Hippophae rhamnoides/Cassia fistula Extracts

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The work deals with the in vitro evaluations of the pod extracts of C. fistula which are shown to exert better antioxidant and enzymatic properties than those exhibited by the fruit extract of H. rhamnoides.

Keywords: C. fistula ; H. rhamnoides ; Antioxydant ; Phytomedicine ; Antiaging ; Cosmetics

1. Introduction

Antioxidants prevent oxidative damages (e.g., 8-hydroxyguanine, cell membrane lipid peroxidation) and subsequent diseases (e.g., inflammatory state-diseases such as cancers, Alzheimer's, diabetes, and strokes), by effectively quenching or inhibiting free radicals (e.g., hydroxyl and superoxide radicals). For a long time, synthetic antioxidants have been employed as food additives, but safety concerns have restricted their use, due to their possible involvement in chronic diseases. Therefore, much attention has been directed toward the isolation of natural antioxidants from botanical sources, especially edible plants [1][2][3][4][5]. Furthermore, plant extracts that can inhibit specific enzymes (e.g., β-glucuronidase, α-glycosidase, and α-tyrosinase), particularly involved in the alteration of skin during aging, are appreciated for their potential use in original cosmetic formulations.

β-glucuronidase, an acid hydrolase, plays a crucial role in catalyzing the hydrolysis of glucuronide into glycones (i.e., alkyl, acyl, aryl groups) and free glucuronic acid [6][7]. This catalysis releases the terminal glucuronide unit linked through the β-configuration by Carbon 1 (C1) [8]. β-glucuronidase was first discovered in the rumen of sheep, although this enzyme has been recorded as present in all plants, animals, and bacteria so far studied [9]. The research and development (R&D) of specific β-glucuronidase inhibitors (e.g., baicalin) is growing [10], most notably in the fields of drug detoxification [11] and cancer therapy [12], as well as in its ability to overcome glycosaminoglycan (GAG) impaired metabolism during skin aging [13], treat skin conditions such as psoriasis [14] and formulate cosmetics [15].

α-glycosidase comprises a family of hydrolases, which are enzymes located in the brush-border surface membrane of small intestinal cells [16]. α-glycosidase is implicated in the hydrolysis of the 1,4 glycosidic linkage from the non-reducing end of the α-glucosides, α-linked oligosaccharide, and α-glucans substrates, producing α-d-glucose and other monosaccharides that are employed as carbon and energy sources [17][18]. Therefore, α-glucosidase inhibitors are not only considered in the management of type-2 diabetes (T2D) [19], tumorigenesis [20], but also in the prevention of skin aging and skin damages [21][22].

α-tyrosinase is found in plant and animal tissues, and represents a rate-limiting and copper-containing oxidase, involved in controlling melanin synthesis through two distinct chemical reactions [23][24][25]: (i) hydroxylation of a monophenol; and (ii) conversion of an o-diphenol into the corresponding o-quinone, which then undergoes several reactions, eventually forming melanin. In humans, the tyrosinase enzyme is encoded by the TYR gene expressed inside melanosomes [23][25][26]. When a mutation in the TYR gene results in impaired tyrosinase production, it is usually associated with type I oculocutaneous albinism, or increased melanin synthesis in skin cancer (e.g., melanoma) [27][28]. In addition to molecular strategies for controlling the tyrosinase activity [29], several polyphenols (e.g., flavonoids and stilbenoid substrate analogues), free radical scavengers and copper chelators, have been identified as potent tyrosinase inhibitors, capable of preventing skin hyperpigmentation and inducing skin whitening [24][30][31][32][33].

Hippophae rhamnoides L. (*Elaeagnacea*), commonly known as sea-buckthorn, is a flowering, spiny, deciduous shrub, native to fixed dunes and sea cliffs in Europe (e.g., Germany, France) and Asia (e.g., Nepal, India, China). It is both an agricultural and an ornamental plant. Although *H. rhamnoides* is a relatively expensive raw material, its fruits are quite beneficial due to their higher average content of ascorbic acid (*aka* vitamin C), in comparison to lemons and oranges [34]. Consequently, the fruits of *H. rhamnoides* are used in traditional Austrian medicine to fight infections (e.g., flu), in the form of tea, juice, and syrup [35]. *H. rhamnoides* exerts various pharmacological effects, including cytoprotection, protection

against stress, immunomodulation, hepatoprotection, radioprotection, anti-atherogenicity, anti-tumorigenicity, anti-microbial activity, and tissue regeneration [36]. We have recently shown the beneficial effects of *H. rhamnoides* extracts in the prevention of premature aging of human skin and melasma [5][37].

Cassia fistula L. (*Caesalpinaceae*/*Leguminosae*), also known as the golden shower tree, is a famous yellow flowering plant from Asia (e.g., particularly found in the forests of India, Sri Lanka, Thailand and Pakistan), and displays numerous medicinal properties for protecting against skin conditions and inflammatory diseases [37][38][39]. Thereby, we recently demonstrated that *C. fistula*'s extracts are capable of preventing premature skin aging in healthy individuals [39], and melasma in a good number of patients when compared with treatment using a placebo (i.e., without the plant extract) [37]. These beneficial effects are probably due to their relatively rich content of bioactive ingredients (i.e., phenolic compounds, fatty acids, flavonoids, tannins and glycosides) [40][41], and their ability to significantly decrease the tyrosine activity-mediated melanin level.

2. Results

Extracts from *C. fistula* and *H. rhamnoides* are gaining much attention in medicine and esthetics, because of their relative high content of antioxidants (e.g., vitamin C, polyphenols such as flavonoids and saponins, unsaturated fatty acids (UFAs)), known to counteract naturally-occurring or induced molecular and cellular damage-mediated oxidation [5][34][36][37][38][39][40][41][42][43].

Recent investigations led by our research groups have proven that great skin benefits (e.g., slower skin aging; anti-melasma) can be produced when *C. fistula* and *H. rhamnoides* extracts are topically applied [5][37][39].

The phyto-antioxidant arsenal is composed of several chemicals (i.e., free radical scavenging) and enzymatic reactions. Therefore, the specificity and sensitivity of a single method is insufficient for providing an inclusive examination of all phenolic compounds in a given plant extract. A combination of reliable tests is necessary in order to evaluate a complete antioxidant and enzymatic activity profile (i.e., free radical scavenging and key enzymatic inhibition capacities).

Following this original approach, our data provided a better qualitative and quantitative understanding of the anti-oxidant and enzymatic inhibition abilities of *C. fistula* and *H. rhamnoides*, two traditional plant extracts, valuable in modern medicine.

3. Conclusions and Perspectives

Based on our various in vitro assays, which aimed to assess the antioxidant and key enzymatic activities of two major plant extracts used in traditional medicine, our results clearly confirmed that both *H. rhamnoides* and *C. fistula* extracts present potent antioxidant activities. More importantly, it was recorded that *C. fistula*'s pod extracts exert the best antioxidant and enzymatic activities, when compared to those of *H. rhamnoides*' fruit extracts, which are known to contain a very high content of vitamin C (i.e., about 30 times more than orange fruit). Indeed, *C. fistula*'s pods represent the richest polyphenolic part of the plant and exert valuable enzymatic activities for cosmetic use. Overall, our data strongly state that TPC in a given plant extract shall be attributed to particular free radical scavenging or enzymatic activities, exploitable for cosmetics, medical, or food applications. This implicates the use of multiple antioxidant and enzymatic assays in order to select the most valuable plant extract or phyto-ingredient. Ongoing studies from our lab aim to explore *C. fistula*'s pod extracts in cells, animal models, and in humans of any age, including those suffering of chronic inflammatory-state diseases or premature skin aging. We also intend to characterize the safety and efficacy, both in vitro and in vivo, of nanoencapsulated *C. fistula* extracts.

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