



## Review article

## Tamarillo (*Solanum betaceum* Cav.) wastes and by-products: Bioactive composition and health benefits

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## ABSTRACT

**Introduction:** During processing, a large amount of by-products is produced from tamarillo fruits in the form of stalks, outer skins, and pomace (residual seeds and inner skins). This material is a renewable source of bioactive compounds with high economic value and positive effects on human health. Previous reviews have focused on the ethnobotanical, traditional uses, and phytochemistry of the tamarillo fruit. This report aims to compile production and cultivation data, as well as the valorization of this agro-industrial residue, green extraction methods used for extracting the bioactive compounds, and their biological activity.

**Method:** In this study, a literature search was conducted in five scientific databases: Web of Science, ScienceDirect, Scopus, PubMed, and Google Scholar to retrieve research published in English, Spanish, or Portuguese between 2009 and 2024, which mentions the composition and extraction methods of bioactive compounds from tamarillo wastes and by-products and the health benefits associated with these compounds. The data extracted was compiled and shown in this scoping review.

**Results:** Tamarillo wastes and by products have a rich nutritional and bioactive composition, including high protein, vitamins A and C, minerals, dietary fiber, sugars, terpenes, flavonoids, carotenoids, anthocyanins, and other phytochemicals. Green methods have been effective, yielding high amounts of these compounds while preserving their integrity. Natural polyphenols have shown antioxidant, anticholinesterase, anti-inflammatory, antimicrobial, anti-diabetic, and anti-obesity properties. The antioxidant fibers, mucilage, and pectin of the pomace contribute to improved intestinal health.

**Conclusion:** Therefore, these wastes and by-products have potential uses as natural colorant, antioxidants, supplements, functional foods, active biobased films, and in pharmaceutical and cosmeceutical sectors due to their effective bioactive molecules. Future research should focus on the use of tamarillo by-products as a source of functional ingredients in several other formulations that are still little explored, as well as their use as a natural colorant and antioxidant. More studies are necessary on the composition-activity relationship, physiological mechanisms, and clinical response.

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## 1. Introduction

Recently, in addition to the high consumption of fruits, vegetables, cereals, and their by-products, there has also been a growing demand on the part of consumers for new products, which, besides providing energy in the diet, contain compounds with bioactive properties that promote beneficial effects on human health. In this scenario, the high productivity of fruit-based products has been generating large volumes of by-products from processing, which are mostly discarded or used for fertilizer or animal feed [1]. However, many studies report that these residues, even after processing, are still nutritionally rich and sources of bioactive compounds with high potential for applications in new formulations as functional ingredients [2–4].

According to the Food and Agriculture Organization of the United Nations (FAO), each year around 1.3 billion tons, equivalent to 30 % of total food production, are lost or wasted globally [5]. In this sense, the application of by-products from the food industry has been highlighted, being applied in food formulations, such as cereal bars [6], morning cereals [7], cakes [8], bread [9], yogurts [10], and cookies [11], to enrich the products with fiber, antioxidants, proteins, vitamins, and minerals, or commercialized as dietary supplements, offering an option to increase the intake of bioactive compounds such as carotenoids, polyphenols, tocopherols, and vitamin C [12].

Therefore, tamarillo (*Solanum betaceum* Cav.) wastes and by-products, such as stalks, outer skins, seeds and pomace (containing residual seeds and inner skins) obtained from the processing of whole pulp and powder ingredients, represent about half of the weight of the fruit (49 %) and are generally discarded, a common practice in the food industry, while the population only consumes the raw or cooked fruit pulp [13,14]. However, these by-products are sources of nutrients such as sugars, amino acids, proteins, minerals, and fiber [14], as well as bioactive molecules that can promote benefits for human health [15] such as carotenoids, vitamin C [16], phenolic compounds and anthocyanins with potential antioxidant activity [17].

This manuscript aims to address production and cultivation data, as well as the valorization of this agro-industrial residue which have become an alternative to replacing conventional ingredients in order to nutritionally enrich new products, reduce costs and contribute to sustainability issues.

This study will contribute to bringing a new vision to the field of research into new environmentally friendly extraction technologies for compounds with high added value. These methods have been increasingly employed for extracting compounds from tamarillo waste and by-products, such as supercritical fluid [18,19], ultrasound-assisted [19,20], pressurized liquid [21,22], microwave-assisted [23], high shear dispersion [20] and using a green solvents and hot water extraction [13,24–26], including carotenoids, phenolics acids, hydrocolloids, polyphenols, anthocyanins, pectin, fibers, flavonol, terpenoids and bufanolides that can be used as natural colorant, antioxidants, additives like emulsifiers, thickener, stabilizer, gelling, and glazing agents for use as a functional ingredient, prebiotic, biofilms, supplements/nutraceuticals and pharmaceutical (“multitarget” therapy).

There is a large demand for pectin in various industrial segments, such as beverages and food (5–30 %), pharmaceuticals and nutraceuticals (2–10 %), biotechnology and biomedicine (1–3%), personal care and cosmetics (1–5%), and the pectin supplied commercially comes from citrus or apple pomace, but tamarillo pomace have shown to be a potential source of pectin, being advantageous in both environmental and economic aspects [23].

Tamarillo residues have shown beneficial properties *in vitro* and *in vivo*: anti-diabetic and anti-obesity [13], anti-inflammatory [27], antioxidant [28,29], prebiotic [24,25], antimicrobial [30–32], anticancer [33–35], anticholinesterase [36], hypoglycemic [28], lipid-lowering [37], and neuroprotective activities against Alzheimer’s disease [21].

However, certain conditions are considered important to obtain maximum benefit from fruit by-products, such as guidance on which varieties, quantities and states of ripeness are used, to verify the influence on their impact on health [38]. In this context, the present review discusses the progress of studies on how natural bioactive compounds extracted from tamarillo waste can act beneficially on human health, their mechanism of action and aims to bringing new perspectives for future research to be explored.

## 2. Methods

### 2.1. Literature search strategy and study selection

This review examines the literature to search, analyze, and synthesize the published works on the composition and extraction methods of bioactive compounds from tamarillo wastes and by-products and the health benefits in human health associated with these compounds. In this study, a literature search was conducted in five scientific databases: Web of Science, ScienceDirect, Scopus, PubMed, and Google Scholar to retrieve research published in English, Spanish, or Portuguese, published from 2009 to 2024.

We used a combination of the following keywords to search: “Tamarillo fruit”, “Tamarillo waste”, “Tamarillo seeds”, “Tamarillo skins”, “Tamarillo by-products” “Chilto fruit”, “tree tomato”, “*Solanum betaceum* Cav.”, “*Cyphomandra betacea* Sendt.”, “Tamarillo bioactive compounds”, “Tamarillo health benefits”, “Tamarillo biological activity”, “Tamarillo process”, and “Tamarillo extraction methods”.

The articles were examined based on their title and abstract to assess their relevance to the research questions. The data obtained throughout the search were summarized and classified in tables and figures.

## 3. Tamarillo production and consumption, pulp processing and process waste

The tamarillo fruit, also known a tree tomato, is native mainly to South America (Andean regions of Colombia, Peru, Chile, Ecuador, and Bolivia) [39] and growing cultivation in Brazil [40] that has been introduced in different locations worldwide. In New

Zealand, farmers in search of improvement and continual re-selection of tamarillo cultivars have led to three new high-quality cultivars, yellow (amber), red (Laird's Large), and purple red (Mulligan), for commercial production. Fruit colors vary between purple and red due to anthocyanins, and red, orange, or yellow due to carotenoids [16].

In Brazil, the fruit is still cultivated on a small scale; in Bahia, it is called "tomatão"; in São Paulo, it is known as "French tomato", and in the southern region of Minas Gerais, it is popularly known as "tree tomato", widely cultivated in gardens or backyards and found in some markets in the South and Southeast regions, originating from imports. Each tamarillo tree can produce up to 30 kg of fruit annually [41]. The cultivation of exotic fruits contributes to a movement in the economy and can enable new gastronomic experiences, as a functional food, in addition to being able to be applied in other segments such as pharmaceuticals and cosmeceuticals. Furthermore, fruit growing generates income per area for small producers and strengthens economic growth in producing countries, thus reducing poverty in rural areas [41,42], since its cultivation in Brazil is through family farming. When ripe, the fresh fruit can be consumed in various ways, such as *in natura*, salads, and industrially processed products, such as frozen pulps, juices, jellies, syrup and ketchup, shows desirable characteristics and can be commercially exploited and there is great interest in developing functional products based on tamarillo [39,43,44].

Due to its rich composition and pleasant sensory characteristics, this fruit consumption has been increasing worldwide. New Zealand is one of tamarillo's main producers and exporters, with a yield of approximately 622 tons per year in 2019 with a cultivated area of about 100 ha with 40 producers, with export markets including America, Australia, Hong Kong, Singapore, and Japan. In Northwest Argentina, called chilito, tamarillo is currently widely used for human consumption in different varieties (orange, red-orange, and red), which has begun growing the sustainable exploitation of this fruit on a larger scale to promote its introduction in market locations [16,45]. According to Ref. [46], tamarillo is also grown in the mountainous regions of West Bengal, Maharashtra and the North-Eastern States, with fruit produced from 1.5 to 2 years and bearing fruit for more than 10 years. Tamil Nadu, located in the south-east of the Indian peninsula, is cultivated in Ootachamund and Kodaikanal. In South Asia in Nepal, Taplejung, Solukhumbu, Dhankuta, Khotang, Dolakha, Kavre, Kathmandu and Parbat districts are the major producers [43].

Tamarillo wastes are generally discarded, a common practice in the food industry, and the population only consumes the raw or cooked fruit pulp [14]. This residue generated during the industrial processing of the tamarillo fruit represent about half of the weight of the fruit (49 %) [13]. They may become an environmental problem, with significant economic losses. The diagram shown in Fig. 1 represents the generation of tamarillo by-products (stalks, outer skins, and pomace that contains seeds and inner skins residual) obtained from the processing of whole pulp and powder ingredients.

#### 4. Composition of the tamarillo plant

The tamarillo (*Solanum betaceum* Cav. Syn *Cyphomandra betacea* Sendt.) belongs to the genus *Solanum* of the Solanaceae [39]. The tamarillo tree is fast-growing, reaching a height of between 1 and 5 m, it forms a single trunk that is woody at the base and branches out at a height of 1.5–2 m. The flowers have a pink-white corolla and are fragrant (clusters of 10–50 flowers). It produces between 1 and 6 elliptical fruits, measuring between 4 and 8 cm in length and 3–5 cm in width, containing many seeds larger than those of tomatoes

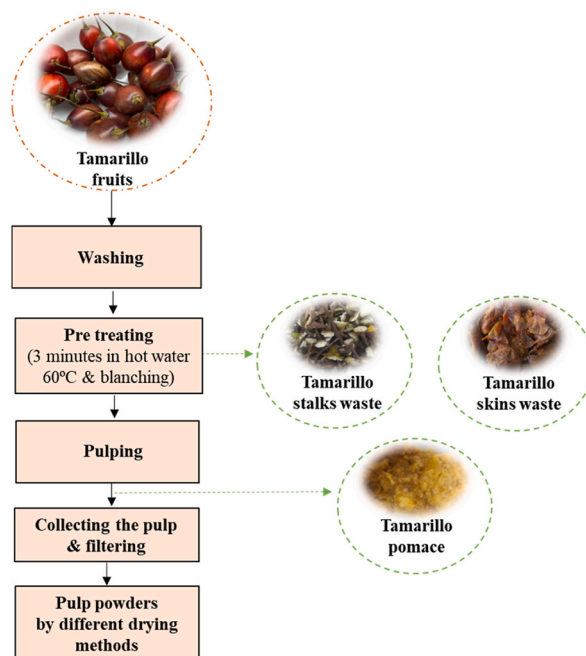


Fig. 1. Tamarillo by-products generation during whole pulp production process.

[52].

The typical representation and anatomy of a tamarillo fruit are shown in Fig. 2a. The self-explanatory figure shows the edible part (pulp - mesocarp) and the inedible parts (outer skin and inner skin - epicarp and seeds). The physical and chemical composition of the fruit is shown in Fig. 2b. The macronutrients of tamarillo by-products (skin and seeds) are represented in Fig. 2c.

The fruits are very attractive and have a distinct sweet and sour taste. They are composed of two zones that can be differentiated internally: a firm outer pulp and the seed zone in the center of the fruit called the placenta, where the seeds are surrounded by a gelatinous substance and a membrane [48].

The color of the fruit can be purple, red, orange, yellow, and reddish yellow, may have faint dark longitudinal stripes, and the flesh can vary from reddish-orange or orange to creamy yellow [41]. The red and purple types are preferred by consumers mainly in the United States and Europe, as the color is more attractive, although the taste is stronger and more acidic than the yellow type. According

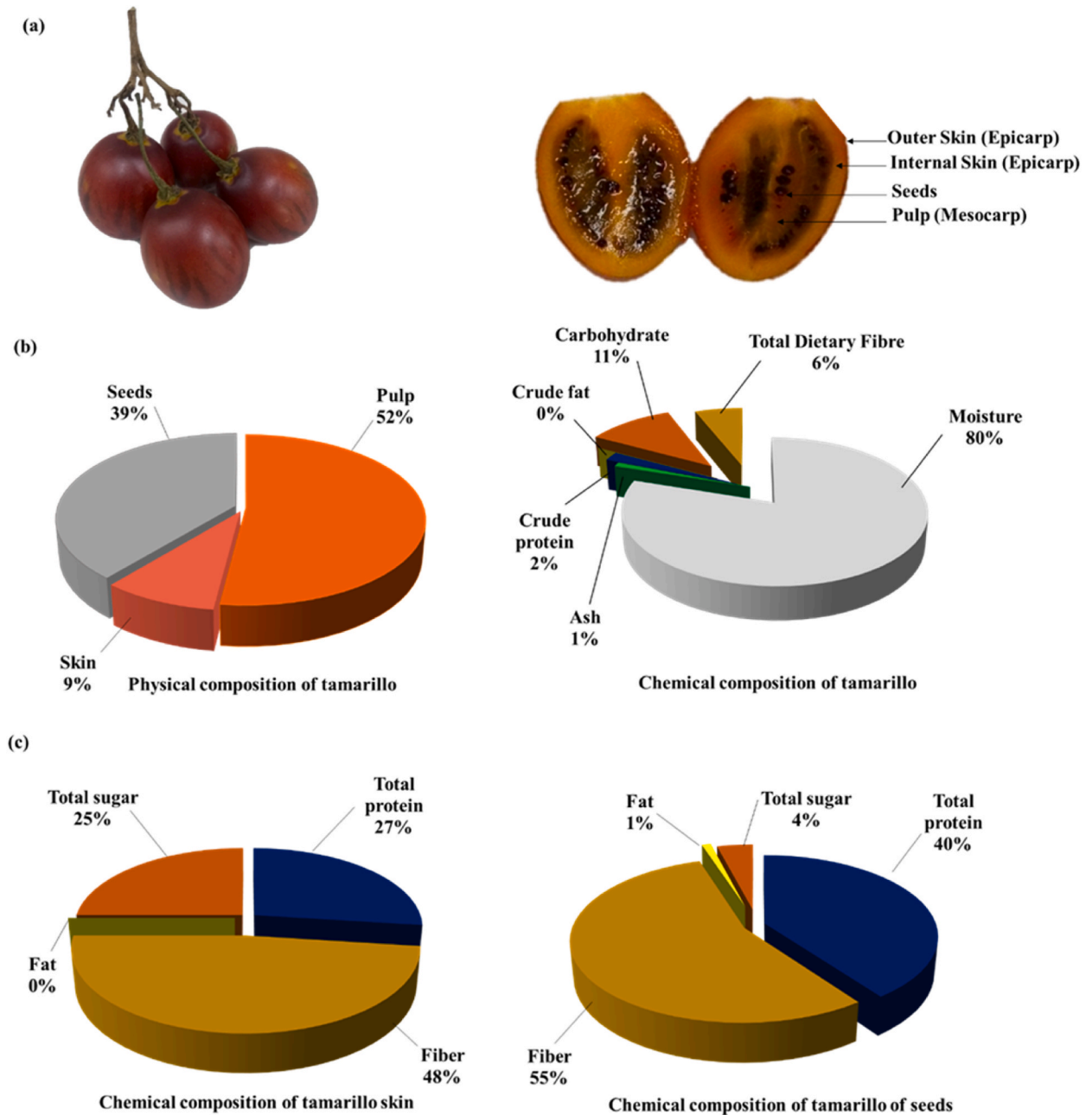


Fig. 2. (a) Representation and typical anatomy of a tamarillo fruit; (b) Physical and chemical composition of the tamarillo fruit; (c) Macronutrients of the skin and seeds [13,80].

to Prohens and Nuez (2001), the red skin type when ripe has a reddish to orange skin with faint, green to brown stripes and orange-colored pulp (50–80 g of weight). The yellow skin type has a bright yellow skin, with brown to green noticeable longitudinal stripes and the flesh is yellow (50–70 g in weight). The purple skin type is known as “dark red” or “black”. The fruits have a vivid dark red skin, with very faint green vertical stripes and the flesh is purple colored (60–100 g in weight) [47].

The pulp, seeds, and skin correspond to 51.5 %, 39.4 %, and 9.1 %, respectively, of the total weight of the fresh fruit [13], which shows the great relevance of the present study since the by-products are equivalent to approximately half the weight of the fruit (48 %).

## 5. Valorization of tamarillo fruit and by-products

The chemical composition of the tamarillo fruit occurs due to the difference in the existing varieties and growing conditions.

Due to the rich composition of nutrients such as sugars, proteins, fibers, and minerals, several products based on tamarillo have been developed as juices, jams, yogurts, or used as a coagulant in the manufacture of cheeses; the rinds have also been reported as lipid antioxidant in cooked beef, emulsifiers, and foam stabilizers in food products [18,41,49–52].

Agro-industrial waste should be treated appropriately, ideally reduced or reused [5]. For this reason, the by-products of the tamarillo processing industries could be better used as a source of functional ingredient in several other formulations that are still little explored since they show desirable characteristics such as low fat and significant fiber and protein contents.

The color of a fruit or a product is an essential acceptance parameter. Most synthetic colorants in food have been removed or banned due to their side effects, such as short, medium, and long-term toxicity, affecting consumer health. On the other hand, natural colorants, in addition to providing a broad spectrum of colors, are of great importance in contributing to the flavor and sensory characteristics of foods, which also guarantees consumer satisfaction [53].

Tamarillo skins and seeds can be considered a good natural pigment source. Diep, Pook, and Yoo (2020) when evaluating three cultivars of tamarillo Amber, Laird’s Large and Mulligan, verified the presence of the anthocyanins delphinidin-3-rutinoside (0.43, 32.41, and 49.11 mg/100 g dry weight, respectively), cyanidin-3-rutinoside (0.29, 68.72, and 114.47 mg/100 g dry weight, respectively), and pelargonidin-3-rutinoside (0.52, 54.36, and 93.63 mg/100 g dry weight, respectively) in the skin of all cultivars and cyanidin-3-glucoside only in the skin of Laird’s Large and Mulligan cultivars (0.33 e 1.97 mg/100 g dry matter, respectively) [17]. Orqueda et al. (2017) also detected anthocyanins in the skin of the orange-yellow cultivar, with a level of 1.78 mg cyanidin-3-glucoside equivalent/100 g powder [13]. Recently, Orqueda et al. (2020), when evaluating the red cultivar, found 62.5 mg C-3GE/100 g in the skin and 65.23 mg C-3GE/100 g in the seeds, which are much higher when compared to the content found in the fruit pulp of 10.6 mg C-3GE/100 g [14].

Antioxidant plant pigments, such as carotenoids and flavonoids, are also called phytochemicals; this term is used for various compounds produced by plants.

In accordance with Varzakas, Zakyntinos, and Verpoort (2016), the most colorful phenolic compounds found in fruit and vegetable by-products are anthocyanins and leucoanthocyanidins, which are potential antioxidants [12]. In addition to anthocyanins, tamarillo skins have a rich composition of other bioactive pigments in the three cultivars Amber, Laird’s Large, and Mulligan, which are the provitamin A carotenoids ( $\beta$ -Carotene and  $\beta$ -Cryptoxanthin), xanthophylls (violaxanthin, antheraxanthin, lutein, flavoxanthin A, zeaxanthin, and flavoxanthin B), and chlorophylls (Chlorophyll A, Chlorophyll C1, Chlorophyll C2, Chlorophyll C3, Chlorophyll D, and Phaeophytin) [16].

Hassan and Bakar (2013) found a higher content of total flavonoids in methanolic extracts of tamarillo skin in a Malaysian cultivar (3.36 mg rutin equivalent/g, dry weight) than in the pulp (2.41 mg rutin equivalent/g, dry weight) [36].

Loizzo et al. (2019) when investigating the phenolic profile of the ethanolic extracts of tamarillo, detected a higher concentration of phenolics in the skin extracts (284.1 mg/kg ethanolic extract) than in the pulp and seed of the fruit (165.1 and 42.1 mg/kg ethanolic extract, respectively) [28]. Chlorogenic acid was the most abundant compound in the skin and seed extracts (253.8 and 37.7 mg/kg ethanolic extract, respectively), followed by sinapic acid (10.3 mg/kg ethanolic extract) and ferulic acid (8.7 mg/kg ethanolic extract) in the skin, and (–)-epicatechin (2.5 mg/kg ethanolic extract) in the seeds. Nonetheless, Orqueda et al. (2020) found a total phenolic content of 408.9 mg GAE/100 g in red tamarillo skin powder, with rosmarinic acid and caffeoylquinic acid being the major compounds (0.291 and 0.354 g/100 g powder, respectively). These authors also reported relevant levels of vitamin C in the skin and seeds (43.5 and 45.2 mg L-ascorbic acid/100 g powder, respectively) [14].

Martin et al. (2021) applied the vibrational spectroscopy technique to the non-edible parts of the tamarillo fruit. They found that the seeds were richer in unsaturated lipids, mainly fatty acid esters and that the skin contained greater amounts of phenolic constituents and terpenoids, with the skin’s outermost surface (epicarp) containing cutin polymers (waxy protective compounds) and proteins. In contrast, the inner skin (in contact with the mesocarp) had more phenols, dietary fiber, and water [44].

The tamarillo skin and seeds have a composition of saturated fatty acids - SFA (25.4 and 16.9 %): 16:0 and 18:0, monounsaturated fatty acids - MUFA (43.7 and 19.3 %): 18:1n-9 and 18:1n-11, and polyunsaturated fatty acids - PUFA (30.9 and 63.8 %): 18:2 n-6, 18:3 n-3; however, 16:1 was found only in the seed [28].

22 free volatile organic compounds were found in the tamarillo fruit, with C6 alcohols and esters being the most important compounds and 83 glycosylated volatile organic compounds, the majority being phenols and terpenoids [54]. 115 compounds were identified in red skins tamarillo collected from Northland region of New Zealand. Methional was the main contributor to the overall aroma in the skins ( $15.4 \pm 4.2$  g/g DW), and the most abundant volatile compound was the (E)-3-Hexen-1-ol (36 %). The major chemical groups in skins were Ketones, Esters, Alcohols, Nitrogen and sulfur compounds, Aldehydes, Fatty acids and in a smaller percentage Furans, Benzenes, Hydrocarbons, Terpenes, carboxylic acids and derivatives, and pyrans [32], however there are still few studies presenting the volatile composition of the seeds and pomace.

Tamarillo by-products are important sources of fiber (23.2 g/100g of skins powder and 29.5 g/100g of seeds powder) [14] and they have high protein content (10.51 g/100g of skins powder and 21.9 g/100g of seeds powder), which makes them ideal for jams and jellies [55]. In addition, they are also source of minerals (Na, Mg, K, Ca, Fe, and Zn) and low in lipids (0.8 g/100g of skin powder and 0.42 g/100g of seed powder) and total soluble sugars (8.9 g of glucose equivalent/100g of skin powder and 20.5 g/100g of seed powder) [14].

Although few studies report the content of tannins in tamarillo skins and seeds, quantifying this anti-nutritional factor is of great importance since when in high amounts they can affect the digestibility of dietary proteins [56]. Orqueda et al. (2017) did not detect condensed and hydrolyzed tannins in freeze-dried pulp, skins, and seed [13].

The nutritional and phytochemical composition of tamarillo skins and seeds show that these by-products can be used as a potential ingredient (Fig. 3) to enrich new formulations with bioactive compounds with possible beneficial effects on health and contribute to the reduction of the environmental impact generated by their improper disposal.

## 6. Extraction of bioactive compounds from tamarillo wastes and by-products

The current scenario has led to demands for more action from waste-generating industries, encouraging integrated management and the recovery of compounds with added value from this material. The large volume of articles published about healthy eating, authored by more than 70 % of countries/regions around the world (an increase from 71 in 2002 to 1764 in 2021/year), shows the need for further in-depth research into new matrices and compounds that bring health benefits [57]. In addition, with the accelerated aging process and increased incidence of chronic non-communicable diseases, there is a growing demand for antioxidant supplements. It is estimated that the global polyphenol market will reach around 1.70 billion dollars by 2029, with growth of 8.72 % over the period 2024–2029 [58].

The extraction of phenolic fractions from by-products is a critical stage in the process, due to the compositional heterogeneity of plant matrices, which can be made up of molecules of different types ranging from 8.000 to 10.000, including monomers (phenolic acids or anthocyanins) and highly polymeric derivatives (such as tannins), glycosylated or aglycons, as well as insoluble conjugates with proteins/carbohydrates from the shikimic or malonic acid pathways [59]. Fast and efficient methods have been used to extract by-products from purple tamarillo, such as supercritical fluid extraction, which is considered a clean method when compared to the traditional method, since it uses environmentally friendly CO<sub>2</sub>, which behaves like a liquid solvent and helps to rapidly increase the yield with low risks of contamination. In addition to this, ultrasound-assisted extraction has also been used, which increases the yield in a short space of time. Rohilla et al. (2022) found that the extraction of anthocyanins and phenolics from purple tamarillo peels showed higher yields in ultrasound-assisted extraction compared to supercritical fluid extraction, especially for organic acids [19].

Castro-Vargas et al. (2013) when using supercritical fluid extraction observed that there was a 2.2-fold increase in extraction yield when using CO<sub>2</sub>/EtOH as a co-solvent compared to using pure CO<sub>2</sub>, this is due to the intensification of the concentration of polar compounds in the extracts, which have limited solubility in CO<sub>2</sub>, in order to stimulate the breaking of solute/solid matrix interactions, accompanied by the replacement of active sites by co-solvent molecules and solubilization of the compounds. Compared to Soxhlet extraction (SE), there was low selectivity, thermal degradation during the process and lower antioxidant results than supercritical fluid extraction [18]. There is an advantage in using water and ethanol as co-solvents, as they are low cost, environmentally friendly and can be used directly in new food, pharmaceutical and cosmeceutical products.

Suárez-Montenegro et al. (2021) using the Pressurized liquid extraction (PLE) technique managed to obtain various bioactive metabolites (phenolics, flavonoids and carotenoids) from tamarillo peels (representing 8–15 % of the fruit), the high pressure and temperature allowed the extraction rate to be accelerated, promoting a significant reduction in extraction time when compared to traditional methodologies and greater efficiency when using a green solvent (100 % EtOH) [21]. Sánchez-Martínez et al., 2022 obtained promising results with red tamarillo peel extract using the PLE technique, as promising sources for obtaining neuroprotective

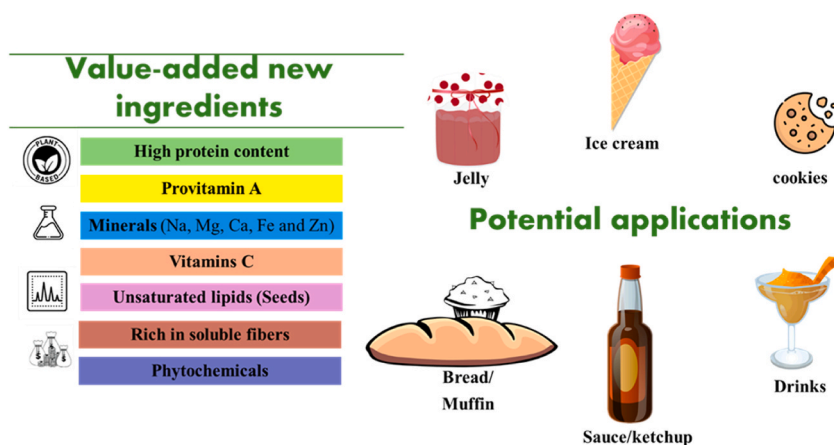


Fig. 3. Components of tamarillo by-products and their potential applications in food industry.

compounds [22].

Phytochemicals extracted from yellow tamarillo peels in extra virgin olive oil, comparing the green extraction techniques High Shear Disperser (HSD) and Ultrasound, and found that the best carotenoid extraction yield was found in samples treated with HSD [20].

Polysaccharides from food industry by-products such as soluble dietary fiber (SDF) and insoluble dietary fiber (IDF) have also been recovered, such as pectins,  $\beta$ -glucans, gums, mucilage, oligosaccharides, inulin, cellulose, hemicellulose, lignin and resistant starches [60]. Orqueda et al., 2022 extracted pectin from tamarillo skins and seeds using hot distilled water and absolute ethanol, resulting in excellent biofilms to prevent lipid oxidation in fish [26]. Green solvents have also shown sustainable and promising alternatives for extracting bioactive compounds from tamarillo by-products [13,14,24–26]. Table 1 and Fig. 4 shows the extraction methodologies that have been used to recover bioactive compounds from tamarillo wastes and by-products and their potential applications.

## 7. Bioactivities of tamarillo-derived compounds

There are several studies in the literature on the valorization of agricultural by-products and the importance of applying a sustainable circular model that uses renewable resources [8,42,61,62]. At the same time, there is also a growing interest in investigating the potential beneficial health effects of bioactive products extracted from agro-industrial by-products [10,63,64].

The biological effects of tamarillo by-products have been investigated *in vitro* and *in vivo* (Fig. 5), such as antioxidant, anti-inflammatory, anticancer, and anti-obesity activities [39].

When dealing with the functional compounds of tamarillo by-products related to human health, it is possible to separate them into two groups of evidence: compounds with antioxidant activity and carbohydrates.

### 7.1. Antioxidant activity

Antioxidants from agro-industrial by-products have been a viable option with high added value for application in new formulations in the diet [10,61,65,66] and may contribute to reducing the effects caused by oxidative stress. Antioxidants can be exogenous (food or supplements) or endogenous (produced in the human body itself) [29]. Loizzo et al. (2019), through *in vitro* antioxidant assays, such as DPPH, ABTS, FRAP, and  $\beta$ -Carotene Bleaching Test, verified that the lyophilized tamarillo skin extracts showed effective antioxidant capacity. The authors conclude that these results contribute to the body of evidence supporting the possibility of using skins and seeds as source ingredients of bioactive in foods [28].

Phenolic compounds are one of the most studied functional compounds due to their potential antioxidant effect on the human body. Orqueda et al. (2017) analyzed the extract enriched with polyphenols from the powder of the skins and seeds of freeze-dried tamarillo, which showed a good dose-response effect on the ability to reduce the cationic radical ABTS, being similar to the pulp, with values of  $SC_{50}$  0.80, 1.38 and 1.09  $\mu\text{g/mL}$  EAG, respectively. These results showed higher antioxidant capacity than commercial synthetic antioxidants, such as BHT ( $SC_{50} = 55 \mu\text{g/mL}$ ). These results allowed the authors to conclude that skin and seed flours can be considered alternatives for obtaining a product that is a source of natural antioxidants [13].

The consumption of tamarillo juice with skins and seeds for two weeks by rural workers daily exposed to pesticides was associated with a reduction in malondialdehyde, a biomarker of oxidative stress, and an increase in superoxide dismutase and acetylcholinesterase, endogenous antioxidants. The authors suggest that the varied composition of phenolic compounds characteristic of tamarillo can explain these results [29].

Free radicals are the cause of aging. Smoking causes the accumulation of free radicals in the body and leads to lipid peroxidation, cell damage and DNA damage. One study showed that when male Wistar rats were exposed to cigarette smoke for 1 h/day for 21 days and given ethanolic extract of tamarillo seeds 80mg/200gBW/day before exposure, there was an inhibition of the decrease in Leydig cells and testosterone levels (causing oxidative stress) compared to a control group that received a placebo aquadest 2 ml/day, with an increase in antioxidant capacity and inhibition of inflammation [67].

### 7.2. Anticholinesterase

The anticholinesterase activity was verified in the lyophilized tamarillo skin and pulp through an enzymatic assay using acetylcholinesterase and verified a higher anticholinesterase effect in the powder of the skins compared to the control. According to the authors, these results may be associated with the significant amount of phenolics, flavonoids, anthocyanins, and carotenoids in tamarillo, all these compounds related to this effect on human health [36].

### 7.3. Anti-inflammatory activity

In a recent *in vitro* study, extracts from tamarillo skin reduced the production of pro-inflammatory biomarkers PGE-2, IL-1 $\beta$ , and TNF- $\alpha$  in RAW 264.7 cells stimulated by LPS, with potential anti-inflammatory effect [27]. There is a demand for herbal medicines that can reduce pain and inflammation. In general, drugs prescribed for pain and inflammation, non-steroidal anti-inflammatory drugs (NSAIDs), are effective; however, they can have many adverse effects, such as gastrointestinal bleeding, cardiovascular reactions such as acute myocardial infarction, atrial fibrillation, cardiovascular thromboembolic event, increased blood pressure, and damage the kidney [68].

**Table 1**  
Methodologies for extraction compounds from tamarillo wastes and by-products.

Wastes/By-products	Extracted compounds	Treatment conditions	Results/Extraction improvement	Potential applications	References
<b>Supercritical Fluid Extraction (SCFE)</b>					
Purple tamarillo skins	Polyphenols Anthocyanins	The flow rate was 1 mL/min of modifier EtOH: H <sub>2</sub> O (1:1), pH 2.0 and 5 mL/min CO <sub>2</sub> –49.42 min, 49.28 °C and 176.63 bar pressure.	In optimized conditions: TPC was 16.12 mg GAE/g and anthocyanins was 0.62 mg C3G/g in the extract.	Natural colorant Antioxidants	[19]
Tamarillo skins	Antioxidant compounds	CO <sub>2</sub> and CO <sub>2</sub> /EtOH as co-solvent 50 °C/30 MPa and CO <sub>2</sub> density of 0.8713 g/mL	Increased in the extraction yield in 2.2 times from pure CO <sub>2</sub> (0.835 ± 0.017 %) versus CO <sub>2</sub> with 5 % of EtOH (1.9 ± 0.1 %) with higher antioxidant activity.	Antioxidants (protectors against lipid oxidation of cooked beef meat).	[18]
<b>Ultrasound-Assisted Extraction (UAE)</b>					
Purple tamarillo skins	Polyphenols Anthocyanins	500 W, 20.5 KHz, EtOH: H <sub>2</sub> O (1:1) pH 2.0, 19.14 min, 51.53 °C, and 50.53 % amplitude	In optimized conditions: 21.06 mg GAE/g TPC and 0.71 mg C3G/g anthocyanins.	Natural colorant Antioxidants	[19]
Yellow tamarillo skins	Carotenoids	Phytochemicals were extracted in extra virgin olive oil. The solid to solvent ratio (1:10). Conditions: 8 min, 50 °C, and 76 % amplitude.	2.01 mg βCE/100 g of the carotenoids. Gallic acid (24.56 μg/g), chlorogenic acid (137.05 μg/g), caffeic acid (61.93 μg/g), and p-coumaric acid (15.83 μg/g).	Functional food (source of carotenoids)	[20]
<b>Pressurized liquid extraction (PLE)</b>					
Tamarillo skins	Phenolics Flavonoids Carotenoids	EtOH-formic acid 98:2 was used at 60 °C 1500 ± 200 psi, 20min.	Highest yields extracts were achieved with 100 % water (98 % water, 2 % formic acid) and with water:ethanol (50:50). Extraction yield (36.25 %), TPC (92.09 mg GAE/g extract), TFC (4.4 mg QE/g extract), TCC (107.15 mg CE/g extract).	Antioxidants Pharmaceutical (“multitarget” therapy) Food industry	[21]
Red tamarillo skins	Flavonoids Terpenoids Bufanolides Phenolic acids	100 % EtOH, 180 °C, 20 min and 10 MPa	PLE led to a decrease in solvent surface tension and viscosity, whereas the solubility of analytes increased, ultimately improving the mass transfer rates. Extract maintained maximum cell viability (120 μg/ml), non-cytotoxic.	Food additives Supplements/nutraceuticals (neuroprotective properties)	[22]
<b>Microwave extraction</b>					
Tamarillo pomace	Pectin	EtOH and acids (citric, tartaric, HCl, and HNO <sub>3</sub> ), dried 40 °C, HPLC and FTIR methods. Rheological and Emulsifying Properties.	FTIR revealed that the pectin extracted from the bagasse presented the same characteristic bands as commercial pectin (HMP). Higher yield with nitric acid and tartaric acid as extractants. Protein in the extracted pectin may enhance the stability of the emulsions.	Food additives (emulsifier, thickener, stabilizer, gelling, and glazing agents) Functional ingredients	[23]
<b>Green solvent's extraction/Hot water extraction</b>					
Red tamarillo skins and seeds	Phenolics Flavonol	Extracted three times with EtOH 95 %, ultrasonic bath for 30 min	The percent recovery of chlorogenic acid and rosmarinic acid were in the range 96–100 % and 100–105 %. Main phenolic: 3-caffeoyl-quinic acid 1724.1 and 1663.4 mg/100 g extract in the skins and seeds. Flavonol: 195.3 mg QE in the skin extract and 180.5 mg QE in the seeds.	Natural antioxidants Functional ingredient Nutraceutical properties	[13,14]
Red tamarillo skins	Dietary fiber	The skins were macerated in EtOH 96 % for three days	8.58 % of the total dietary fiber. Prebiotics with similarity to inulin.	Health foods (prebiotic added)	[25]
Red tamarillo skins and seeds	Polyphenols Anthocyanins Pectin	Polyphenols and anthocyanins: extracted with EtOH 95 % and ultrasonic for 30 min. Pectin: hot distilled water, 2 h, 100 °C and precipitation with absolute ethanol	The antioxidant films were effectively improving their shelf-life and reducing lipid and protein oxidation during 10 days of storage at 4 °C. Films containing polyphenolic extract of the skin showed better barrier properties.	Active biobased films (extend the shelf-life of fish)	[26]
Red tamarillo seeds	Hydrocolloid	Water and 1 % citric acid	It was possible to extract hydrocolloid from seed mucilage, composed of pectin associated with the protein arabinogalactan.	Natural gelling and thickening agents	[24]
<b>High Shear Dispersion (HSD)</b>					
Yellow tamarillo skins	Carotenoids Phenolics acids	Phytochemicals were extracted in extra virgin olive oil. The solid to solvent ratio (1:10). The optimized conditions: 5.50 min, 49 °C, 15.000 rpm	3.81 mg βCE/100 g; Gallic acid (27.59 μg/g), chlorogenic acid (135.49 μg/g), caffeic acid (62.47 μg/g), and p-coumaric acid (16.50 μg/g).	Functional food (physiological action of the carotenoids in Mayonnaise)	[20]



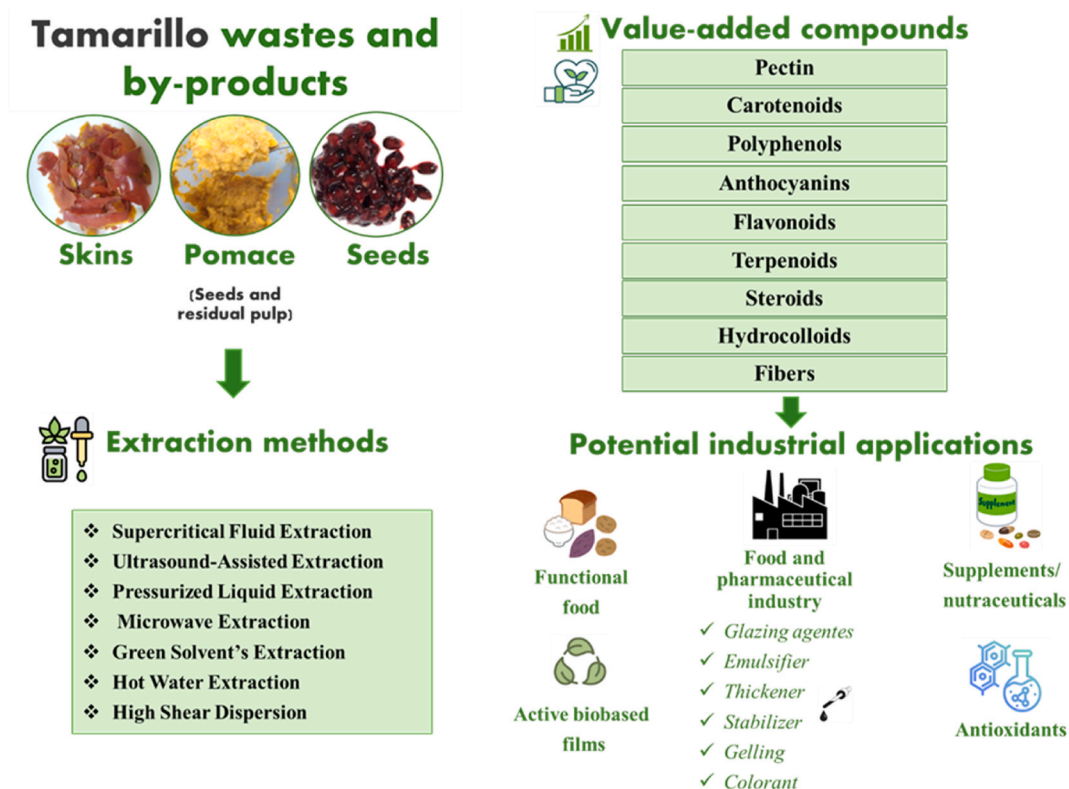


Fig. 4. Extraction of bioactive compounds from tamarillo wastes and by-products and potential applications.

#### 7.4. Antimicrobial activity

Five main active compounds were found in the ethanolic extract of tamarillo skin, including phenolics, flavonoids, alkaloids, tannins, and terpenoids. In addition to these compounds, it contains less saponin, which showed effective inhibition of the growth of *Enterococcus faecalis* [31]. Tamarillo skin extracts have shown great potential for use as natural antibacterial therapies, effectively inhibiting *E. faecalis*, *E. coli*, and *S. enteritidis* [87].

#### 7.5. Anticancer activity

Cancer is defined by abnormal cell growth. Bioactive compounds have been used in herbal medicines to prevent the occurrence of the initiation phase the carcinogenesis process [69].

Oral cancer is a malignant disease, 90 % is squamous cell carcinoma, with its most frequent predilection in the tongue, and the ethanolic extract of tamarillo skins at 5 % has shown *in vitro* efficacy in decreasing the viability of squamous cells of the tongue which can be explained by the presence of phenolic acids, flavonoids [34]. Salfabila and Sudiono 2022 found that a low concentration of tamarillo seed ethanol extract (2  $\mu\text{g}/\mu\text{L}$ ) with a high flavonoid content (275.30 mg/g) had the highest cytotoxicity against tongue cancer cell (human oral squamous carcinoma cell line HSC-3) [35].

The pomace (insoluble fraction) from tamarillo obtained after juice preparation remains in the gastrointestinal tract for a long time and may help in quenching the free radicals that are continuously formed in the intestine and that could be involved in the etiology of degenerative diseases, such as colon cancer, and prevent oxidative stress-induced cell death in HepG2 cells in a dose-dependent manner. Total phenolic compounds and flavonoids showed a better correlation with the free radical scavenging effect than anthocyanins [33].

#### 7.6. Prebiotic

Carbohydrates from agro-industrial by-products, such as fructooligosaccharides (FOS), xylooligosaccharides (XOS), pectic oligosaccharides (POS), arabinoxy-oligosaccharides (AXOS), and isomaltoligosaccharides (IMOS) can confer prebiotic effects and be used as an abundant low-cost ingredient [70].

The pectin associated with the low molecular weight arabinogalactan protein present in the mucilage fraction of tamarillo seed, increase the number of bifidobacteria and lactobacilli, being a fermentable substrate or prebiotic for the intestinal microbiota [24].

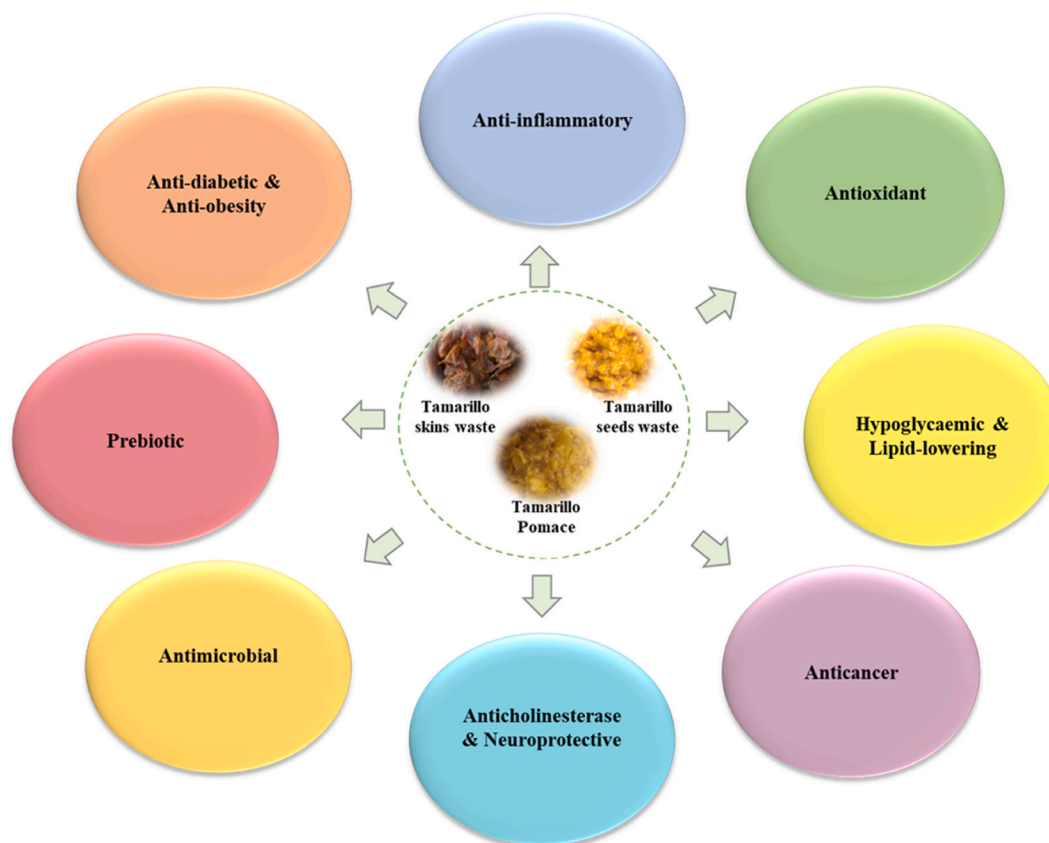


Fig. 5. Biological effects of Tamarillo by-products.

Studies with pectic oligosaccharides from fruit skins have been increasing due to their bioactive properties in the modulation of the intestinal microbiota [71]. Prebiotics is associated with the prevention and remediation of several infections and intestinal disorders, the treatment of diarrhea in children and the elderly, stimulating immunity, increasing the intestinal barrier, remission of intestinal inflammation and Irritable Bowel Syndrome (IBS), in addition to cancer prevention and positive effects on lipid metabolism, mineral adsorption, and immunomodulation [72].

Intake of fiber-rich foods and antioxidant compounds has been widely associated with a decreased risk of several chronic diseases. Dietary fibers promote beneficial effects on human health with increased fecal volume, stimulation of colonic fermentation, reduction of postprandial blood glucose, serum lipid levels, and lowering blood pressure. They are also associated with reducing the risk of cardiovascular diseases, type II diabetes, and some cancers [73]. The tamarillo skin and seeds powder an excellent fiber content and can be used dietary intake [55]. The prebiotic activity is based on the probiotic lactic acid bacteria's performance in the presence of a pathogenic strain, in order to be the dominant flora. Tamarillo skins flour presented a prebiotic activity similar to inulin, hydrocolloids are resistant to digestion in the upper part of the intestinal tract, producing an increase in microbial biomass as a result of fermentation [25].

#### 7.7. Lipid-lowering, anti-diabetic, hypoglycemic, and anti-obesity

54 volunteers consumed tamarillo juice (100g of fruit containing the seeds and mucilage in 150 ml of water) daily for 6 weeks, and there was a perceived reduction in abdominal obesity (67 %–53 %), and total cholesterol, LDL, and glucose concentrations decreased significantly after drinking the juice in all volunteers [37].

Researchers have been looking for alternatives to prevent and treat conditions related to metabolic syndrome (MetS), which is a global health problem. There is a high occurrence of obesity, carbohydrate metabolism disorders, hypertension and atherogenic dyslipidemia that affect 20–30 % of adults worldwide [74].

Phenolic acids and flavonoids present in skins and seeds extracts inhibited enzymes associated with metabolic syndrome, including  $\alpha$ -glucosidase,  $\alpha$ -amylase and lipase, and exhibited antioxidant activity by different mechanisms [13].

Tamarillo skins and seeds extracts were able to inhibit both carbohydrate-hydrolyzing enzymes  $\alpha$ -amylase and  $\alpha$ -glucosidase, inhibit sodium-dependent glucose transporter 1, stimulate insulin secretion, reduce hepatic glucose production and increase insulin-dependent glucose uptake, with flavonoids being the main compound with potential for the treatment of Type 2 Diabetes Mellitus [28].

### 7.8. Neuroprotective activity/against Alzheimer's disease

Around 40 million people over the age of 60 suffer from Alzheimer's disease worldwide, the damage caused by which is the impairment of acetylcholine neurotransmission and the abnormal function of cholinesterases, the enzymes responsible for degrading this neurotransmitter; the extraneuronal deposits of amyloid beta ( $A\beta$ ) fibrils and plaques and.

Intracellular accumulations of neurotoxic  $A\beta$  oligomers; the intracellular hyperphosphorylated tau protein leading to the formation of neurofibrillary tangles (NFTs); and neuronal loss in key brain regions involved in memory and cognition [75].

In vitro studies of tamarillo skin extracts showed metabolites with multi-target (antioxidant, anti-inflammatory and anti-cholinergic) properties against Alzheimer's disease, including hydroxycinnamic acid derivatives and other phenolic acids, as well as quercetin hexoside and rutin [21].

Table 2 indicates some scientific studies on *Solanum betaceum* Cav. wastes and by-products effects on human health.

## 8. Functional ingredients and technological innovations

According to Brazil bakery and confectionery trends 2020 the macro trends is a growth in the functional foods market that promotes opportunities for the incorporation of new ingredients, which can enrich with omega-3, plant sterols, soluble fibers in general, vitamins and antioxidants new formulations [76]. New bioactive substances have been investigated to not only verify the health benefits, but also to provide technological solutions for the incorporation of these substances into processed products.

Active biobased films containing polyphenolic extract of the skin effectively improved their shelf-life and reduced lipid and protein oxidation during 10 days of storage at 4 °C [26].

Maltol present in the skins can be used to enhance oral bioavailability of gallium as well as iron-based drugs, which adds to the potential of using it as a therapeutic adjunct, and the 5-hydroxymethylfurfural can be used as a food additive and flavoring agent in the food industry. Peel volatiles had fruity, caramel, and burnt pineapple-like odors, which are characteristics of furaneol that is the most important aroma compounds in tamarillo similar to tomato [32].

Tamarillo pomace was able to retain a wide range of bioactive compounds and should also be explored as a possible antioxidant ingredient [33].

Studies have shown that extracts of tamarillo, rich in the fruit's species-specific protease, Tamarillin, can be used as a natural clotting agent in milk [77]. Furthermore, preliminary studies of emulsification tests suggest that tamarillo pulp and seed mucilage hydrocolloids can be used as emulsifiers [24]. Still related to the tamarillo polysaccharides, their extracts can be a gelling agent [78]. Finally, studies have observed the ability to extend the shelf life of foods by preventing or delaying lipid oxidation, demonstrating its potential as a natural additive [18,79].

## 9. Conclusion and future prospects

Tamarillo wastes and by-products (stalks, skins, pomace, and seeds) are renewable resources of bioactive compounds and has received substantial interest. These by-products, produced during the pulp processing, contain a rich nutrition composition such as dietary fiber, sugars, a high amount of proteins, low lipids, vitamins A and C, and phytochemicals, such as phenolics, tannins, anthocyanins, flavonoids, terpenoids, and alkaloids.

Overall, there are several findings showing that the bioactivity compounds have been extracted by different techniques, including supercritical fluid, ultrasound-assisted, pressurized liquid, microwave-assisted, high shear dispersion and using a green solvents, such as ethanol and hot water. New ingredients in powder also have been obtained for spray drying, oven or freeze dryer and showed potential physicochemical and technological characteristics are being used in the development of different functional food products. Nevertheless, more other green methods of recovery need to be investigated, such as enzymatic, pulse electric field extraction and use of Natural Deep Eutectic Solvents (NADES) which have low toxicity, are biodegradable and sustainable, as well as more optimized methods.

Phytochemicals extracted from tamarillo waste and by-products, in addition to having a high added value, have demonstrated potential effects on human health, including anti-diabetic and anti-obesity, anti-inflammatory, antioxidant, prebiotic, antimicrobial, anticancer, neuroprotective activity, and others. However, it is noteworthy that due to the different varieties of tamarillo and their by-products, and the chemical structure and biological effects in vivo studies is a key factor for emitted a precise clinical documentation.

Red tamarillo skins have shown excellent characteristics as a biofilm based on polysaccharides and polyphenols as edible coatings to replace non-biodegradable plastics and extend the shelf life of fish [26], encouraging further studies of biofilms from other varieties and matrices such as pomace and stalks, as well as the shelf life of other types of food.

By-products have excellent properties as gelling agents (pectin), coagulants (tamarillin), emulsifiers (hydrocolloids) and natural preservatives/colorants (carotenoids and anthocyanins) [24,77,78], but new technological properties and applications can also be need explored in food, pharmaceutical and cosmeceutical industries.

In this context, tamarillo is still little known and little explored, but this unconventional food plant it is easy to grow and is an excellent option for adding to the food menu, due to its rich nutritional and bioactive compounds with excellent sensory characteristics.

**Table 2**Main functional compounds found in tamarillo (*Solanum betaceum* Cav.) wastes and by-products and their effects on human health.

Wastes/By-products	Functional compounds	Extraction method	Assay type	Potential health benefits/Mechanism of action	References
<b>Anti-diabetic and Anti-obesity</b>					
Skin and seeds	Phenolics acids and flavonoids	Extraction with 70 % EtOH in an ultrasonic bath for 30 min. HPLC-ESI-MS/MS and Gastroduodenal test.	In vitro	Inhibited enzymes associated with metabolic syndrome, including $\alpha$ -glucosidase, $\alpha$ -amylase and lipase, and exhibited antioxidant activity by different mechanisms (SC50 0.80 and 1.38 $\mu$ g/mL EAG).	[13]
<b>Anti-inflammatory</b>					
Skins	Flavonoids, saponins, alkaloids and tannins	70 % EtOH by maceration. ELISA test. Concentration: 12.5 g/ml and 75 g/ml.	In vitro	Inhibition against inflammatory markers such as PGE-2, IL-1 $\beta$ and TNF- $\alpha$ in the LPS-induced macrophage cell line (RAW 264,7).	[27]
<b>Antioxidant</b>					
Skins and seeds	Phenolics	Cold extraction with absolute EtOH, 24 h, UHPLC-MS. Relative Antioxidant Score (RACI) and Global Antioxidant Score (GAS) values. a-Amylase and a-Glucosidase Inhibitory Assays.	In vitro	Active as hypoglycaemic agent with IC50 values of 32.9 g/mL against $\alpha$ -amylase and $\alpha$ -glucosidase.	[28]
Seeds	Phenolics, flavonoids, vitamin C, tannins and anthocyanins	80mg/200gBW/day EtOH extract just before being exposed to cigarette smoke 1 h/day for 21 days. Testosterone levels using the ELISA method and testicular surgery was done for microscopic evaluation and Leydig cell counts.	In vitro/ In vivo	Inhibition of the decrease in the number of Leydig cells and testosterone levels in male Wistar rats exposed to cigarette smoke.	[67]
Juice (Skins and seeds)	Phenolics	40 farmers were given pure tamarillo juice 250 ml/day every day for 2 weeks. Measurement of AChE, malondialdehyde (MDA), and superoxide dismutase (SOD) levels was analyzed by HPLC/Colorimetric methods.	In vivo	Reduction in malondialdehyde, a biomarker of oxidative stress, and an increase in superoxide dismutase and acetylcholinesterase, endogenous antioxidants.	[29]
<b>Prebiotic</b>					
Seeds	Acetate, propionate, and butyrate fatty acids	Extraction of the hydrocolloid with water and 1 % citric. FT-IR and RP-HPLC. Gastrointestinal test.	In vitro	Growth of bifidobacteria and lactobacilli and suppressed some pathogenic bacteria, acting as a fermentable substrate or prebiotics for the gut microbiota.	[24]
Skins	Antioxidant dietary fiber	Extracted by maceration in EtOH 96 % for three days		<i>L. plantarum</i> showed prebiotic activity for as carbon sources. Hydrocolloids were resistant to digestive enzymes and gastrointestinal conditions, indicating that they are available for fermentation by gut microbiota.	[25]
<b>Microbial growth inhibition</b>					
Skins	Phenolics, flavonoids, alkaloids, tannins and terpenoids	Extracted by maceration with absolute for five days. Disk diffusion method.	In vitro	Extract can be an alternative in root canal irrigation to limit the growth of <i>Enterococcus faecalis</i> bacteria (diameter of inhibition zone: 100 % of tamarillo skin extract with sealer was 16.95 $\pm$ 3.39 mm.	[31]
Skins	Phenolics	Extracts in distilled water, acetone, methanol, and ethanol (40, 50, 60, 70, and 80 %), shaken (200 rpm) at 30 °C for 1 h. Disk diffusion method.	In vitro	Inhibition of <i>E. faecalis</i> (60 % and 70 % acetone, DIZs of 10.0 and 9.0 mm), <i>E. coli</i> (70 % and 80 % ethanol, DIZs of 12 and 13.5 mm), and <i>S. enteritidis</i> (80 % methanol, DIZ of 9.0 mm).	[30]
Skins	Volatile (E)-3-Hexen-1-ol	Extracted with MilliQ, n-hexane, ethanol, and methanol. SPME-GC-MS and TD-GC-MS. Disk diffusion method. 36 and 29 % of (E)-3-Hexen-1-ol.	In vitro	Inhibitory effect of water extract on growth of the bacteria tested (Gram-negative and Gram-positive).	[32]
<b>Anticancer</b>					
Skins	Phenolic acids, flavonoids	Extracted by maceration in 70 % EtOH for 72 h. Colorimetric method. Cell Counting Kit-8 (CCK-8) test. Concentration: 5 %	In vitro	Induced tongue squamous cancer cell apoptosis. Effective in reducing the viability of HSC-3.	[34]
Seeds	Phenolics, flavonoids triterpenoids, tannins and alkaloids	Extracted by maceration in 70 % EtOH for 3 days. Colorimetric method. Cell Counting Kit-8 (CCK-8) test. Concentration: 2 $\mu$ g/ $\mu$ L	In vitro	Decrease the viability of HSC-3 cells. High flavonoid content (275.30 mg/g).	[35]
Pomace (Insoluble Fractions) and juice	Phenolics and flavonoids	Washing cycles with EtOH and water, centrifugation, the residual precipitate was lyophilized. Spectrophotometric method.	In vitro	Prevent oxidative stress-induced cell death in HepG2 cells.	[33]

(continued on next page)

Table 2 (continued)

Wastes/By-products	Functional compounds	Extraction method	Assay type	Potential health benefits/Mechanism of action	References
Analysis of H <sub>2</sub> O <sub>2</sub> -Induced HepG2 Cell Death.					
<b>Anticholinesterase</b> Skins	Phenolics, flavonoids, anthocyanins, and carotenoids	80 % methanol or distilled water (1:50) for 2 h, shaker at 200 rpm. Anticholinesterase Inhibition Assay	In vitro	The anti-cholinesterase activity showed a moderate, and strong positive correlation with DPPH, FRAP, and ABTS assays with the values of $r = 0.199$ , $r = 0.445$ , and $r = 0.945$ , respectively.	[36]
<b>Hypoglycaemic</b> Skins and seeds	Flavonoids	Cold extraction with absolute EtOH, 24 h, UHPLC-MS. Relative Antioxidant Score (RACI) and Global Antioxidant Score (GAS) values. $\alpha$ -Amylase and $\alpha$ -Glucosidase Inhibitory Assays	In vitro	Inhibition carbohydrates-hydrolyzing enzymes; Inhibition sodium-dependent glucose transporter 1 (SGLT1); Stimulate insulin secretion; Reduce hepatic glucose output; Enhance insulin-dependent glucose uptake (IC <sub>50</sub> of 32.9 g/mL in the skin extract).	[28]
<b>Lipid-lowering</b> Juice (pulp and seeds)	Phenolics	Juice: mix 100g of peeled fruit in 150 ml of water daily for 6 weeks. Hematological parameters.	In vivo	Total Cholesterol, LDL and glucose concentrations decrease significantly.	[37]
<b>Neuroprotective activity/Against Alzheimer's disease</b>					
Skins	Phenolics Flavonoids Carotenoids	Pressurized liquid extraction EtOH-formic acid 98:2, 60 °C, 1500 psi, 20min. Spectrophotometric and UHPLC-q-TOF-MS/MS. Anti-butyrylcholinesterase enzyme (BChE), reactive oxygen species (ROS), and reactive nitrogen species (RNS) inhibition, cytotoxicity in HK-2, THP-1 monocytes, and SH-5YSY neuroblastoma cell lines.	In vitro	Anti-BChE inhibitory activity IC <sub>50</sub> (85.462 ± 0.68 µg/ml). TPC (92.09 mg GAE/g extract), TFC (4.4 mg QE/g extract), TCC (107.15 mg CE/g extract), antioxidant capacity (ABTS, IC <sub>50</sub> = 6.33 mg/ml extract), LOX (IC <sub>50</sub> = 48.3 mg/ml extract), and AChE (IC <sub>50</sub> = 97.46 mg/ml extract).	[21]

## Ethics statement

The authors state there are no Ethical matters involved in the study, since the study did not enroll human beings and, also, did not deal with animals.

## Data availability statement

The authors confirm that the data supporting the review paper are available within the article, in the cited references and are also available on request from the corresponding author, **Allien Monique Rosa Machado**.

## CRedit authorship contribution statement

**Allien Monique Rosa Machado**: Writing – review & editing, Methodology, Investigation, Conceptualization. **Anderson Junger Teodoro**: Writing – review & editing, Supervision. **Lilian Regina Barros Mariutti**: Writing – review & editing, Supervision. **Juliana Cortes Nunes da Fonseca**: Writing – review & editing, Supervision.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Lilian Regina Barros Mariutti reports a relationship with Cell Press that includes: board membership. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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