Prunus avium L.(Sweet Cherry) By-Products

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Prunus avium L. (sweet cherry) is one of the most appreciated fruit due to its organoleptic and nutritional value. Interestingly, cherry leaves, stems, and flowers are agri-food by-products rich in bioactive compounds that are mostly still unexploited. Stems and leaves have been used in folk medicine since ancient times.

Keywords: L. (sweet cherry) ; by-products ; phenolic compounds ; diabetes ; biological properties

1. Introduction

Many plants have been used as a source of phytochemicals with excellent bioactive properties as well as health-promoting activities. Prunus avium L., commonly known as sweet cherry, is one of the most appreciated red fruits, and it is part of the Mediterranean diet [1]. Furthermore, many scientific reports have shown interesting biological effects [1][2]. The cultivation and consumption of cherries are rising globally, with Turkey, the United States of America, Uzbekistan, and Chile as the main producers [1][3]. According to the Food and Agriculture Organization (FAO) of the United Nations Statistical Database in 2018, the world production of sweet cherries was about 2,923,723 tons [4]. In Portugal, there is a long tradition of cherry cultivation, particularly in the northeast of the country, in the Cova da Beira region (Fundão). In this area, the production of cherries is at around 17,461 tons per year [5][6][7]. Most cherry production is for fresh consumption, although it can also be processed into other products such as juice, jam, marmalade, and toppings. Thus, this fruit production and processing lead to several by-products, which are often discarded.

Nowadays, the valuation of by-products based on the recovery of bioactive phytochemicals from the eliminated plant material has aroused interest, namely because it has high levels of natural antioxidants and/or other constituents with biological properties [8][9][10][11]. In recent years, the identification of phenolic compounds and the evaluation of the biological potential of P. avium by-products have been the subject of a few studies [7][10][12][13][14][15]. Additionally, to avoid agro-wastes, special attention has been paid to their vegetal parts, including stems, leaves, and flowers, also because their infusions are largely used in traditional medicine as diuretics, sedatives, as draining and anti-inflammatory agents, and also to boost the cardiovascular system and improve smooth muscle [12][16][17].

Considering the relevance of sweet cherry stems, leaves, and flowers from a biological and agro-economical point of view, the main purpose of this review is to address the phenolic composition of these agro by-products. Moreover, the biological potential of P. avium by-products regarding antioxidant and anti-hyperglycemic activities are described. The increase of oxidative stress is an important trigger in the development and progression of DM, so the discovery of biological activities in underexplored and valued products is attractive. Furthermore, more recently, scientific reports from our research group and others have started to unveil the remarkable effects of P. avium fruits and their by-products against oxidative stress-related diseases [5][6][7][10]. Additionally, the recovery and valuation of these by-products may be a new strategy for obtaining bioactive compounds, encouraging their incorporation in functional foods, pharmaceutical drugs, dietary supplements, and nutraceuticals, while also contributing to the circular economy.

This review is organized as follows: the second part of the review presents an overview of the origin, production, botanical characteristics, and traditional uses of P. avium . A detailed description of the phenolic composition of cherry leaves, stems, and flowers compared to cherry fruits is presented in part three. The fourth part describes the main in vitro, in vivo, and human studies on the antioxidant and anti-hyperglycemic potential of these P. avium by-products. Finally, part five concludes the paper and presents several guidelines for further research work.

2. Prunus avium L.

There are more than 100 cherry cultivars (e.g., Burlat, Saco, Summit, Sweetheart, Brooks, among others), and can be red- or yellow-fleshed [18]. Most red-fleshed sweet cherries have dark-red flesh, juice, and skin, while the yellow-fleshed sweet cherry varieties may have yellow flesh and skin with clear or yellow flesh, clear juice, and yellow skin [19].

Sweet cherry is very appreciated by consumers due to its bright color, texture, pleasant aroma and taste, and richness in several bioactive constituents [20]. In recent years, the P. avium fruit and its by-products have attracted growing interest from the scientific community because of its nutritional and bioactive composition and the consequent biological properties [5][6][7][10][12][21].

Regarding their by-products, cherry stems are generally green due to their chlorophyll content. The color change in stems is used as an indicator for evaluating the degree of fruit freshness [22]. During the industrial processing of cherries, the stems are removed and discarded, and little attention has been paid to the valuation of these vegetal parts. On other occasions, they are used in traditional medicine for the treatment of urinary infections.

Although cherry blossoms are not used directly in traditional medicine, they may also be of interest as a source of bioactive compounds, and their phytochemical composition deserves to be investigated.

3. Phenolic Compounds of Sweet Cherry By-Products

Phenolic acids are abundant in red fruits and belong to a non-flavonoid group [23][24]. They can be divided into hydroxybenzoic (C 6-C 1) and hydroxycinnamic (C 6-C 3) acids (**Figure 1**) [1][23]. Hydroxybenzoic acids are aromatic compounds composed of simple phenols, including gallic, p-hydroxybenzoic, protocatechuic, vanillic, and syringic acids. In plants, hydroxybenzoics occur mostly in the glycoside form [1]. On the other hand, hydroxycinnamic acids are phenolic acids with a three-carbon side chain. Chlorogenic, caffeic, ferulic, p-coumaric, and sinapic acids are examples of hydroxycinnamics [1].

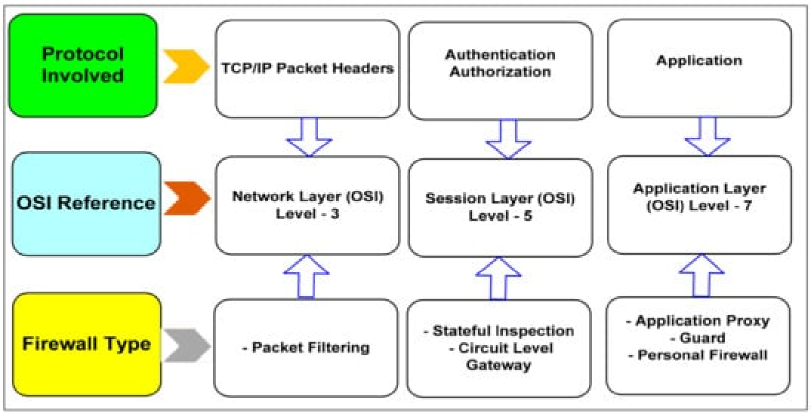

Figure 1. Firewall practice and level of controls according to the OSI reference model.

Regarding the sweet cherry fruit, two hydroxybenzoics have been reported, such as a protocatechuic acid derivative and a protocatechuic acid-glycoside [25]. The first compound was identified for the first time in this study and presented higher amounts (1538.92 µg/g dw) in the Satin cultivar of P. avium [25]. The same research team obtained similar results in previous work with Portuguese sweet cherries [6]. Other hydroxybenzoic acids such as gallic, p-hydroxybenzoic, and 2,5-dihydroxybenzoic acids have also been found in cherries [1].

With regard to the cherry fruit, its hydroxycinnamic composition has also been evaluated and reported in some studies [25][26]. In a study conducted by Martini et al. [26], the total content of hydroxycinnamic acids ranged between 39.75% and 57.67% in six different cultivars of sweet cherry. Cis-3-Coumaroylquinic acid, trans-3-coumaroylquinic acid, cis-3-caffeoylquinic acid, trans-3-caffeoylquinic acid, and trans-5-caffeoylquinic acid were the main phenolic acids found in this study, representing an average of 42.85% of total phenolic compounds [26]. In another study, Gonçalves et al. [25] identified nineteen hydroxycinnamic acids in P. avium fruit extracts, with chlorogenic acids being the most predominant, comprising 66.16% of total non-colored phenolics and 37.13% of total phenolics, followed by caffeoylquinic acids ranging from 32.6% to 57.7% of total phenolics. Caffeoylquinic acid glycosides, p-coumaric acids, and ferulic acids were other phenolic acids identified in this work, but found in minor amounts [25].

In P. avium by-products and cherry fruit, the hydroxycinnamics were the main class of phenolic acids present [5][6][7][10][12][25].

4. Biological Properties of Prunus avium L. By-Products

The biological properties of P. avium stems, leaves, and flowers have been attributed to their phytochemical composition, mostly to their content in phenolic compounds. Several studies on extracts and aqueous infusions from cherry by-products have described many bioactivities such as antioxidant and anti-hyperglycemic activities [1][9][27]. This section will summarize the reports about the therapeutic potential of P. avium by-products in relation to antioxidant and anti-hyperglycemic activities.

In sum, P. avium by-products such as sweet cherries may be a new promising source of phenolic compounds, given that they have already been proven to possess considerable antioxidant activity.

Healthy lifestyle habits such as the practice of physical exercise and eating a balanced diet, and treatment with oral hypoglycemic drugs are the main strategies for DM prevention and control [28]. However, the pharmacological strategy has led to the appearance of adverse effects caused by allopathic drugs. Accordingly, the search for new procedures that control the early stages of hyperglycemia and/or type 2 DM (T2DM) based on safe and effective antidiabetic medicinal plants, including phenolic compounds, has been proposed [28]. The anti-hyperglycemic activity of the P. avium fruits and by-products as well as some of their main compounds were evaluated by different studies described in **Table 1** .

Table 1. Anti-hyperglycemic activity of *Prunus avium* L. fruits and by-products.

Part of Plant/Compounds	Extract	Type of Study	Main Outcomes	References
Stems, leaves and flowers	**Ethanol/Water 1:1 (*v/v*) Aqueous Infusion**	***In vitro***	**Inhibition of α-glucosidase enzyme in a concentration-dependent manner.**	[7]
Fruits	**Ethanol 70%**	***In vitro***	**Inhibition of α-glucosidase enzyme in a concentration-dependent manner.**	[5][6]
Cyanidin-3-rutinoside	**n.a.**	***In vitro***	**Inhibition of α-amilase enzyme in a concentration-dependent manner.**	[29]
Hydroxycinnamic acids, flavonols, and anthocyanins	**Hydroxycinnamic acid-rich fraction Flavonol-rich fraction Anthocyanin-rich fraction**	***In vitro***	**Promotion of cellular glucose consumption by HepG2 cells.**	[30]
Kaempferol and quercetin	**n.a.**	***In vitro***	**↑ Insulin-stimulated glucose uptake in mature 3T3-L1 adipocytes.**	[31]
Rutin, quercetin, kaempferol, genistein	**n.a.**	***In vitro***	**Improved basal glucose uptake in HepG2 cells.**	[32]
Fruits	**Ingestion of 200 mg/kg body weight of cherries**	***In vivo***	**↓ Blood glucose; ↓ Urinary microalbumin; ↑ Creatinine excretion level in urea.**	[33]
Caffeic, ferulic, gallic, and protocatechuic acids	**Gavaged (40 mg/kg body weight)**	***In vivo***	**↓ Hyperglycemia; ↓ Insulin resistance; ↓ Dyslipidemia; ↓ Oxidative stress.**	[34]
Fruit	**Anthocyanin-depleted cherry powder**	***In vivo***	**Protective effects in the liver; Prevent hepatic inflammation in diabetic conditions; ↓ Fasting glucose levels.**	[35]
Caffeic acid	**0.5–3 mg/kg body weight**	***In vivo***	**↓ Plasma glucose level in insulin-resistant rats; ↑ Glucose uptake into the isolated adipocytes in a concentration-dependent manner.**	[36]
Cinnamic acid	**5–10 mg/kg body weight**	***In vivo* and *in vitro***	**↓ Blood glucose levels in a time- and dose-dependent manner; ↑ Glucose tolerance; ↑ Glucose-stimulated insulin secretion in isolated islets.**	[37]

Legend: n.a.—not applicable; ↑—Increase; ↓—Decrease.

According to the studies mentioned above, the anti-hyperglycemic activity of phenolic compounds comprises reducing dietary carbohydrate digestion and consequently intestinal absorption, the modulation of enzymes involved in glucose metabolism, and the improvement of β-cell function and insulin action [28]. Thus, it is essential to identify the molecular mechanisms involved in these processes, develop new therapies to prevent, reverse, or delay the development and progression of DM through the use of bioactive compounds of the P. avium fruit and its by-products.

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