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Agronomic Cultivation, Chemical Composition, Functional Activities and Applications of Pereskia Species – A Mini Review

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ABSTRACT

Background: The exploration of the plant biodiversity as a natural source to obtain sustainable food products and new bioactive pharmaceutical compounds has been growing significantly due to their abundance, safety and economy. Natural pharmaceutical and edible compounds present some advantages when compared to synthetic ones, such as being chemically inert and widely available.. In this sense, plants of the genus *Pereskia* belonging to the Cactaceae family, have been studied. It is an unconventional wild edible plant that contains a large amount of protein and minerals. Studies have demonstrated their biological activities and potential application in different areas such as pharmaceutical, medicinal and food.

Objective: This review is focused on the chemical composition, functional properties, applications on pharmaceutical, nutraceutical and food areas and formulation techniques to enhance stability and bioavailability of bioactive compounds from the underutilized wild edible plant known as *ora-pro-nobis* (*Pereskia aculeata* or *Pereskia grandifolia*).

Conclusion: The latest studies involving ora-pro-nobis demonstrated its great potential due to its biological activities, which could stimulate further investigations. The utilization of this plant as a natural source to supplement the diet, or to prepare new food formulations and pharmaceutical products is an attractive approach to explore and fully realise the potential of the rich biodiversity found in Brazil and in other countries.

Keywords: ora-pro-nobis, *Pereskia aculeata*, *Pereskia grandifolia*, Cactaceae, unconventional plant, nutritional value, medicinl food.

1. INTRODUCTION

Biodiversity is essential for food security and nutrition, and could offer options for sustainable livelihoods (FAO, 2018). The world population is increasing and the fast depletion of natural resources are essential factors to propel the search for diversification on agriculture. Unconventional wild edible plants are those that are available from their natural habitat, easy access, affordable and could be used as food source due to their high nutritional value (Bhati and Jain, 2016; Beluhan and Ranogajee, 2010). In general, the consumption of underutilized plants is local or regional (Akinnifesi *et al.*, 2006). The less importance to unconventional wild plants than conventional agricultural commodities is associated to the production and market value (Eleazar and Cesoiv, 2012). The total dietary energy intake of humans has been focused on relatively few plants species obtained from domesticated species: Cereals (*e.g.*, barley, maize, millet, rice, rye, sorghum, sugar cane and wheat), tubers (*e.g.*, cassava, potato, sweet potato and yam) (Grivetti and Ogle, 2000). Many underutilized and neglected species are nutritionally rich (*e.g.*, high levels of essential minerals, vitamins, proteins, etc.) and adapted to low input agriculture. These plants can make an important contribution to a better and sustainable diet for local communities (Salvi and Ss, 2016).

The integration of indigenous trees of fruits and unconventional edible plants into farming systems could provide people's need for food and nutritional security. This implies a better knowledge of the nutritional quality of unconventional foods produced in agroforestry farming systems (Leaky *et al.*, 1999). Many species of unconventional wild plants could be an effective way to help a diverse and healthy diet to combat micro- and macro-nutrients deficiencies in vulnerable social groups, particular in developing countries (Salvi and Ss, 2016). Leterme *et al.* (2006) studied the mineral composition of a large number of fruits and unconventional foods including nuts, leaves and tubers, produced by agroforestry programmes in the Andes and the rain forests of Colombia. They observed that the leaves were outstanding mineral sources, mainly calcium and iron. It was found that the cultivation conditions (*e.g.*, soil fertility, pH, water supply, climate and seasonal variation) resulted in nutritional composition variability.

Tropical and subtropical countries concentrate a great diversity of plants including unconventional wild plants (Barreira *et al.*, 2015). It has become increasingly evident that the nutritional potential of these unconventional wild plants could improve the macro- and micronutrients health status in human diets. The therapeutic potential of many indigenous plant species has also been studied and the discovery of new bioactive compounds in unconventional wild and traditional medicinal plants is an active field of research (Azam *et al.*, 2014).

Collaborative efforts among scientists and regional consumers should be stimulated to establish and develop innovative production and exploitation systems of promising unconventional wild plants. In this way, it could be possible to improve the availability of feed resources, while protecting the biodiversity (FAO, 2012). This is particularly relevant given the current climate change challenges and the increasing need to identify resilient crops.

A unique complete published list or online database with the total edible plants available in the world is not easy to find. Kunkel (1984) listed about 12,500 species with edible potential. Rapport & Drausal (2001) proposed that there are 27,000 species. Kinupp & Lorenzi (2014) listed 600 species of unconventional edible plants, including 351 most promising species found in the Brazilian flora, such as *Pereskia aculeata, Xanthosoma taioba, Talinum paniculatum, Smallanthus sonchifolius, Acanthosyris spinescen*s, *M. fluminensis* and *Vasconcellea quercifolia,* among others.

There are reports of the potential use of *Pereskia* species in different areas, food, pharmaceutical, medicinal, others. However, our knowledge of *Pereskia* and many other unconventional wild plants is scarce, and there is an urgent need to shift the focus of interest towards these type of plants, given their environmental and potential public health impact (Mattila *et al.*, 2018). In this review we aim to present an overview of the current state of knowledge about *Pereskia*. We have kept the focus on its botanic, taxonomic and agronomical aspects, chemical composition, as well as its documented biological activities and current uses in pharmacy and foods.

2. THE GENUS *Pereskia*

Pereskia, a genus with 17 species, presents regular leaf development and function, generally viewed as representing the "ancestral cactus". It includes *P. aculeata*, *P. aureiflora*, *P. bahiensis*, *P. bleo*, *P. diaz-romeroana*, *P. guamacho*, *P. grandifolia*, *P. horrida*, *P. lychnidiflora*, *P. marcanoi*, *P. nemorosa*, *P. portulacifolia*, *P. quisqueyana* Alain, *P. sacharosa*, *P. stenantha*, *P. weberiana* and *P. zinniiflora* (Leuenberger, 1986). In the present classification, it has been proposed the division of subfamily Pereskioideae in two genera only: *Pereskia* (17 spp.) and *Maihuenia* (2 spp.) (Hunt, 2016).

These species are primarily distributed in dry and arid regions of Caribbean, Central and South America (Edwards *et al.*, 2005). It is believed that the northwest region of South America was the original centre of the diversification and spread of the genus *Pereskia* (Butterworth and Wallace, 2005). In Brazil, the main species commonly found are *P. aculeata* and *P. grandifolia* (Pinto and Scio, 2014).

Members of *Pereskia* genus have been described as having superior to inferior ovaries, broad, flattened leaves with C_3 photosynthesis, areoles with leaf production, dense, fibrous wood, a simple cortex without cortical bundles, poorly developed stem epidermal and hypodermal layers, non-succulent tissues or partially succulent leaves, and as inhabiting relatively mesic environments (Mauseth and Landrum, 1997).

Pereskia aculeata Miller and *Pereskia grandifolia* Haw.

P. aculeata Miller and *P. grandifolia* Haw., known as ora-pro-nobis or Barbados gooseberry (Pinto and Scio, 2014) are an unconventional wild edible plants. Both species are climbing vines plants that can reach up to 10 m in length (Figure 1a), with long branches and thorns (Figure 1b) in the armpit of the elliptical and succulent leaves (Duarte and Hayashi, 2005; Lorenzi and Souza, 1995). They are found in Brazil from the northeastern (Bahia) to the southern region (Minas Gerais, Paraná, Santa Catarina and Rio Grande do Sul) of the country (Conceição *et al.*, 2014). Ora-pro-nobis, from the Latin means "pray of us", is a species that belongs to the kingdom Plantae, class Magnoliopsida, order Caryophyllales, family Cactaceae and genus *Pereskia* (Almeida and Corrêa, 2012). Its natural habitat is the tropical forest, but it can be grown domestically in rural and urban areas (Souza *et al.*, 2016a). *P. grandifolia* and *P. aculeata* are perennial plants that have mucilaginous leaves and present different colour of their flowers: in *P. aculeata* the flower is white (Figure 1c) and in *P. grandifolia* is pink (Figure 1d) (Kinupp and Lorenzi, 2014). They produce edible fruits with few seeds and which are dispersed by birds. The propagation of these type of plants can be carried out sexually or asexually, although the first method is minimally employed. It occurs due to the scarce information and expertise about the propagation. Despite the production time beings lower in sexual propagation, plants with desirable morphological characteristics are needed to ensure sustainable cultivation and identify the existing genetic diversity in these species (Souza *et al.*, 2016b; Gibson and Nobel, 1990).

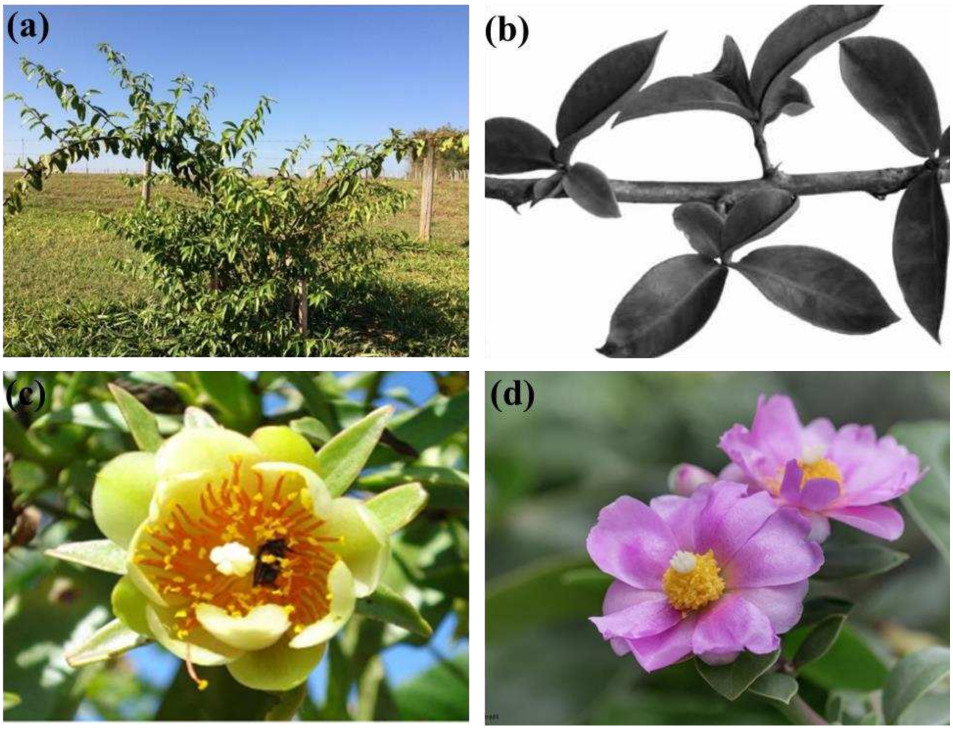

Figure 1. *Pereskia* (Cactaceae) species: (a) *Pereskia aculeata* Miller cultivated experimentally (6 months after cultivation) in University of São Paulo campus (Pirassununga, Brazil); (b) Detail of vegetative branch in *Pereskia aculeata* Miller, evidencing the leaves arrangement and presence of thorns (Duarte and Hayashi, 2005); (c) *Pereskia aculeata* Miller flower[1] (Santos *et al.*, 2012); (d) *Pereskia grandifolia* Haw. Flower (image captured on 3rd May of 2018 and available in https://www.flickr.com/photos/marcusviniciuslameiras/4894377091).

Duarte and Hayashi (2005) developed a thorough anatomical study of the leaf and stem of *Pereskia aculeata*. They observed that leaves are simple and elliptical, and has uniseriate epidermis, paracytic stomata on both surfaces, dorsiventral-like mesophyll, several druses of calcium oxalate and large isodiametric cells. In the midrib a collateral bundle in open arc is embedded. The petiole exhibits a plain-convex transection and a collateral bundle in closed arc shape. In the stem part, in early secondary growth, has uniseriate epidermis, angular collenchyma, cortical parenchyma with many amiloplasts, perivascular fibre caps and collateral vascular organization. In the cortex and pith, numerous cavities containing mucilage and druses of calcium oxalate are seen, the latter also in the phloem.

There are isolated studies on growth characteristics and agronomic management of the *P. aculeata* and *P. grandifolia* species, but these are still scarce. Leuenberger (1992) addressed general aspects of *Pereskia* species growth. Toffaneli and Resende (2011) studied the growth of *P. aculeata* in three different conditions: No support – free growth; espalier in the double string on the first thread; and espalier in the double string on the second thread. They observed that the treatment with no support presented the most promising results. Queiroz *et al*. (2015) evaluated the growth response of the *P. aculeata* under periodic drought through controlled reductions in the substrate matric potential. They found smaller dry mass accumulation in leaves (reduction of 21.4 %) than in stems (reduction of 48.1 %) and roots (reduction of 63.7 %). These results were noteworthy because the leaves are the main commercial part of the plant. Souza *et al*. (2016a) studied the effect of nitrogen fertilization on mineral, protein and nitrate contents, as well as the yield of *P. aculeata* leaves and verified that doses up to 400 kg ha^{-1} of nitrogen ensure adequate leaf yield, protein and mineral contents within the desired range for the species, being a food rich in proteins, iron and calcium.

The form of propagation and multiplication using stem cuttings is the commonly applied. However, few studies have been published involving ora-pro-nobis cultivation. Souza *et al.* (2016b) studied the thermal effects on the germination of the *P. aculeata* and *P. grandifolia* species at different temperatures (24, 27, 30, 33 and 36 °C). The best germination response for *P. aculeata* and *P. grandifolia* occurred at 30 and 33 °C, respectively, with greater germination strength and fewer days to attain 63.21 % of germinations. Campos *et al*. (2017) evaluated the profile of buds of ora-pro-nobis in substrate of carbonized rice husk containing three treatments: apical, medial and basal cuttings. They concluded that medium and basal cuttings of the plant branches were more viable and showed more shoots at 37 days.

2.2 Chemical composition of *Pereskia aculeata* and *Pereskia grandifolia*

Nutritional compounds

Unconventional wild plants such as *Pereskia* species show, typically, higher nutrient levels (*e.g.*, protein, minerals, vitamins) than the conventional ones. However, its production and consumption potentials are reduced and sometimes has been neglected (Oliveira *et al.*, 2013). Thereby, the studies involving its nutritive potential are based on material obtained from institutional gardens or private yards (usually native plants) (Almeida and Corrêa 2012; Takeiti *et al.*, 2009; Almeida Filho and Cambraia, 1974).

Leaves of *P. aculeata* are consumed as a vegetable, although its fruit is also edible (Souza *et al.*, 2016a). The leaves present high levels of protein and minerals (Takeiti *et* *al.*, 2009; Almeida Filho and Cambraia 1974), and hydrocolloids (Conceição *et al.*, 2014; Lima Junior *et al.* 2013). Furthermore, the significant content of fiber and the absence of leaf toxicity (Almeida Filho and Cambraia, 1974) of this species makes it a useful and atractive food source (Lima Junior *et al.*, 2013).

The first report about the protein content of the ora-pro-nobis leaves was given by Almeida Filho and Cambraia (1974) as being high (17.4-25.4%) when compared with other common vegetables sources, such as corn (7.6-10 %, w/w), beans (18-20 %, w/w), spinach (2.2 %, w/w), kale (1.6 %, w/w) and lettuce (1.3 %, w/w). They observed that ora-pro-nobis leaves are extremely rich in high-quality proteins. Studies conducted on its leaves showed protein contents ranging between 17.4 g kg^{-1} (Almeida Filho and Cambraia, 1974) to 28.9 g kg^{-1} of dry matter (Almeida *et al.*, 2014) and a high digestibility (85 %, Lima Junior *et al.*, 2013). In addition to presenting a well-balanced composition, the leaves have an exceptionally high content of specific essential amino acids, particularly L-lysine. According to Mercê *et al.* (2001), the lysine constitutes 5.4 % w/w of the total protein content, which is 2–23 times the content found in any other previous cited vegetables. These authors affirmed that this observation is noteworthy, since lysine is an essential amino acid in animal nutrition, and it is deficient in cereals, which are the main source of food in many low-income communities (Pinto and Scio, 2014). The protein and essential amino acid levels reported are substantially higher than the minimum amount recommended by the Food and Agriculture Organization of the United Nations (FAO) as necessary for human consumption (Sierakowski *et al.*, 1987). Furthermore, the protein content of ora-pro-nobis is similar or higher than those observed in taro (*Xanthosoma sagittifolium*, 27.59 %; Pinto *et al.*, 2001), nightingale (*Urtica circularis*, 28.00 %), mestruz (*Coronopus didymus*, 28.17 %) and nightshade (*Solanum americanum*, 29.90 %) (Kinupp and Barros, 2008).

Takeiti *et al.* (2009) performed a complete study with ora-pro-nobis leaves evaluating the nutritional components regarding the proximal chemical composition, minerals, vitamins, amino acids, protein content and digestibility. The amino acids content, general composition and mineral contents are given in Tables 1, 2 and 3, respectively.

Table 1. Amino acid composition, FAO/WHO (1990) recommended allowances for preschool children (2-5 years old), *in vitro* protein digestibility of *Pereskia aculeata* leaves (Takeiti *et al.*, 2009).

Amino acid	**g/100 g (dry basis)**[a]	**% of total**	**FAO/WHO (1990)**
Essential			
Arginine	1.44 ± 0.02	5.32	
Histidine	0.59 ± 0.01	2.17	114
Isoleucine	1.07 ± 0.01	3.95	141
Leucine	2.00 ± 0.02	7.40	112
Lysine	1.43 ± 0.05	5.29	91
Methionine	0.23 ± 0.01	0.85	
Phenylalanine	1.27 ± 0.01	4.71	
Threonine	1.00 ± 0.01	3.71	109
Valine	1.28 ± 0.01	4.75	136
Tryptophan	5.52 ± 0.19	20.46	1860
∑ subtotal	15.83	59.61	181
Non-essential			
Aspartic acid	1.71 ± 0.22	6.32	
Serine	1.00 ± 0.01	3.71	
Glutamic acid	2.67 ± 0.03	9.90	
Proline	1.11 ± 0.01	4.10	
Cystine	0.35 ± 0.02	1.28	
Glycine	1.31 ± 0.01	4.86	
Alanine	1.36 ± 0.01	5.04	
Tyrosine	1.21 ± 0.03	4.49	
∑ subtotal	11.13	39.7	
Total sulphur amino acids (Met + Cys)	0.58	2.13	85
Total aromatic amino acids (Phe + Tyr)	2.48	9.2	146
In vitro protein digestibility (%)	75.90 ± 0.02		

[a] Values are means of duplicate determinations carried out by Takeiti *et al.* (2009).

The ora-pro-nobis leaves contain high amounts of dietary fibre, minerals, such as calcium, magnesium, potassium, zinc and iron, besides vitamins C, B9 and E. Many of these nutritional components, mainly protein and minerals, are detected in higher proportions than those observed in other conventional leafy vegetables, such as kale, cabbage and spinach (Oliveira *et al.*, 2013; Takeiti *et al.*, 2009; Mercê *et al.*, 2001; Morton, 1987; Almeida Filho and Cambraia, 1974).

Table 2. General composition of *Pereskia aculeata* leaves (g 100^{-1}) (Takeiti *et al.*, 2009).

	***P. aculeata* (leaves)[a]**	***Spinacia oleracea* (spinach)[b]**	***I. batatas* poir (sweet potato leaves)[c]**
Moisture, fresh leaves	85.9 ± 0.2	90.7	87.1
Total protein[d]	28.4 ± 0.4 (3.1)[e]	3.2	3.8
Lipids	4.1 ± 0.3 (0.4)[e]	0.3	0.3
Ash	16.1 ± 0.1 (1.7)[e]	0.7	1.9
Crude fibre	9.8 ± 0.2 (1.0)[e]	0.6	-
Soluble dietary fibre	5.2 (0.5 ± 0.02)[e]	-	6.8 (0.9)[e]
Insoluble dietary fibre	33.9 (3.3 ± 0.07)[e]	-	39.1 (5.1)[e]
Total dietary fibre	39.1 (3.8 ± 0.06)[e]	3.5	45.9 (5.9)[e]

[a]Values are means in triplicate determinations. Values expressed on a dry basis, except for moisture.
[b]Values refer to g/100 g raw leaves according to Salazar *et al.* (2006).
[c]Values refer to g/100 g raw leaves according to Ishida *et al.* (2000).
[d]6.25_N g/100 g.
[e]Values in parentheses are related to fresh green leaves.

Oliveira *et al*. (2013) determined the ascorbic acid (vitamin C) content in ora-pro-nobis leaves and compared it to the others unconventional wild plants. They found similar values of vitamin C for ora-pro-nobis and taro (*Xanthosoma sagittifolium*) ranging between 192.21 and 198.33 mg 100^{-1} (fresh weight), respectively. Comparing these results with others observed in vegetables commonly used as food, such as kale (96.7 mg 100 g^{-1}) and rocket (46.3 mg 100 g^{-1}), it was concluded, that ora-pro-nobis leaves could be a good alternative source to supply the daily requirement of vitamin C.

Table 3. Mineral composition of fresh green *Pereskia aculeata* leaves (mg 100 g^{-1}) (Takeiti *et al.*, 2009).

Minerals	***P. aculeata* (*ora-pro-nobis* leaves)[a]**	***Spinacia oleracea* (spinach)[b]**	***I. batatas* poir (sweet potato leaves)[c]**
Calcium	3420	106	187
Magnesium	1900	62	79
Potassium	1632	662	639
Phosphorus	156	51	68
Manganese	46.4	-	-
Zinc	26.7	0.2	0.8
Iron	14.2	3.1	5.4
Boron	5.55	-	-

Copper	1.4	0.2	0.4

[a]Values are expressed in triplicate determinations (wet weight basis).
[b]Values refer to mg/100 g raw leaves according to Salazar *et al.* (2006).
[c]Values refer to mg/100 g raw leaves according to Ishida *et al.* (2000).

3. BIOLOGICAL ACTIVITIES

Anti-inflammatory activity

An intense chronic and acute topical anti-inflammatory activity against irritant agents were observed in hexane fractions of methanol extract of *P. aculeata* leaves applied in ear dermatitis in mice. This effect was associated to the presence of significant amounts of phytosterols (taraxerol, taraxasterol and phytol) (Pinto *et al.*, 2015a). The authors concluded that the acute and chronic anti-inflammatory activity of *P. aculeata* leaves found is very promising and corroborates the need to understand their ethnopharmacological applications better.. Salt *et al.* (1987) identified sitosterol in *P. aculeata*, *P. bleo* and *P. grandifolia* leaves, which could indicate anti-inflammatory, antibacterial and antifungal characteristic. Purified plant sterols, including sitosterol, are known to have similar structure and functions as cholesterol. They are used in commercial functional foods in Europe (e.g., Benecol® and Pro-Activ®), with approved health claims to reduce cholesterol (Katan *et al.*, 2003). Whether *Pereskia* leaves, either as a direct food source or its extracts, could have potential in these regards or not, is yet to be established.

Antioxidant activity

The antioxidant effect was observed in extracts of *P. grandifolia* leaves (Sim *et al.*, 2010), *P. bleo* (Wahab *et al.*, 2009) and *P. aculeata* (Pinto *et al.*, 2012), and it was associated to the presence of phenolic compounds. The data obtained in their testing systems establish the antioxidant potency of *Pereskia* species. Souza *et al.* (2014) identified antioxidant activity with respect to DPPH radical in *P. aculeata* extracts prepared in acetone (80 %) and ethanol (70 %). They mentioned that the leaves of this species could be considered as a potential source of antioxidant compounds. According to Diplock *et al.* (1998), the presence of antioxidants could prevent and/or reduce the risk of major diseases such as heart diseases, arteriosclerosis, some cancers, Alzheimer and diabetes, associated with an excess of reactive free radicals.

Antimicrobial activity

Antimicrobial activities were found applying ethyl acetate extracts of *P. grandifolia* leaves against *Pseudomonas aeruginosa, Staphylococcus aureus* and *Bacillus subtilis* (Philip *et al.*, 2009). A moderate activity against *P. aeruginosa* and *Salmonella choleraesuis* was observed for *P. bleo* hexane and methanol leaves extract (Wahab *et al.*, 2009). The ether extract of *P. sacharosa* leaves indicated an antimicrobial activity against *Helicobacter pylori*, a bacterium associated with gastric ulcers (Uyub *et al.*, 2010).

Cytotoxicity

Recent studies have addressed the cytotoxic activity of *Pereskia aculeata* ethyl acetate extracts against different human cell lines (Carvalho *et al.*, 2014; Nurestri *et al.*, 2009). For example, nasopharyngeal epidermoid carcinoma cell line (KB), cervical carcinoma cell line (CasKi), colon carcinoma cell line (HCT 116), hormone-dependent breast carcinoma cell line (MCF-7), lung carcinoma cell line (A549) and the non-cancer human fibroblast cell line (MRC-5) were identified using *in vitro* cytotoxicity assay. The results indicated that *P. grandifolia* possessed remarkable cytotoxicity effect against KB and MCF-7 cell lines. The authors also identified the compounds β-sitosterol, vitamin E, phytone, 2,4-di-tert-butylphenol and a mixture consisting of 2,4-ditertbutylphenol, methyl palmitate, methyl oleate and methyl stearate, isolated from the extract of *P. grandifolia* in ethyl acetate. The observed cytotoxic activity against KB cells was attributed to the compound 2,4-di-tert-butylphenol. Malek *et al.* (2009, 2008) also found the presence this compound in *P. bleo* extracts and confirmed the cytotoxicity against KB cells. By contrast, in our own studies (Maciel *et al.*, 2018), we have shown that *P. aculeata* aqueous extracts administered to Caco-2 cells did not show any cytotoxic effects within the dose range studied (185-890 ng mL^{-1}). The results seem to indicate that the type of phytochemicals present in the aqueous extracts of ora-pro-nobis differ notably from those present in the less polar extracts and are far less cytotoxic.

Diuretic and hypotensive activities

Pereskia grandifolia is well recognized in Brazilian traditional medicine as a diuretic agent. Kazama *et al.* (2012) reported diuretic activity in aqueous extract of *P. grandifolia* leaves tested in rats. They associated the results to the inhibition of arginine vasopressin release. The authors also evaluated the ethanolic extract from *P. grandifolia* leaves. They observed that besides of the low capacity of this extract in to induce potassium and chloride excretion, without showing signs of acute toxicity. The results indicated that its bioactive components have a high potential as an adjuvant in some kidney diseases and disorders of arginine-vasopressin secretion.

Antinociceptive activity

This bioactivity has not been reported in the more common *P. aculeata* and *P. grandifolia* extracts. However, in *P. bleo* was studied by Abdul-Wahab *et al.* (2012). They found reasonable antinociceptive activity in mice from the leaves used to produce different extracts and suggested this effect to peripheral mechanisms of pain control. Guilhon *et al.* (2012) investigated the antinociceptive activity of the ethanolic extract and fractions obtained from *P. bleo* leaves. The authors suggested that the results could be mediated, probably, by the central mechanisms related to the opioid system. Pinto *et al.* (2015b), evaluated the antinociceptive activity of the hydromethanolic fraction obtained from the methanol extract of *P. aculeata* leaves. The results suggested peripheral and central antinociception devoid of an opioid effect. According to those authors, it was the first time that this bioactivity (analgesic potential) is reported for *P. aculeata*.

4. APPLICATIONS IN PHARMACEUTICAL, NUTRACEUTICALS AND FOOD

Unconventional wild plants commonly serve multiple functions on dietary and therapeutic uses, such as dye, dietary fibre, food, medicine and oil (Grivetti and Ogle, 2000). The applications of *Pereskia* species are usually limited and need more research to explore the species of this genus. The published data indicates the *Pereskia* species potential as active biological agent and nutritional supplements (Pinto and Scio, 2014).

Pharmaceutical uses

Plants produce metabolites, and many of them show versatile pharmacological activities (Wahab *et al.*, 2009). The chemical compounds of *Pereskia* species are of potential pharmaceutical application relevance. The fruits of *P. aculeata* are rich in carotenoids (namely, α-carotene, β-carotene, lutein, α-cryptoxanthin/zeinoxanthin, and β-cryptoxanthin) (Agostini-Costa *et al.*, 2012). The high levels of α-carotene and zeaxanthin found in berries and leaves, respectively, could be carotenoid biomarker characteristics for *Pereskia* species, which may be important sources of functional compounds for health-promotion (Agostini-Costa *et al.*, 2014).

The fruits of *P. aculeata* and *P. grandifolia* are used in folk medicine as antisyphilitics and expectorants, while leaves of *P. aculeata* are applied as an emollient, treatment of inflammation and skin diseases (Duarte and Hayashi, 2005; Farago *et al.*, 2004; Cruz, 1995). The leaves of both species are used in regional cuisine by natives in some regions of Brazil (Pinto and Scio, 2014; Almeida and Corrêa, 2012), and *P. grandifolia* is cultivated mainly as an ornamental plant and to form hedges (Moran and Zimmermann, 1991). Malaysia is another country that use largely *P. grandifolia*, where the plant was introduced since ~50-60 years ago. It is employed by traditional medicine to treat several types of diseases: cancer, headache, stomachache, gastric ulcers, haemorrhoids, dermatitis, diabetes, hypertension, rheumatism, inflammation, and as a tonic to revitalize the body (Sim *et al.*, 2010). Murilo *et al.* (2010) indicated the use of *P. bleo* in traditional medicine in Panama to treat gastrointestinal disorders and for human nutrition.

Wound healing activity has been attributed to the mucilage of cactus leaves (Thornfeldt, 2005; Aburjai and Natsheh, 2003). However, this property has never been tested under experimental conditions (Carvalho *et al.*, 2014). Wound healing is a complex process involving steps of cellular migration and proliferation, especially, but not only, of fibroblast cells (Krishnan, 2006). It is expected that the compound to be tested should be effective in promoting the cellular proliferation and migration of fibroblast, as indication of wound healing property. In studies performed by Carvalho *et al.* (2014) with hydroethanolic extract obtained from *P. aculeata* leaves, it was evidenced the beneficial effect of the mucilage containing extract on the fibroblast cell culture. It corroborates the folk use of *P. aculeata* for wound healing properties. Sartor *et al.* (2010) also observed the healing capacity of the crude extract of *P. aculeata* leaves applied directly on skin wound of rats. Pinto *et al.* (2016) investigated the topical wound healing activity of gels containing the methanol extract and hexane fractions of the *P. aculeata* leaves in a model of excisional wound healing in mice. The wound healing process was considerably accelerated, mainly by the hexane fraction gel formulation.

Nutraceutical and food application

Consumers' concerns about quality and healthy foods are increasing. Sobrinho *et al.* (2015) incorporated 1 and 2 % (w/w) of ora-pro-nobis (*P. aculeata*) leaves flour in sausage formulations aiming to make this meat product healthier. This addition promoted an increase of the protein and fibre contents in sausages, improving the sensory properties, particularly colour and texture of the product. Fermented milk beverages were obtained adding mucilage extract from *P. aculeata* as a gelling or emulsifier ingredient. The final product showed higher protein content, firmness and adhesiveness (Amaral *et al.*, 2018).

Fortified bread was developed adding 6 % (w/w) of ora-pro-nobis flour (*P. aculeata*), increasing the fibre and protein content with good sensory global acceptance (Martinevski *et al*., 2013). Rocha *et al*. (2008) developed a pasta containing 1.0, 1.5 and 2.0 % of ora-pro-nobis flour, increasing the protein, fibre and mineral contents when compared the product with the control pasta. Zem *et al*. (2017) produced flour of *P. aculeata* and investigated its effects on a diet applied in rats. They concluded that it might not be adequate to warrant satisfactory growth levels of the animals when provided in the diet a single protein source (*P. aculeate* flour). However, the authors suggested that due to few limiting factors, it may be targeted for protein supplementation with other vegetal sources and thus it may provide for the protein needs in human diets.

Prajapati *et al*. (2013) elaborated a review involving the pharmaceutical applications of various natural gums, mucilages and their modified forms. They mentioned that a large number of gum and mucilage plant-based pharmaceutical and cosmetic excipients are available today. These excipients are attractive for a wide range of formulations, given their natural abundance, safety, and amenability for "bio" or "organic" products.. Natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. Recent trend toward the use of plant based and natural products demands the replacement of synthetic additives with natural ones. Some recent works has been published in this context involving *P. aculeata*. Conceição *et al.* (2014) and Lima Junior *et al.* (2013) investigated the extraction process of the gum and hydrocolloids from the extract of *P. aculeata* leaves. They proved that this plant could be an alternative source of viable hydrocolloids, founding the final product rich in protein and minerals. The authors also evaluated the potential use of the powdered product as an emulsifying and stabilizing agent in food applications. Studies of the complex nature of the biopolymers such as arabinogalactans, extracted from ora-pro-nobis leaves and their interactions with Co^{2+}, Cu^{2+}, Mn^{2+} and Ni^{2+} regarding the thermal stability of the metallic compounds were performed by Sierakowski *et al*. (1990) and Mercê *et al.* (2001). In their results, it was suggested the potential use of the hydrocolloids in food and pharmaceutical industries. Silva *et al.* (2017) also produced mucilage derived from *P. aculeata* evaluating different temperatures (30, 45 and 60 °C) to obtain the extract.

Barbalho *et al.* (2016) studied the *P. aculeata* flour on metabolic profile and intestinal motility of Wistar rats, and observed a total decreased of lipids, weight gain, visceral fat and increased levels of HDL-c (high density lipoprotein). They found that the flour ingestion reduced the risk of cardiovascular disease by 67.1 %. The beneficial effects of *P. aculeata* flour were attributed to the higher content of vitamin C, carotenoids and fibres. Almeida and Corrêa (2012) studied rats fed with hypercaloric diet and concluded that the daily ingestion of *P. grandifolia* flour ingestion could prevent obesity and cardiovascular diseases due to the effectiveness reduced weight gain, body mass index, glycemia and lower levels of triglycerides.

5. FORMULATION TECHNIQUES TO ENHANCE STABILITY AND BIOAVAILABILITY OF BIOACTIVE COMPOUNDS

The functionality of plant extracts and pure compounds isolated from medicinal plants is highly dependent on the stability, appearance, taste and flavour, formulation and active ingredient availability. Often, active ingredients such as food supplements (*e.g.* omega-3 fatty acids) or micronutrients (*e.g.*, iron), can often cause detrimental changes in product formulation. These can be associated with their inherent properties or with their interactions with other ingredients. Colloidal delivery systems are used to achieve an adequate balance between the solubility and dispersibility of active ingredients to overcome the technical challenges associated with chemical stability, taste, bioavailability, sedimentation and solubility (Velikov, 2012).

Studies in our laboratories (Maciel *et al.*, 2018), have aimed to develop a colloidal carrier system loaded with ora-pro-nobis (*P. aculeata*) aqueous extract, as a potential formulation for iron food fortification. To this end, we prepared chitosan/pectin polyelectrolyte electrostatic self-assembled complexes and evaluated their physicochemical and cellular iron bioavailability in Caco-2 cells. The thus obtained particles were in the dimeter size range of ~1.0 to 7.0 µm, depending on the relative molar charge ratio (n+/n-) of oppositely charged chitosan (positive) and pectin (negative). We gained proof-of-concept that the systems comprised by an excess of chitosan (n+/n- > 1.0) led to higher cellular ferritin levels than, although these were lower than for the free ora-pro-nobis extract (6.81 ± 0.36 *vs.* 174.96 ± 15.44 ng/mg cell protein, respectively). In other studies (Omwenga *et al.*, 2018; Qin *et al.*, 2018), we have also demonstrated the effectiveness of associating lipophilic flavonoid compounds such as quercetin, baicalein and cinnamaldehyde in oil-core nanocaspules coated with chitosan. These studies show consistently, that the encapsulation of these bioactive compounds leads to enhanced bioactivity against bacterial quorum sensing and biofilm formation. Also, the encapsulation of the flavonoids quercetin and baicalein, has a cytoprotective effect.

Whether some of the bioactive lipophilic compounds present in ora-pro-nobis non-polar extracts would be amenable for nanoencapsulation to modulate their bioactivity, is yet to be established in future studies.

6. CONCLUSION

Few reports on the identified phytochemical compounds, nutrients and functional properties suggest that the ora-pro-nobis (*Pereskia aculeata* and *Pereskia grandifolia*), an underutilized indigenous edible plant, should be better investigated. From the ongoing research worldwide, and with the current available database it was evidenced that the ora-pro-nobis possess high nutritional value and still presents interesting potential for the development of supplementation and fortification formulation of minerals, vitamins and protein, as well as other health benefits that are yet to be discovered. This review has sought to present an updated account of the current knowledge on the different applications of ora-pro-nobis. It is clear that further investigations should be conducted so that the potential uses observed in pharmaceutical, nutraceutical and food area of this plant are fully realised. In the years to come, there will be continued interest in both novel and traditional natural plant sources and their uses in the development of novel materials as health enhancers.

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