles and nerves. In addition, its consumption has health benefits including reduced blood pressure, reduced risk of stroke and a potential beneficial effect on bone health and insulin sensitivity (Lee *et al*., 2020). Calcium is another essential mineral with critical functions in the skeletal, cardiovascular, endocrine, and neurological systems. Its relatively low level in goldenberry fruits could contribute to blood pressure regulation and weight control. In addition, it allows avoiding the harmful effects of this element since, in inadequate amounts, calcium has been linked to complications during pregnancy, various types of cancer, and cardiovascular disease (Shlisky *et al*., 2022). Phosphorus is used to regulate acid-base balance and enzymatic and hormonal activity. Finally, magnesium stabilizes the nervous system and activates alkaline phosphatase, with studies suggesting potential benefits in cardiovascular disease, osteoporosis and diabetes (Eken *et al*., 2016).

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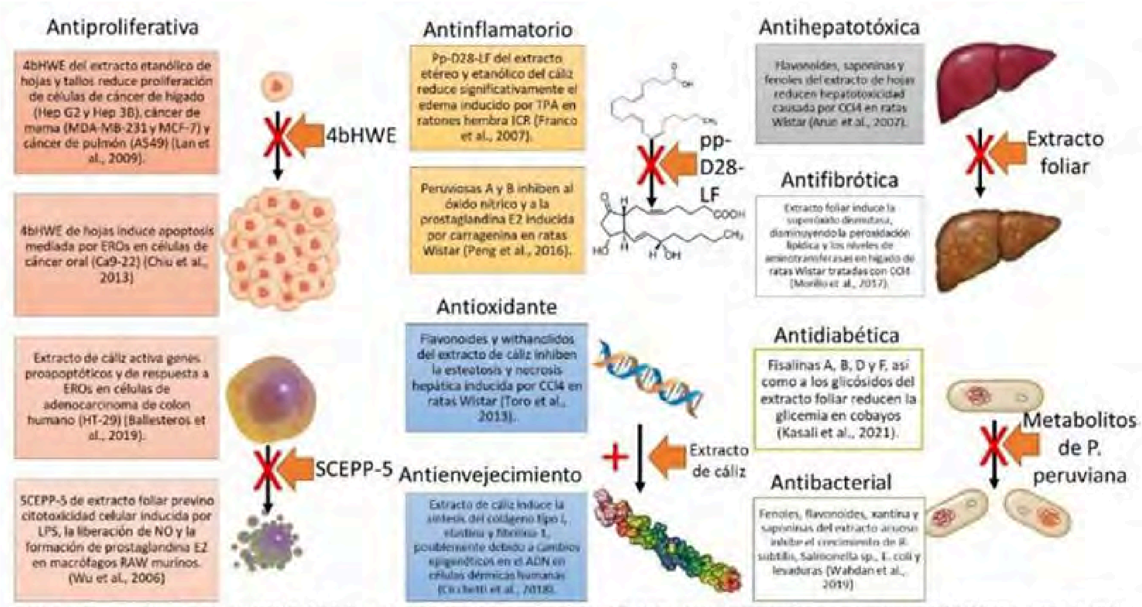
Table 4. Mineral content in the fruit of *Physalis peruviana* L.

Minerals (mg per 100 g of fruit)	Eken *et al*. (2016)	Bazalar *et al*. (2019)
Potassium	-	373.3
Magnesium	145	48.7
Calcium	19.1	11.2
Sodium	1.7	8.8
Copper	-	0.4

Health benefits

Figure 2 shows the main biological effects of *P. peruviana* calyxes that have been documented in the literature, which have been classified as antiproliferative, anti-inflammatory, antioxidant, anti-aging, antihepatotoxic, antifibrotic, antidiabetic and antibacterial effects, as described in the following paragraphs. These effects have been evaluated mainly using extracts of goldenberry calyxes, which mainly contain phytochemicals, such as withanolides, flavonoids, phenols, saponins, and peruvioses, which probably act in a combined and synergistic way promoting beneficial effects on health (Figure 2).

Figure 2. Biological effects of phytochemicals found in *Physalis peruviana* L.



EROs: especies reactivas de oxígeno; 4bHWE: 4-b-hidroxiwithanolido E; LPS: lipopolisacáridos; NO: óxido nítrico; CCl4: tetracloruro de carbono; TPA: 12-O-tetradecanoyl-phorbol-13 acetato; SCEPP-5: extracto de dióxido de carbono supercrítico de *Physalis peruviana*.

P. peruviana leaf extract exhibits antiproliferative, antihepatotoxic, antifibrotic, antidiabetic, and antibacterial properties. Thus, since ancient times, goldenberry leaves have been used in folk medicine for the preparation of infusions and the treatment of jaundice, ulcers, fever, skin conditions, and as an antiseptic in tribal communities in southern India (Sharmila *et al*., 2014). On the other hand, in another study carried out in the same country, the use of goldenberry leaves in the treatment of vomiting episodes has also been reported (Sathyavathi and Janardhanan, 2014).

In a study using cell lines, Lan *et al*. (2009) found that 4bHWE from ethanolic extract of leaves and stems reduces proliferation of cells of liver cancer (Hep G2 and Hep 3B), breast cancer (MDA-MB-231 and MCF-7), and lung cancer (A549). In the same vein, Ballesteros *et al*. (2019) demonstrated that calyx extract activates pro-apoptotic and ROS-response genes in human colon

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adenocarcinoma cells (HT-29). The response to ROS had previously been demonstrated by Chiu *et al*. (2013), who observed that leaf 4bHWE induces ROS-mediated apoptosis in oral cancer cells (Ca9-22).

The anti-inflammatory action of these compounds has been demonstrated through different studies. For example, Wu *et al*. (2006) found that SCEPP-5 from leaf extract prevented LPS-induced cellular cytotoxicity, NO release, and prostaglandin E2 formation in murine RAW macrophages. In addition, Franco *et al*. (2007) found that Pp-D28-LF from the ethereal and ethanolic extract of the calyx significantly reduces TPA-induced edema in female ICR mice. Later, Peng *et al*. (2016) observed that peruvioses A and B inhibit nitric oxide and carrageenan-induced prostaglandin E2 in Wistar rats, exerting a potent anti-inflammatory effect.

At the liver level, Toro *et al*. (2013) used flavonoids and withanolides from calyx extract, inhibiting CCl4-induced steatosis and hepatic necrosis in Wistar rats. In a similar study, Arun *et al*. (2007) had succeeded in reducing the hepatotoxicity caused by CCl4 in Wistar rats by applying the flavonoid, saponin, and phenol fraction of the leaf extract. The explanation for these effects could lie in enzymatic activation, as demonstrated by Morillo *et al*. (2017) by using the leaf extract of this species to induce the enzyme superoxide dismutase, decreasing lipid peroxidation and aminotransferase levels in the liver of Wistar rats treated with CCl4. Varied effects of phytochemicals present in *P. peruviana* have also been demonstrated.

For example, as an antioxidant, Wahdan *et al*. (2019) used phenols, flavonoids, xanthine, and saponins from the aqueous extract, which inhibits the growth of *B. subtilis*, *Salmonella* sp., *E. coli*, and yeasts. The effect on chromatin has also been evaluated in the study by Cicchetti *et al*. (2018), who found that calyx extract induces the synthesis of type I collagen, elastin and fibrillin 1, possibly due to epigenetic changes in DNA in human dermal cells. Finally, there is the hypoglycemic effect induced by physalins A, B, D and F, as well as glycosides of the leaf extract, observed in guinea pigs by Kasali *et al*. (2021).

Conclusions

Exhaustive research on *Physalis peruviana* goldenberry has allowed us to have a complete profile of the phytochemicals present in different organs of this plant, which include vitamins, minerals, essential fatty acids, and antioxidants, as well as secondary metabolites, such as withanolides, flavonoids, phenols, saponins and peruvioses, distributed at the level of different organs of the plant.

The phytochemicals present in *Physalis peruviana* provide exceptional nutritional value with antiproliferative, antihepatotoxic, antifibrotic, antidiabetic and antibacterial properties, which positions this plant and its derivatives as a valuable component in healthy eating with applications in the phytomedicine as an adjuvant for the treatment of diseases, such as cancer, hypertension, diabetes, oxidative stress and metabolic syndrome.

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