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Review

Potential applications of ferulic acid from natural sources

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ABSTRACT

Ferulic acid (FA), a ubiquitous natural phenolic phytochemical present in seeds, leaves, bothin its free form and covalently conjugated to the plant cell wall polysaccharides, glycoproteins,polyamines, lignin and hydroxy fatty acids. FA plays a vital role in providing the rigidity to the cell wall and formation of other important organic compounds like coniferyl alcohol, vanillin, sinapic, diferulic acid and curcumin. FA exhibits wide variety of biological activities such as antioxidant, antiinflammatory, antimicrobial, antiallergic, hepatoprotective, anticarcinogenic, antithrombotic, increase sperm viability, antiviral and vasodilatory actions, metal chelation, modulation of enzyme activity, activation of transcriptional factors, gene expression and signal transduction.

Contents

1. Introduction

First time, ferulic acid (4-hydroxy-3-methoxycinnamic acid, FA) was isolated from *Ferula foetida* for its structure determination, and its name was based on the botanical name of plant [27]. In 1925, FA was chemically synthesized and structurally confirmed by spectroscopic techniques, depicted the presence of an unsaturated side chain in FA, and also existence of both *cis* and *trans* isomeric forms [14,56]. The double bond present in the side chain is subjected to *cis*–*trans* isomerization (Fig. 1), and the resonance stabilized phenoxy radical accounts for its effective antioxidant activity. It catalyzes the stable phenoxy radical formation upon absorption of ultra-violet light, which gives the strength to FA for terminating free radical chain reactions. FA is an enormously copious and almost ubiquitous phytochemical phenolic derivative

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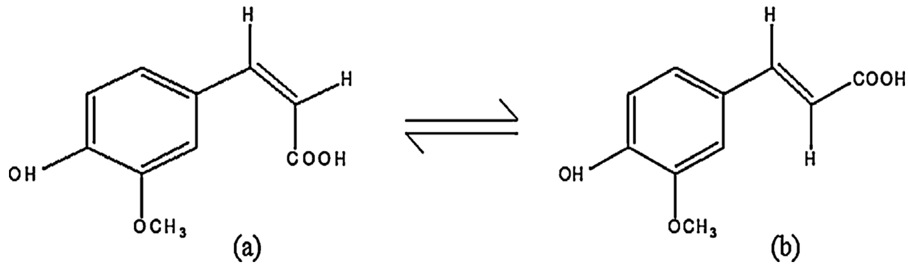

Fig. 1. Schematic representation of two different isomeric forms of ferulic acid found in nature (a) *cis* conformation and (b) *trans* conformation of ferulic acid.

of cinnamic acid, present in plant cell wall components as covalent side chains [66]. Collectively with dihydroferulic acid, it is the component of lignocelluloses, where it confers rigidity to the cell wall by making the crosslink between polysaccharides and lignin. It has been found that FA is linked with a variety of carbohydrates as glycosidic conjugates, different esters and amides with a broad range of natural products [73]. It makes esters by binding with a variety of molecules such as polysaccharides, long chain alcohols, various sterols of plant, tetra-hydroisoquinoline-monoterpene glucoside, a cyanogenetic glycoside and an amino-hydroxy-cyclopentenone, flavonoids and different types of hydroxycarboxylic acids including gluconic, tartaric, malic, hydroxycitric, tartronic, quinic, and hydroxy fatty acids [9,17,24,25].

The aim of this review is to provide the organized outline about natural sources, metabolism, and different applications of FA in biomedical, pharmaceutical, food, cosmetic and other industries, which will provide vast information to a wide range of researchers, working on the different applications of natural products.

2. Ferulic acid: natural sources and isolation

FA is commonly found in commelinid plants (rice, wheat, oats, and pineapple), grasses, grains, vegetables, flowers, fruits, leaves, beans, seeds of coffee, artichoke, peanut and nuts [8,47–49,72,85]. Cell walls (1.4% of dry weight) of cereal grains and a variety of food plants (pineapple, bananas, spinach, and beetroot) contains 0.5–2% extractable amount of FA, mostly in the *trans*-isomeric form, and esterified with the specific polysaccharides [21,22,23,57]. Table 1 summarizes the content of FA in different known sources.

Extraction of FA offers accessible business fortuity, and provides supplementary environmental and economic encouragement for industries as it is used in ingredients of many drugs, functional foods and nutraceuticals. Numerous alkaline, acidic and enzymatic methods for the extraction of FA from different sources have been proposed in literature [3,35,45,46,71,86]. However, optimization of critical parameters for isolation of FA such as time of extraction, pH and temperature is essential for its high yield. Study was conducted with the help of response surface methodology which showed 1.3 fold increases in the production of FA as compared to the unoptimized conventional extraction technique [78]. FA is insoluble in water at room temperature but it is soluble in hot water, ethyl acetate, ethanol and ethyl ether, and it has been found that ethanol (60%) is suitable for the successful extraction of FA [18].

Although, FA is found ubiquitously in the cell wall of woods, grasses, and corn hulls, but it is not effortlessly available from these natural sources as it is covalently linked with a variety of carbohydrates as a glycosidic conjugate, or an ester or amide. Therefore, it can only be released from these natural products by alkaline hydrolysis [78]. Generally, FA obtained from the chemical process cannot be considered as natural, so various attempts have been made for enzymatically release of FA from natural sources. Isolation of FA for commercial production by enzymatic means is a difficult challenge because most of the FA contents in plants are covalently linked with lignin and other biopolymers. Recently, Uraji et al. successfully enhanced the enzymatic production of FA from defatted rice bran, and suggested that the enzymes (α-L-arabinofuranosidase, multiple xylanases, and an acetyl xylan esterase) from *Streptomyces* can also be used for the extraction of FA from other sources viz., raw rice bran, wheat bran and corncob [80]. The TLC separation of crude extracts and visualization by a range of spraying reagents and UV-light offers a quick way for the regular high-throughput detection of FA. Approximately >45% (>2.0%/g dry weight) of total FA content was released during enzymatic treatment of sweet potato stem that had been achieved through the incubation period of 12 h with 1.0% Ultraflo L [51]. Biotransformation studies for the production of FA from eugenol

Table 1
Content of ferulic acid in different known sources.
Source: [91]

Source	Ferulic acid (mg/0.1 kg)
Bamboo shoots	243.6
Water dropwort	7.3–34
Eggplant	7.3–35
Redbeet	25
Burdock	7.3–19
Soyabean	12
Peanut	8.7
Spinach/frozen	7.4
Redcabbages	6.3–6.5
Tomato	0.29–6
Radish	4.6
Broccoli	4.1
Carrot	1.2–2.8
Parsnip	2.2
Mizuna	1.4–1.8
Pot grown basil	1.5
Chinese cabbage	1.4
Pot grown lettuces	0.19–1.4
Green bean/fresh	1.2
Avocado	1.1
Grapefruit	10.7–11.6
Orange	9.2–9.9
Banana	5.4
Berries	0.25–2.7
Rhubarb	2
Plum, dark	1.47
Apples	0.27–0.85
Sugar-beet pulp	800
Popcorn	313
Whole grain rye bread	54
Whole grain oat flakes	25–52
Sweet corn	42
Pickled red beet	39
Rice, brown, long grain parboiled	24
Coffee	9.1–14.3
Boiled spaghetti	13.6
Pasta	12
White wheat bread	8.2