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Review

Phytochemical composition and biological activity of *Physalis* spp.: A mini-review

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Abstract

The main objective of this mini-review was to synthesize recent data about the phytochemical composition, the nutritional properties, and the biological and pharmacological activities of a now cosmopolitan genus, *Physalis* (Solanaceae), being in the focus of intensive research over the last two decades. Six *Physalis* species with nutritional and pharmacological promise are considered in particular – *P. peruviana* L., *P. philadelphica* Lam., *P. ixocarpa* Brot. ex Horm., *P. angulata* L., *P. pubescens* L., and *P. alkekengi* L. Summarized contemporary data on the metabolite profile and the biological activities of *Physalis* species support their century-long use in traditional medicine and human nutrition. The fruit represent a rich source of minerals, vitamins, fibers, carotenoids, proteins, fructose, sucrose esters, pectins, flavonoids, polyphenols, polyunsaturated fatty acids, phytosterols and many other beneficial nutrients. Individual phytochemicals and complex fractions isolated from *Physalis* plants demonstrate various biological and pharmacological activities, the most promising of which include antimicrobial, antioxidant, anti-diabetic, hepato-renoprotective, anti-cancer, anti-inflammatory, immunomodulatory and others. Most of these activities are associated with the presence of flavonoids, phenylpropanoids, alkaloids, physalins, withanolides, and other bioactive compounds. The accumulated data disclose the potential of *Physalis* spp. as highly functional foods, as profitable crops for many regions over the world, and as sources of valuable secondary metabolites for phytopharmacy, novel medicine and cosmetics. Information provided by this review is also important for a more intensive promotion of *Physalis* species in Bulgaria and for future studies on their composition and benefits.

Keywords: *Physalis* spp., phytochemicals, biological activity, health benefits

Abbreviations:

FW – fresh weight; RAE – retinol activity equivalent

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Introduction

The genus *Physalis* of family Solanaceae is among the largest genera in subfamily Solanoideae, with about 100 species, although the estimation of the species within the genus varies considerably – from 75 to 120 (Martínez 1998; Feng et al. 2018). The genus is generally recognized by the inflated balloon or lantern-like calyx (husk, fruit basket), which completely envelopes the berry, protecting it against insects, birds, diseases and adverse climatic conditions (Puente et al. 2011). *Physalis* species show great morphological variation: by life form (annual, rhizomatous perennial and shrubby or arborescent perennial genotypes); by height (from a few centimetres up to 2 m, profusely branching or single-stem); by leaf morphology (petiolate or sessile, from ovate to lanceolate in form, with long or short glandular hairs); by flower morphology (corolla colour varying from yellow to light green, but purple in *P. solanaceous* (Schltdl.) Axelius and white – in *P. alkekengi* L.); by calyx morphology (either strongly 5-angled or 10-angled in shape, green when fresh and turning light brown or yellow at maturity, but bright orange in *P. alkekengi* and almost black in *P. melanocystis* (B.L.Rob.) Bitter); by fruit and seed morphology (berries have either juicy or rather dry pericarp, the colour of ripe berries varying from green to yellow to orange or purple; seed colour varying from light yellow to brown, and seed size – from 0.6 to 3.0 mm) (Kindscher et al. 2012; Martínez 1998; Puente et al. 2011; Sharma et al. 2015). On the other hand, several *Physalis* species have highly similar morphological traits and misidentification in the genus is common, as in the case of *P. minima* L., which is confused with *P. angulata* L. or *P. pubescens* L. in traditional Chinese medicine preparations, or *P. angulata* being confused with *P. peruviana* L. (Feng et al. 2018). Moreover, many of the common names used in different regions of the world may be applied to more than one *Physalis* species, for example "goldenberry", "gooseberry", "tomatillo", "Chinese or Japanese lantern" or the French "amour en cage" (love-in-a-cage). These specifics of the genus should be taken into account, especially in the case of interpretation of data for locally collected specimens, without sound botanical identification.

Physalis is now considered a cosmopolitan genus, which has its origin in America and has been introduced post-Columbian to the Old World. The exception is *P. alkekengi*, which is the only species native to Asia and Europe. The country with the greatest diversity in the genus is Mexico with over 70 species, most of them being endemic (several endemic species are also found in the United States, Central and South America).

Most of *Physalis* species have a long history of ethnomedical use in the treatment of various ailments, including malaria, asthma, hepatitis, liver and kidney problems, dermatitis, and many others, and as immunomodulatory, antitumor, antibacterial or antipyretic agents (Zhang and Tong 2016). Additionally, some of the species are cultivated (and some are collected from wild populations) for their edible fruit and have nutritional importance – mainly *P. peruviana* L., and to a lesser extent *P. philadelphica* Lam., *P. ixocarpa* Brot., *P. pubescens* L. and *P. alkekengi* L.

The last two decades have witnessed a constantly increasing interest in *Physalis* species, with a specific focus on their phytochemistry and pharmacology. As it it is well known, medicinal plants are the largest reservoir of secondary metabolites, and the major sources of chemical diversity that has driven many pharmaceutical breakthroughs in the last century (Sang-ngern et al. 2016). More than 200 chemical constituents representing secondary metabolites with various carbon skeletons and interesting biological activities have been identified from the genus *Physalis* over the past two decades (Lv et al. 2018; Olivarez-Tenorio et al. 2016; Puente et al. 2011; Sharma et al. 2015; Zhang and Tong 2016). They include steroids (Men et al. 2014; Qiu et al. 2008), flavonoids (Qiu et al. 2008), alkaloids (Li et al. 2018), carotenoids (Etzbach et al. 2018; de Rosso and Mercadante 2007; Wen et al. 2017; Wen et al. 2019), phenylpropanoids (Chen et al. 2014), sucrose esters (Zhang and Tong 2016), vitamins (Puente et al. 2011; Sharma et al. 2015), labdane diterpenes (Zhang and Tong 2016), and others (Li et al. 2018).

Withanolides (steroidal lactones; a group of modified, highly oxygenated C_{28} ergostane-type phytosterols, synthesized mainly by Solanaceae plants) are the most frequent secondary metabolites and are considered as taxonomic markers of the genus (Zhang and Tong 2016). In fact, withanolides and their analogues, either as pure substances or extracted fractions from fruit and aerial parts, are the hot topic in recent research on *Physalis* species. In total, 169 withanolides, divided into different types and subgroups on the basis of the steroidal skeleton, have been reported in the genus and have been classified as promising antimicrobial, antitumor, anti-inflammatory, hepatoprotective, immunomodulatory, and antiparasitic agents (Cirigliano et al. 2008; Puente et al. 2011; Zhang and Tong 2016). Among them, more than fifty physalins with a 13,14-*seco*-16,24-cycloergostane skeleton and their derivatives have been identified in extracts from the aerial parts of several species (*P. angulata*, *P. minima* L., *P. alkekengi* var. *franchetii*, *P. divericata* D. Don, *P. peruviana*). Most of these are firstly discovered structures and have been pointed out as the characteristic bioactive components responsible for the antitumor, anti-microbial and anti-inflammatory properties of various fractionated extracts by a series of *in vitro* and *in vivo* studies (Ji et al. 2012; Li et al. 2014; Li et al. 2018; Pinto et al. 2016; Rivera et al. 2018; Yang et al. 2016).

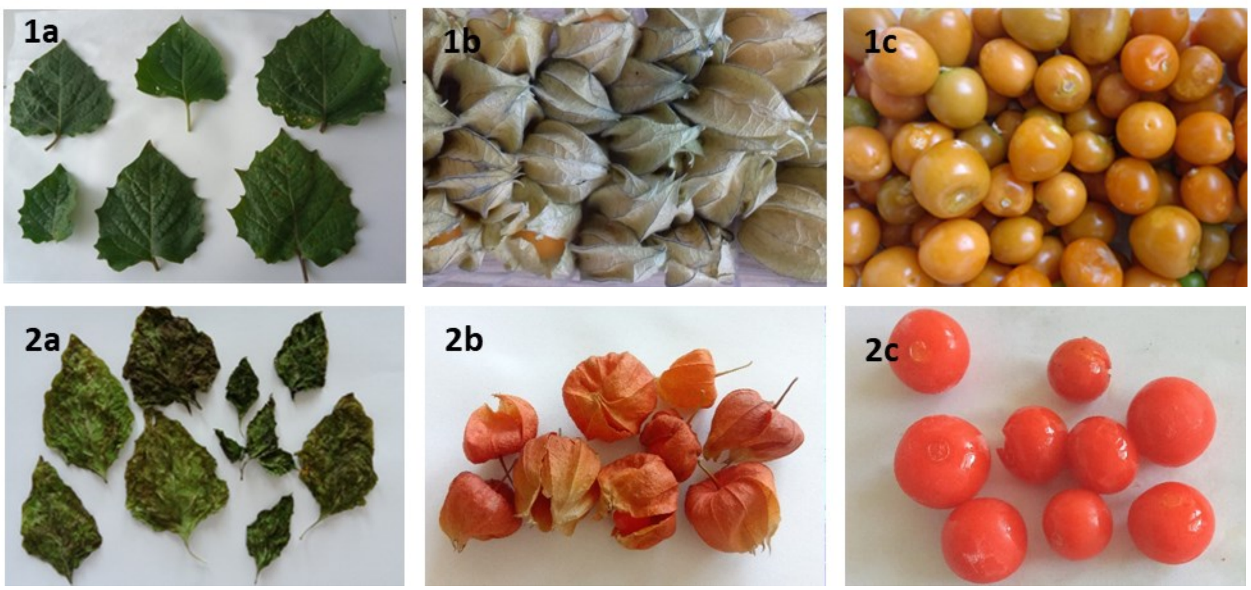

Figure 1. Leaves, whole fruits and berries of *P. peruviana* L. (1a-c) and *P. alkekengi* L. (2a-c) (authors' images)

In this review are considered just a few of the *Physalis* species, sharing the common trait of having edible fruit and a pharmacological promise, with a special accent on the only two species common to Bulgaria – *P. peruviana* (cultivated) and *P. alkekengi* (wild growing) (Figure 1). The review synthesizes recent data about the phytochemical composition, the nutritional properties, and the biological and pharmacological activities of these species.

Chemical composition, biological activities and use of *Physalis* species

Physalis peruviana L.

P. peruviana (Cape gooseberry, Inca berry, goldenberry) is the most widely distributed species from the genus, developed into numerous commercial varieties over the world. It is a native plant from the Andean region (the Peruvian and Ecuadorian Andes), spreading throughout South America as early as the pre-Incan and Incan periods. The species was introduced in South Africa by the Spanish and from there moved to different countries of the tropics and subtropics where it is grown commercially. Nowadays its cultivation extends to Central and South Europe, the United States, Asia and the Pacific (Puente et al. 2011). Columbia is the largest producer of Cape gooseberry fruit, followed by South Africa, and the national export of fresh or dehydrated fruit is second only to that of banana (Muniz et al. 2014; Puente et al. 2011; Zhang et al. 2013). *P. peruviana* is an herbaceous, semi-shrub, upright plant, annual in the temperate zones, but perennial in the tropics and subtropics. The plant is adapted to a wide range of altitude, soils and climatic conditions (Muniz et al. 2014). The optimal annual temperatures are between 13 and 18°C (or between 8 and 20°C), but higher temperatures (27-30°C) are also well tolerated, as is the case of fruit production in the Mediterranean or Hawaii. The plant requires plenty of sunshine, especially in the fruit ripening stage, and protection from excessive wind. Water demand is at least 800 mm during the growing period, but excessive rainfall (up to 4300 mm) is not a problem for well-drained soils. The ideal soil type is sandy-clayey, rich in organic matter (more than 4%), slightly acidic (with a pH between 5.5 and 6.8, although pH values up to 7.3 are also tolerated well) (Muniz et al. 2014; Puente et al. 2011). Plants grow to 1-1.5 m high and in some cases up to 1.8-2 m. Leaves are simple, heart-shaped, 5-15 cm long and 4-10 cm wide. The flowers are hermaphrodite, bell-shaped and pedunculate, about 15-20 mm in diameter, with 5-lobed corolla and yellow with purple-brown spots inside. The fruit is an ovoid berry, with a diameter between 1.25 to 2.50 cm and weight between 4 and 10 g, containing around 100 to 300 small seeds. As in all *Physalis* species, the berry is protected by a calyx, formed by five sepals around 5 cm long, which color changes from green to beige and brown in the ripening stage (Licodiedoff et al. 2013; Sharma et al. 2015; Yıldız et al. 2015). Ripe berries are bright yellow to orange in color, shiny, with a tender and juicy texture, rich in flavor (sweet and sour, with a hint of citrus). The berries are consumed mostly fresh, as fruit desserts or salads; fresh fruit in partly open calyces make an excellent exotic decoration to various dishes. Considering the fact that the shelf life of ripe fruit is relatively short, up to one month with calyx and 4 to 5 days without the calyx, in a cooled environment (Olivares-Tenorio et al. 2017a; Puente et al. 2011), much of the produced fruit is being dehydrated (Junqueira et al. 2017; Nawirska-Olszanska et al. 2017) or processed to value-added dry products (Dag et al. 2017; Hernandez-Sandoval et al. 2014; Vega-Galvez et al. 2014). Additionally, Cape gooseberry fruit is favorable for processing into a variety of culinary products, such as jams, jellies, juices, beverages, dressings and sauces for meat and sea food, which nutritional, organoleptic, rheological and other characteristics have been extensively studied (Erkaya et al. 2012; Hegazy et al. 2019; Hemalatha et al. 2018; Ramadan and Mörsel 2007; Sharoba and Ramadan 2011; Vega-Galvez et al. 2014). Cape gooseberry fruit, as well as fruit pomace (seeds and skins, accumulated as waste in juice production) have been identified as an excellent source of edible oil, both in terms of oil yield and oil composition (Ramadan and Mörsel 2003, 2009; Ramadan et al. 2008).

The nutritional value and the ethnobotanical use of Cape gooseberry fruit are related to the presence of various classes of chemical constituents and their activities (Puente et al. 2011; Ramadan 2011; Sharma et al. 2015; Zhang et al. 2013). The fruit are rich in minerals (K, Mg, Ca, Fe, P, Na, Zn, Cu, Mn) (Bazalar Pereda et al. 2019; Hegazy et al. 2019; Rodrigues et al. 2009), vitamins (A, B, C, E, K_1) (da Silva et al. 2016; El-Beltagi et al. 2019; Licodiedoff et al. 2013; Olivares-Tenorio et al. 2016; Ordonez-Santos et al. 2017), carotenoids (de Rosso et al.

2007; El-Beltagi et al. 2019; Etzbach et al. 2018; Ordonez-Santos et al. 2017; Ramadan and Mörsel 2003), carbohydrates (Hegazy et al. 2019; Mayorga et al. 2002; Puente et al. 2011), protein (Yıldız et al. 2015), fatty acids and phytosterols (Puente et al. 2011; Ramadan and Mörsel 2003; Rodrigues et al. 2009; Sharma et al. 2015; Zhang et al. 2013), flavonoids and phenolic acids (da Silva et al. 2016; Ertürk et al. 2017; Hegazy et al. 2019; Licodiedoff et al. 2013; Ordonez-Santos et al. 2017; Sathyadevi and Subramanian 2015; Yıldız et al. 2015), alkaloids (El-Beltagi et al. 2019), and others (El-Beltagi et al. 2019; Fukushima et al. 2016; Kupska et al. 2016; Ramadan et al. 2017). Summarized nutrient data for *P. peruviana* fruit are presented in Table 1.

Recently, *P. peruviana* is legitimately considered as one of the promising members of the "supefruits" family (Chang et al. 2019; Kupska et al. 2016). Typically, the term "superfuit" has been introduced with the marketing strategy to promote the health benefits of exotic fruits with less popularity worldwide, which have numerous phytochemicals (such as phenolic acids, flavonoids, proanthocyanidins, coumarins, hydrolysable tannins, carotenoids, and anthocyanins) together with the corresponding antioxidant activities (Chang et al. 2019).

Table 1. Nutrient data of *P. peruviana* fruit (USDA, ARS 2018).

Nutrient	Nutritional value per 100 g
Proximates	
Water, g	85.40
Energy, kcal (kJ)	53 (222)
Protein, g	1.90
Total lipid (fat), g	0.70
Ash, g	0.80
Carbohydrate, g	11.20
Minerals	
Ca, mg	9.00
Fe, mg	1.00
P, mg	40.00
Vitamins	
Vitamin C, mg	11.00
Thiamin, mg	0.11
Riboflavin, mg	0.04
Niacin, mg	2.80
Vitamin A, RAE, µg	36.00

The berries, the calyces or the whole plants of *P. peruviana* are an integral part of folk medicine traditions in many countries. In Peruvian and Columbian medicine fruit is used empirically to treat cancer, hepatitis, asthma, malaria, dermatitis, rheumatism; to reduce blood glucose; to decrease albumin; to control cataract, pterygium and amebiasis (Puente et al. 2011; Sharma et al. 2015), and as antimycobacterial, antileukemic, antipyretic and diuretic agents (Zhang et al. 2013). In Chinese medicine, fruit is used as a remedy for abscesses, coughs, fevers and sore throat (Shah et al. 2013). Leaves and dried seeds are used as curing agents for skin diseases, jaundice, ulcer, fever, glaucoma, abdominal upsets; as antiseptics, diuretics and antibiotics (Anjalam et al. 2016; Sharmila et al. 2014; Zhang et al. 2013), and fruit calyces – as anticancer, antimicrobial, antipyretic, diuretic, and anti-inflammatory immunomodulatory agents (Puente et al. 2011).

Contemporary studies support many of the traditional medicinal uses of *P. peruviana*, by revealing different aspects of the biological and pharmacological activities of isolated pure phytochemicals or complex plant extracts. These activities include: antimicrobial (El-Beltagi et al. 2019; Hegazy et al. 2019), antioxidant (Bazalar Pereda et al. 2019; da Silva et al. 2016; Eken et al. 2016; El-Beltagi et al. 2019; Ertürk et al. 2017; Licodiedoff et al. 2013; Olivares-Tenorio et al. 2017b; Ramadan et al. 2008; Vega-Galvez et al. 2014), analgesic (Sharma et al. 2015), anti-diabetic and hypocholesterolemic (Dewi et al. 2018; Hassan et al. 2017b; Puspaningtyas 2014; Ramadan 2012; Ramadan et al. 2013; Zhang et al. 2013), hepato-renoprotective (El-Gengaihi et al. 2013; Sharma et al. 2015; Zhang et al. 2013), anti-tumor (Dkhil et al. 2014; El-Beltagi et al. 2019; El-Gengaihi et al. 2013; Hassan et al. 2017a; Hassan et al. 2017b; Ramadan et al. 2017; Sathyadevi and Subramanian 2015), anti-inflammatory and immunomodulatory (Sang-ngern et al. 2016; Zhang et al. 2013), and others (Cirigliano et al. 2008; Lim 2013; Zhang and Tong 2016). Substantial research has been devoted to the identification, extraction and fractionation of withanolides from the aerial parts of *P. peruviana* plants in the last two decades, and the number of newly reported structures (such as physalins A, B, D, F, phyperunolids A-F, peruvianoxid, physaperuvins G-J, M, N, 4β-hidroxiwithanolid E and its acetate derivatives, withanolid E, S, C, withaperuvin D, physalolactone, withaphysanolid, and others) has been constantly growing (Cirigliano et al. 2008; Puente et al. 2011; Sang-ngern et al. 2016; Sharma et al. 2015; Zhang et al. 2013).

At present, *P. peruviana* remains pretty unknown, “exotic” and “mysterious” crop in Bulgaria, although its potential has been appraised more than 20 years ago. The first (and still the only) Bulgarian variety named “Plovdiv” has been selected in the Department of Horticulture at the Agricultural University of Plovdiv, in the period between 1996 and 2001 (Panayotov 2009). The variety is characterized by very good distinctiveness, homogeneity and stability. In 2006 it was registered for the first time in the Official Variety List of Bulgaria by the Executive Agency for Variety Testing, Field Inspection and Seed Control. According to the production scheme recommended for the environmental conditions of Bulgaria, seedlings are transplanted around the middle of May, and fruit harvest begins from the middle of August. The plant is intensely branched, with an average height of 158 cm. The flowers are single, yellow, with a diameter of 10-11 mm. The leaves are heart-shaped, with indented periphery, 9.5 cm wide and 7.8 cm long. The fruit is with a spherical-oblong shape, length of 20.5 mm and width of 19.6 mm, and with an average weight of 3.02 g. Fruit yield is estimated to 3785 kg/ha, or 132 g per plant (Panayotov 2009), although yield variation is observed depending on environmental conditions, fertilization, weed control, and other factors (Panayotov 2016; Panayotov and Popova 2014b; Panayotov and Popova 2016a; Panayotov et al. 2016). Ripe berries have a typical strawberry flavor, with a hint of vanilla, and a pleasant, balanced, sweet to slightly sour taste (Panayotov 2009). Fruit is best stored with the calyx, in a refrigerator (1-4°C), for up to 30 days, but longer storage (up to 3 months) is also tolerated well (Panayotov and Pevicharova 2002). Fruit contains 17.79% dry matter, 35.45 mg% vitamin C, 10.72% total sugar (as glucose), 1.03% pectin, 1.03% total acids, and 0.51% flavonoids (as rutin) (Panayotov 2009). The share of unripe fruit by the end of the growing season in Bulgaria is relatively big (between 8.7 and 17.3%) (Panayotov and Popova 2016b), and the dynamics of post-harvest ripening indicates that it may be continued for up to 14-21 days after harvest (Panayotov and Popova 2014a; Panayotov and Popova 2015). Thus, the secured supply period for the variety is from 4 to 5 months, i.e. supply from direct harvest for 3 months, August to October, and supply from storage and post-harvest ripening – for the rest of the period (Panayotov and Popova 2016b). Authors summarize that *P. peruviana* is suitable for growing in almost all regions of Bulgaria, especially on small-scale farms, and it can contribute to the diversity of fresh production on the market (Panayotov 2009; Panayotov et al. 2012). To the best of our knowledge, present-day production of Cape gooseberry in Bulgaria – despite the favorable ecological, social and market environment – is limited to a single truly operating farm, i.e. the Versol Bio-farm (Versol Ltd.), located in Lik village, municipality of Mezdra, North-West Bulgaria, at altitude of about 400 m. Our own observations and web-based surveys suggest that *P. peruviana* and probably some of the other species from the genus are relatively more popular in the country as ornamental plants grown in home gardens or in pots.

P. philadelphica Lam. and *P. ixocarpa* Brot. ex Horm.

The species *P. philadelphica* Lam. (Mexican groundcherry, Mexican husk tomato) and *P. ixocarpa* Brot. ex Horm. are native to Mexico and have been domesticated by the native peoples long before the Columbian era, playing an especially important role in Aztec and Mayan cultures (Zamora-Tavares et al. 2015). The classification of the two species, often categorized as synonyms, has been (and remains) rather controversial, as they share the same common names, “tomate verde” (green tomato), “tomate de cáscara” (husk tomato) or “tomatillo”, as well as origin, history of introduction and naturalization, growing areas and use (Svobodova and Kuban 2018). *P. ixocarpa* has been introduced to India, Australia and Africa about 60 years ago. In Mexico, it grows both in the wild and in traditional polyculture production systems, as a tolerated weed amid crops such as corn and sorghum. The species is widely grown for food use, giving an average yield of approximately 14.5 t/ha, although potentially it can provide as much as 40 t/ha (Magaña-Lira et al. 2019). Today, *P. philadelphica* is one of the main vegetables grown in Mexico, both for domestic sale and export (the annual production exceeds 800 000 t), as well as in some other countries in Latin America. It is considered as one of the most studied and widely used species of the genus, existing in numerous varieties and genotypes with significant morphological variation. There are great differences between wild and commercially cultivated forms and within each of these categories – a variation in characteristics such as fruit size, colour, taste, shape, and firmness, calyx colour and length, growth habit, reproductive cycle, number of seeds per fruit and others (Zamora-Tavares et al. 2015). Berries can be 1.5 cm in diameter when wild to 6 cm or even 10 cm when cultivated, with whitish-yellow, yellow, green, purple or green with purple hues color; the flavor may vary from acidic to sweet and sour (Zamora-Tavares et al. 2015).

In contrast to Cape gooseberry (*P. peruviana*), tomatillo varieties are used as vegetable, and not as fruit. *P. philadelphica and P. ixocarpa* fruit is usually harvested before full ripening and the green berries are the basic ingredients (along with chili peppers) of the famous Mexican "salsa verde" (a spicy green sauce used in traditional Mexican-style foods, such as enchiladas, chicharrónes, tacos and quesadillas). The purple and red-ripening cultivars often have a slight sweetness, so they generally are used in jams and preserves. The diverse culinary uses of tomatillos include also stews, soups, salads, curries, stir-fries, meat dips, and desserts. Fruit can be dried, and the resins are described as similar to dried cranberries, with a hint of tomato flavour (Kindscher et al. 2012). Fruit is rich in pectin and is an excellent thickener and rheology modifier, both in raw and cooked form (Moralez-Contreras et al. 2018). In Mexican and Ecuadorian folk medicine the fruit of *P. ixocarpa* is used as eyewash, tonic, diuretic and laxative, as treatment for gastrointestinal and respiratory problems, and as an application in inflammations, enlargement of the spleen, ascites and bladder ulceration. Crushed leaves are applied over snakebites (Khan et al. 2016). The medicinal benefits of *P. philadelphica and P. ixocarpa* are related to the presence of various bioactive phytochemicals, such as sucrose esters (Zhang et al. 2016), phenolics and flavonoids (da Silva et al. 2016; Medina-Medrano et al. 2015), vitamins (da Silva et al. 2016; Naumova et al. 2019), withanolides and physalins (Svobodova and Kuban 2018; Zhang et al. 2016). Recently reported biological activities of extracts from various plant parts include antimicrobial (Khan et al. 2016), anti-oxidant (Medina-Medrano et al. 2015), anti-cancer (Choi et al. 2006; Xu et al. 2018), and anti-inflammatory (Zhang et al. 2016).

Physalis pubescens L.

Natural habitats of the species are found in a large zone including the southern part of the United States, throughout the Mexican lowlands to Argentina and the West Indies. It has been further introduced, or spread as weed, into several regions in Central America and North Africa, Australia, and has been reported recently as introduced to Europe (Belgium, France and Italy). Some of the common names used are ground cherry, low hairy ground cherry, pineapple ground cherry, husk tomato or tomatillo. *P. pubescens* is an annual herbaceous shrub plant, with a height of 0.45 - 0.60 m and a shallow, fibrous root system; the leaves are heart-shaped or ovate, with smooth or toothed edges, 3 - 9 cm long. Distinguishing characteristics for the species are the yellow corollas of the flowers, 0.9-1.5 cm in diameter, with 5 dark purple spots inside, and the hairy, strongly angled calyces (El Sheikha et al. 2010; Martínez 1998). The plant is highly adaptable to environmental conditions, and can be grown on different soil types (loamy, clay, or sandy, all well-drained), in semi-shade or no shade, on dry or moist soil; therefore it is a suitable crop for new reclaimed lands and desert regions. Fruit yield is about 0.5-1.1 kg per plant, securing the production of about 12 t/ha. The ripe berries are relatively small, with an average diameter of 1.25-2 cm, green-purple to golden yellow, with a juicy pulp, described as sweet and tangy (El Sheikha et al. 2010). According to the same authors (El Sheikha et al. 2010) fruit contains considerable amounts of carotenoids (70 µg/mL FW), polyphenols (76.6 µg/mL FW), ascorbic acid (38.8 µg/mL FW), and minerals (in concentrations higher than those in lemon, lime and orange juices - K 1210 mg/g FW; Na 40 mg/g FW; P 590 mg/g FW; Ca 70 mg/g FW; Mg 20 mg/g FW; Zn 2 mg/g FW). According to Wen et al. (2017, 2019) fruit contain β-carotene (0.5 mg/100 g FW), organic acids (257-305 mg/100 g FW tartaric, 176-247 mg/100 g FW citric, 130-182 mg/100 g FW malic, 7-9 mg/100 g FW ascorbic acid), sucrose (5.41-6.63 g/100 g FW), D-fructose (1.28-2.03 g/100 g FW), D-glucose (1.02-1.79 g/100 g FW). The analysis of individual phenolic metabolites found 21 compounds, including amino acids, cinnamoyl- and hydroxycinnamoylamides and glycosides, quinic acids, HDMF glycosides, etc. The total phenol and flavonoid fractions from the calyces of *P. pubescens* are reported to have antioxidant, anti-proliferation and induced-apoptotic activity and to be potential candidates for the development of antihepatoma ingredients, in contrast to those extracted from *P. pubescens* fruit (Wang et al. 2016). The bioactive components of *P. pubescens* are relatively less studied, but a number of new and known withanolides and glycosides have been recently isolated and their potential in cancer prevention and treatment has been documented (Chen et al. 2016; Fan et al. 2018; Xia et al. 2017a; Xia et al. 2017b).

Physalis angulata L.

Compared to the *Physalis* species described above, *P. angulata* (angular winter cherry) is a less popular species, used sporadically in culinary (as a vegetable) and in folk medicines, but has been recently studied for its medicinal properties. It is an annual, erect, branched herbaceous plant found as weed in the tropical and sub-tropical regions. The plant reaches up to 1 m height, and has ovate to elliptic leaves, about 9-10 cm wide, and pale yellow to white flowers, up to 6 mm long. Berries are small (1.2-1.5 cm in diameter), ovate, orange to orange-red in colour (Sharma et al. 2015; Svobodova and Kuban 2018). Extracts or infusions of *P. angulata* aerial parts have been used as traditional medicine for the treatment of diseases such as malaria, asthma, hepatitis, dermatitis, rheumatism, liver disorders, fever, bronchitis and others (Kusumaningtyas et al. 2015; Rengifo-Salgado and Vargas-Arana 2013; Tuan Anh et al. 2018). *P. angulata* extracts are found to be rich in polyphenols (gallic acid, ellagic acid, caffeic acid, rutin, mangiferin), and to have antioxidant, antipyretic, antimicrobial, anti-inflammatory and analgesic effects. Recent phytochemical studies reveal the presence of many other biologically active constituents, e.g. flavonoids, carotenoids, alkaloids (phygrine), diterpene glycosides, as well as that of physalins and other withanolides (Cobaleda-Velasco et al. 2017; Kusumaningtyas et al. 2015; Lim 2013; Meira et al. 2015; Men et al. 2014; Pinto et al. 2016; Rengifo-Salgado and Vargas-Arana 2013; Rivera et al. 2018; Svobodova and Kuban 2018; Tuan Anh et al. 2018).

Physalis alkekengi L.

P. alkekengi (known as Chinese lantern, Japanese lantern, winter cherry, strawberry groundcherry) is an indigenous plant to Central and South Europe and South Asia (China, Indochina, Japan), subsequently naturalized in many other regions worldwide (Namjoyan et al. 2015). It is the only *Physalis* species native to Bulgaria, where it can be found growing in the wild at altitude up to 1500 m. The common name of the plant in Bulgarian is "mekhunka" (husk). *P. alkekengi* is included within the scope of the national Law on Medicinal Plants (State Gazette, issue 29 of April 7, 2000). It is a perennial, herbaceous plant, typically 0.40-0.60 m high, with spirally arranged leaves (6-12 cm long and 4-9 cm broad) and white 5-lobed corolla flowers (10-15 mm). The most distinctive morphological feature of the species, making it easily identifiable, is the large, bright orange to red calyx covering over the fruit at maturity. Berries are small (less than 1-1.5 cm in diameter), globular, shiny and orange-red. The species is used for ornamental and medicinal purposes, and as food. As an ornamental plant it is cultivated in many countries with temperate climate, although considered as relatively invasive with a tendency to escape from cultivation (Zhang et al. 1994). Like the other *Physalis* species, *P. alkekengi* accumulates various specialized metabolites and nutrients (alkaloids, vitamins, flavonoids, phenolic acids, saponins, tannins, withanolides, carotenoids, glucocorticoids, etc.), responsible for its activities and use (Bahmani et al. 2016; Fukushima et al. 2016; Li et al. 2014; Li et al. 2018; Liu et al. 2015; Lv et al. 2018; Qiu et al. 2008; Wen et al. 2017; Wen et al. 2019). In many countries across Europe and South Asia folk medicines recommend the use of *P. alkekengi* fruit as a diuretic for renal and urinary tract ailments, and in the treatment of gout and rheumatism (Bahmani et al. 2016; Namjoyan et al. 2015; Sharma et al. 2015). As a traditional Chinese medicine *P. alkekengi* fruit, calyces, roots and whole plants have been used (internally or externally) for a variety of conditions, such as sore throat, cough, eczema, hepatitis, urinary problems, and tumors (Qiu et al. 2008; Shu et al. 2016). Other therapeutic effects used in traditional medicine include anti-inflammatory, antibacterial, antiseptic, analgesic, laxative, diuretic, antimitotic, hypoglycemic, antispasmodic, liver corrective and sedative, as well as relief of malaria and syphilis symptoms (Bahmani et al. 2016; Namjoyan et al. 2015; Sharma et al. 2015). Bulgarian folk medicine recommends fresh or dried fruit for liver diseases occurring with jaundice and ascites, while leaves are used as infusion for tooth pain or as poultice for rheumatism and joint pain (Petkov 1982). The topical use of the fruit addresses mild skin irritation, wounds, and skin inflammation. Recent studies prove the correlations between the ethnobotanical use, the phytochemistry and the pharmacological effects of *P. alkekengi* (Li et al. 2018). The most promising pharmacological activities of the species include anti-diabetic (Hu et al. 2018; Ji et al. 2012; Tong et al. 2008; Zhang et al. 2018; Zhao et al. 2017), anti-tumor (Esmailpoor et al. 2019; Li et al. 2014), anti-inflammatory (Bahmani et al. 2016; Shu et al. 2016), vasodilative (Li et al. 2018), anti-oxidant (Bahmani et al. 2016), and others (Liu et al. 2015; Namjoyan et al. 2015; Shu et al. 2016; Zhang and Tong 2016). According to Li et al. (2018), the majority of these pharmacological functions are associated with the presence of physalins, flavonoids and phenylpropanoids, in a synergy with other chemical constituents. Physalins in particular are responsible for anti-inflammatory, antimicrobial, anti-diabetic, anti-cancer (the anti-tumor effects of physalins being the hot topic in the pharmacological aspects of the plant) and immunosuppressive activities; flavonoids for anti-diabetic, anti-inflammatory and anti-cancer activities; phenylpropanoids for anti-diabetic, antimicrobial and anti-cancer effects.

The ripe berries of *P. alkekengi* are also a highly functional food; a source of vitamins (A and C), phenolic antioxidants, minerals (P, Ca and Fe), pectin and other nutrients (Sharma et al. 2015). They make an excellent supplement to various meat and vegetarian meals, salads and desserts.

Conclusions

This review, although in brief, demonstrates that the different species of genus *Physalis* have been in the focus of scientific research during the last two decades. The accumulated data disclose the potential of *Physalis* spp. as highly functional foods ("superfruits"), as profitable crops for many regions over the world, and as sources of valuable secondary metabolites for phytopharmacy, novel medicine and cosmetics. The review supports the evolving interest in *Physalis* species in Bulgaria, as well as the need for future studies and in-depth characterization of their phytochemical profile, nutritional and pharmacological prospects.

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