IJPSR (2022), Volume 13, Issue 2 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 05 February 2021; received in revised form, 09 June 2021; accepted, 11 June 2021; published 01 February 2022

FERULIC ACID: A NATURAL ESSENTIAL COMPOUND HAVING POTENTIAL INDUSTRIAL AND MEDICINAL PROPERTIES

Meghna Diarsa and Akshaya Gupte *

Natubhai V. Patel College of Pure and Applied Sciences, Vallabh Vidyanagar - 388120, Gujarat, India.

Keywords:

Ferulic acid, Antioxidant, Shikimate pathway, Pharmacokinetics

Correspondence to Author:
Dr. Akshaya Gupte

Head, Department of Microbiology, Natubhai V. Patel College of Pure and Applied Sciences, Vallabh Vidyanagar - 388120, Gujarat, India.

E-mail: meghnadiarsa19@gmail.com

ABSTRACT: The ubiquitous compound 4-Hydroxy-3-methoxy cinnamic acid, also known as ferulic acid, constitute. A bioactive ingredient of many food that may offer a potential therapeutic effects useful in the treatment of cancer, diabetes, lung and cardiovascular disease. It is also effective against the disorders relative to oxidative stress, including certain neurodegenerative diseases. Ferulic acid is widely distributed in plants in either free or conjugated forms. Overall the pharmaceutical potential of ferulic acid can be attributed to its ability in scavenging free radicals. In recent years, it is also known to inhibit HNG-CoA reductase and activate glucokinase, thus contributing to the reduction of hypercholesterolemia and hyperglycemia. This review discusses the different properties of ferulic acid, establishing a relationship to several biological activities. FA is also used in a substantial amount in the food and cosmetic industries. So also, in recent years, it has been used as a cross-linking agent to manufacture edible food films. The review also discusses compound distribution, metabolism, and physiological role uses in the production of vanillin.

INTRODUCTION: Ferulic acid (FA) is the most important hydroxycinnamic acid found abundantly in plant tissue [1-3]. In the plants, FA is rarely found in the free form. It is mainly found as an ester crosslinked with polysaccharides in the cell wall [4-5]. Ferulic acid was first isolated and purified from the plant *Ferula foetida* in 1866 and was chemically synthesized in 1925 [6-8]. FA is basically a phenylpropanoid and exists as a crystalline solid. FA also play a functional role in the structural integrity of the cell wall as it is associated with cellulose, hemicellulose, and lignin [9, 10]. Polyphenolic acids are secondary metabolites of a varying chemical structures and biological properties.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(2).603-11

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(2).603-11

Naturally, FA is present in various plants and their residues such as corn bran, artichoke, peanut, wheat bran, coffee seeds, rice, oats, eggplant, beets, citrus, spinach, sugar beet, cane bagasse, neem, and pineapple [11]. FA exhibits low toxicity and possesses various bioactive properties such as antioxidant agent, antimicrobial, anti-inflammatory, antihyper-lipidic, anti-carcinogenic, anti-viral, anti-carcino-genic, anti-allergic, antithrombotic, and helpsin lowering cholesterol activity [1, 12-18]. One of the most important properties of FA is its antioxidant nature.

It is easily absorbed into the body and stays in the bloodstream for a longer period of time as compared to any other phenolic compounds. FA is also widely used in the food industry as a preservative because of its antioxidants and antimicrobial actions [19]. It is also used in cosmetic industries, especially in skincare formulations, as a photoprotective agent. It can also be used as a

supplement because it has free radical neutralization properties.

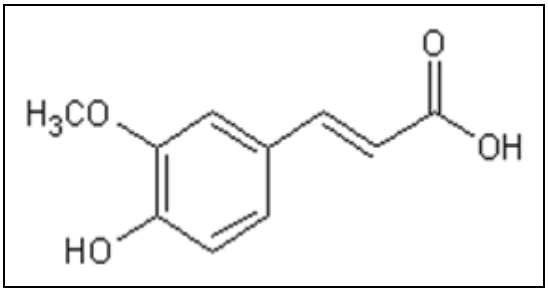
Source of Ferulic Acid: Ferulic acid is one of the important metabolites of lignin biosynthesis from phenylalanine and tyrosine and is ubiquitous in plant [20]. It occurs in plants in two forms: free and conjugated with hydroxyl acid or polysaccharides. Both forms together indicate the total FA. It is usually concentrated in the bran of grains, peel of fruits and roots, and peel of vegetables. The level of FA in various foods is summarized in **Table 1**.

TABLE 1: THE CONTENT OF FERULIC ACID IN DIFFERENT FOOD SOURCES

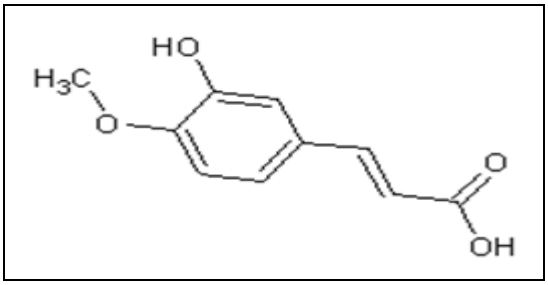
Source	Ferulic acid content (mg/gm %)
Barley extract	1358-2293
Rye bran	280
Corn flour	38
Oat bran	33
Orange	9.2-9.9
Banana	5.4
Apple	0.27-0.85
Eggplant	7.3-35
Soybean	12
Carrot	1.2-2.8
Sugar-beet pulp	800
Coffee	9.1-14.3

In the fruits and vegetables ferulic acid found in conjugated form of hydroxyl acids, or with mono/disaccharides. In root vegetables, FA mainly occur as a dimer and /or esterified with arabinose. FA-Oryzanol is well-known example of sterol esterified ferulic acid, generally found in the grain. The extraction of FA provides environmental and economic encouragement for the production of pharmaceutical drugs, food, and nutraceutical industries. For the extraction of FA, various methods such as alkaline, acidic and enzymatic treatments are used. However, optimization of critical parameters such as time of extraction, pH and temperature are important for obtaining a high yield of ferulic acid. Alkaline treatment is a chemical method that involves hydrolytic cleavage of ester linkages between lignin and plant polysaccharides thereby leading to the release of the phenolic acids. The enzymatic treatment involves feruloyl esterase enzyme (E.C. 3.1.1.73) (FAE), a key enzyme for the extraction of the ferulic acid from the plant cell wall [21-27]. The enzyme acts through delignification and de-polymerization of polysaccharides and is able to hydrolyze the ester linkages between the arabinose sugar and ferulic acid [28-33]. Ferulic acid is insoluble in water at room temperature; however, it is soluble in hot water and solvents like ethyl acetate, ethanol, and ethyl ether, where 30% ethanol is also found to be the most suitable for FA extraction.

Structure and Chemical Properties of FA: Hlasiwetz and Barth in 1866 isolated proto-catechuic acid and resorcinol from a commercial resin of *Ferula foetida* [34]. Simultaneously they also obtained a yellow precipitate on the addition of divalent lead to an alcoholic resin solution. They washed the precipitated lead salt with alcohol, reconstituted the free acid, and determined its composition as $C_{10}H_{10}O_4$ (ferulic acid). In 1925 it was first synthesized chemically by amine catalyzed condensation of vanillin with malonic acid. The two isomers cis- and trans- isomers of FA were separated in 1957. The stereo clarity of ferulic acid was studied by ^{13}CNMR in 1976 and was confirmed by X-ray crystallography analysis in 1988. The compound 3-(4-Hydroxy-3-methoxyphenyl)-2 propenoic acid is commonly known as ferulic acid. It is also known as 3-methoxy-4-hydroxycinnamic acid, caffeic acid 3-methyl ether, and confidence acid. **Fig. 1** represents the structure of Ferulic acid and Isoferulic acid [35].



Ferulic acid



Isoferulic acid

FIG. 1: CHEMICAL STRUCTURE OF FERULIC ACID AND ISOFERULIC ACID

Ferulic acid extracted and isolated from plant exist as the trans- isomer. During the storage of cis and trans ferulic acid in water at room temperature,

slow isomerization results in an equilibrium ratio of 23% cis and 77% trans.

Other Properties of Ferulic Acid: Ferulic acid is a strong dibasic acid. The dissociation of the first proton generates a carboxylate anion whereas the second proton generates a phenolate anion. A high degree of the phenolate anion increases its acidity relative to other phenolic acids. Cis-phenolic acid does not crystallize but forms a yellow oil with a UV maximum at 316 nm in ethanol [36]. Trans-ferulic acid is a colorless substance that possesses orthorhombic needle-like structure and is crystallized in hot water. FA has a molecular weight of 194.18 with a melting point of 170°C [37, 38]. It is soluble in ethanol, ethyl acetate, and hot water and sparingly soluble in benzene and petroleum ether too. Trans-ferulic acid absorbs UV strongly with an absorption maxima at 284 nm and at 307 nm in solution at pH 6.0 exhibits a strong fluorescence. Numerous chromatographic methods are available to determine the quality as well as quantity of ferulic acid. The detection methods include High-pressure liquid chromatography (HPLC), Gas chromatography (GC), Capillary electrophoresis, electrochemical (EC), Thin-layer chromatography (TLC), High-performance thin layer chromato-graphy (HPTLC), and UV spectrometry method, HPLC-MS, Ultra performance liquid chromato-graphy (UPLC) coupled with electrospray ionization [39].

Metabolism and Physiological Function: The principal pathway for the biosynthesis of ferulic acid in the plant is shown in **Fig. 2**. Ferulic acid is formed through the shikimate pathway starting from the two amino acids *i.e.*, L-phenyl amine and L- tyrosine [40]. The two reactions are initiated by the enzyme phenyl amine-lyase and tyrosine ammonia-lyase [41]. These enzymes convert the amino acids to trans-cinnamates and ρ-coumarate, respectively. Furthermore, ρ-coumaric acid gets converted into FA by hydroxylation followed by methylation with methionine acting as a donor of a methyl group which is catalyzed by S-adenosyl l-methionine. The subsequence of oxidation and methylation reactions give rise to other aromatic compounds like di- and tri-hydroxycinnamate derivatives, which can be further employed in the formation of lignin. Oxidative degradation of ferulic acid leads to vanillin and guaiacol. Flavonoids can also be synthesized as a byproduct.

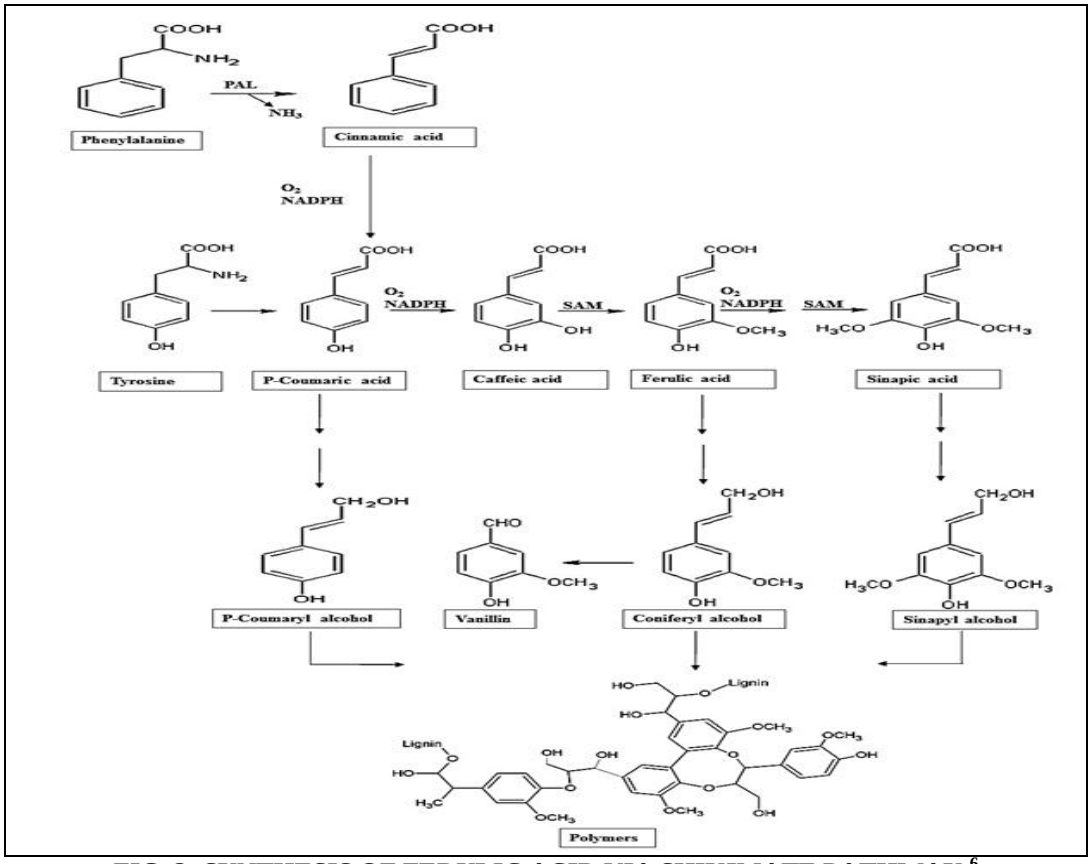


FIG. 2: SYNTHESIS OF FERULIC ACID VIA SHIKIMATE PATHWAY [6]

In-vivo studies in rats have shown that FA can be metabolized to a number of other metabolites such as FA glucuronide, FA-sulfate, FA-sulfoglucuronide, di-hydroferulic acid *etc*. Many researchers reported that major pathway of FA metabolism is in the conjugation with glucuronic acid/ sulfates. The conjugation of FA takes place in the liver by the action of sulfotransferase and UDP glucuronosyl-transferase [42].

FA has various physiological roles such as it crosslinking with vicinal pentosane chain arabin-oxylase, and hemicelluloses in cell walls which increases extensibility during cell elongation. It also acts as a germination inhibitor. FA has capability topromote the reduction in the release of ferritin iron. FA exhibits allelopathic function in the plant by regulation of plant growth via root interaction.

Uses and Potential Application of Ferulic Acid:

Ferulic Acid as an Antioxidant: The human body is affected by the formation of free radicals through endogenous and exogenous factors, which may cause many diseases. These exogenous factors include Ultraviolet light, air pollutions, and cigarette smoke, which may generate free radicals like Superoxide, H_2O_2, O^-_2, $^{\cdot}OH$, and NO[43]. 1990. Superoxide and hydroxyl radicals can also be formed by the endogenous process in the presence of oxygen, adrenaline, flavone nucleotide, thiol compound, and sugars. These oxidative free radicals may affect healthy human cells adversely; thus, it becomes necessary to remove such toxic-free radicals [44]. The human body possesses several enzymes in order to neutralize the above mention free radicals. Enzymes known as superoxide dismutase (SOD), catalase and glutathione peroxidase have an antioxidant activity against free radicals. When there is an elevated level of oxidative stress, some additional antioxidants are also required to nullify oxidative stress. Ferulic acid is a ubiquitous plant constituent, and its antioxidant potential can be attributed to its structural characters. FA contains phenolic nucleus and unsaturated side chain; it is resonance stabilized phenoxy radical which accounts for its potential antioxidant activity [45]. Ferulic acid enhance the expression of the antioxidant enzymes, including superoxide dismutase (SOD) and catalase. Antioxidant mechanism of ferulic acid is a very complex mechanism. **Fig. 3** represents the resonance stability of ferulic acid. It is based on the inhibition of the formation of reactive oxygen spp. on nitrogen as well as it also neutralizes the radicals [46]. The dibasic activity of FA is mainly due to the presence of carboxyl and phenolic hydroxyl groups. FA has a free radical scavenging activity and it also act as an inhibitor of enzyme which is responsible for generation of free radicals [47]. As a secondary antioxidant, ferulic acid is able to bind transition metals such as iron and copper, thus preventing the formation of toxic hydroxyl radical, which leads to cell membrane peroxidation. The structure of ferulic acid reveals a high degree of conjugated unsaturation and it is absorbed strongly in the UV range. Absorption of UV light initiates the formation of phenoxy radicals leading to its cis-trans- isomerization. Strong absorption of U.V light may also contribute to strong antioxidant activity. 3-methoxy 4-hydroxycinnamic acid injected into the human body, utilized and excreted in the urine in as derivatives of phenyl propionic and glycin conjugates *i.e.* 3-methoxy 4-hydroxyphenyl.

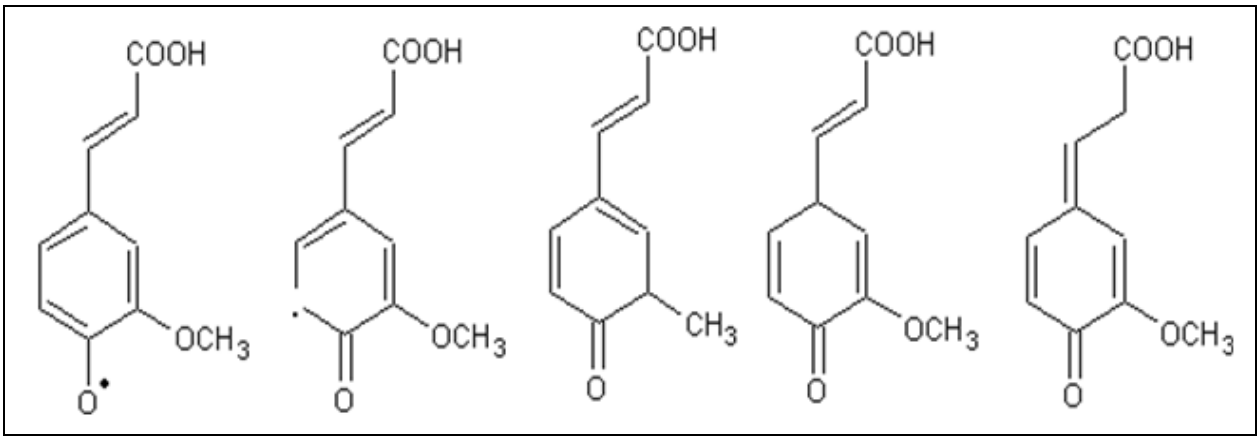


FIG. 3: RESONANCE STABILITY OF FERULIC ACID RADICALS

Anti-diabetic Effect: Diabetes mellitus is a metabolic disease caused due to hyperglycemia and excess production of free radicals, which leads to oxidative stress [48]. Diabetes is defined as an imbalance between the level of prooxidants and antioxidants in the biological system, thereby leading to cellular injury. The formation of free radicals is associated with the most common endocrine disorder. Ferulic acid possesses an antioxidant activity that helps to eliminate noxious streptozotocin agent, which is harmful to the insulin-producing beta cell in the pancreas. It has been reported that the administration of FA reduces blood glucose levels, free fatty acids, and TBARS (Thiobarbituric acid reactive substance) in diabetic rats [49, 50].

Anti-cancer Effect: Cancer is an uncontrolled division of the cells, it is also known as a malignant tumor [43]. Anticancer properties of ferulic acid can be attributed to its antioxidant property to eliminate ROS and to stimulate the activity of antioxidant enzyme. It is known that a high concentration of ROS is produced in cancerous cells. FA has other prooxidant and antioxidant properties, which are considered as an important anticancer and apoptosis mechanism. Certain researchers have suggested that the consumption of grains, fruits and vegetables which have high content of FA help in reducing cancer [51]. FA is a potent component of Chinese medicinal herbs such as *Angelica sinensis, Cimicifaga heracleitolia,* and *Ligustiaum changxiong* [52]. Phytochemicals present in different plants and fruits may cause interference with intracellular signaling pathways. Effect of FA an oral cancer was studied by Mori *et al.,* (1999) [53], after chemically inducing carcinoma in rats where they revealed that the rats with FA administration showed chemo preservative activity against oral cancer. Fang *et al.,* (2016) [54] studied that an innovated hybrid anti-Alzheimer compound *i.e.* Ferulic acid-carbazole, reveal moderate to strong inhibitory action against cholinesterase Azoxymethane induced colon cancer wherein they observed the enzymes glutathione-s-transferase and quinone reductase had high activities in mice treated with FA. Both the enzymes are responsible for the detoxification of liver and colon polyphenols, and FA compromises tumor suppression potential in breast cancer [6, 50, 55-56]. Gao *et al.,* (2018) [22] studied the effect of ferulic acid in the Hela and Caski cells by increasing the concentrations of ferulic acid. They found that a 2.0 mM concentration of phenolic acid inhibits the Hela cell (88%) and Caski cell (85.4%). It also inhibits the migration of the cells by reducing the MMP-9mRNA expression. It also induces protein expression like P53 and P21 and reduces the cyclic D1 and E levels.

Anti-Microbial and Antifungal Effect: Ferulic acid inhibits the growth and reproduction of viruses and bacteria. It shows the effect against various gram-positive, gram-negative organisms along with yeast [57-58]. FA shows a strong inhibitory effect against *Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Citro bacterkoseri, Shigella sonnei, Acinetobacter baumanni* [43, 50, 59]. The antimicrobial activity of FA is related to the inhibition of arylamine N-acetyltransferase, a specific enzyme that catalyzes the acetylation of arylamine in the bacteria. Treatment of ferulic acid also leads to irreversible changes in membrane properties such as hydrophobic changes, surface changes, and pore formation in the cell membranes with consequent leakage of essential intracellular constitutes [60]. FA extended its antifilarial effect through indirect apoptosis and by down regularly and by the attraction of level of some key antioxidants. Ferulic acid also contains antiparasitic properties. Ferulic acid extracted from *Hibiscus mutabilis* (Malvaceae) express microfiralicidal and macro-firalicidal activities in case of microfilaria (L_1) and adult of *Setariacervi.* FA expresses the antifilarial effect in *Setariacervi* through apoptosis, downregulating, and modifying the level of key anti-oxidants such as GSH, GST, and SOD. FA also inhibits the growth of the yeast *Dekkerabru xellensis* [61].

Anti-inflammatory Effect: Acute inflammation is multiple processes which are mediated by activated immune cells. Macrophages play an important role in different immunological phenomenon such as production of pro-inflammatory cytokines and inflammatory mediators (ROS, nitric oxide Posta glands) [62]. The efficiency of some inflammatory mediators like prostaglandin E2, tumor necrosis factor-alpha, and iNOS (inducible nitric oxide synthase) articulate decreases in the presence of 3-methoxy 4-hydroxycinnamic acid and other derivatives [63-64]. Ferulic acid is also used in the anti-inflammatory drug.

Use of FA in Foods and Cosmetics: FA has tremendous applications in the food and cosmetics industries. Ferulic acid has the ability to inhibit the peroxidation of fatty acids. In Japan, ferulic acid used in the preservation of oranges and stabilizes the lard and soybean oil [41]. It also promotes the viscosity and emulsifying properties of food. Another application is, it is widely used in the development of edible films for food and drug packaging. Ferulic acid stabilizes the solution of vitamin C and E, which is used in the skin ointment and sunscreen lotion to doubling the photoprotection of skin (keratinocytes, collagen and fibroblasts) [46]. The researchers revealed that 3-methoxy 4-hydroxycinnamic aid is a competitive inhibitor with tyrosine, which suppresses the formation of melanin [65-66]. The phenolic nucleus and conjugated side chain are present in the structure of ferulic acid, which absorbs the U.V. light and stabilize the phenoxy radicals. It also expresses the defense mechanism against the U.V. rays, bright beams, and photodamage [67].

Bioconversion of Ferulic Acid into Vanillin: Ferulic acid is a precursor of commercially valuable molecules. Vanillin (4-hydroxy 3-methoxybenzaldehyde) is an aromatic flavoring compound is used in the food industries, pharmaceuticals, and other industries. Vanillin forms as an intermediate during the microbial degradation of ferulic acid [6]. Vanillin (75%) is used in the food industries like chocolate and ice cream to give flavor. It is also used for making the good quality of the fragrances [2]. Pharmaceutical industries use vanillin to avoid the unpleasant odor and taste of the medicines [6]. Vanillin is widely used for the production of several drugs such as aldomet, dopamine, papaverine, and L-Dopa and as an antifungal agent [68].

Vanillin was unknown until the vanilla beans found by Cortez in the Aztec kingdom of Montezuma in 1520 [2]. In 1858, Vanillin was isolated from the vanilla pod by the Theodore Nicolas Gobley [50, 68]. Vanilla is a mixture of two different species of vanilla orchids: *Vanilla planifolia* and *Vanilla tahitensis*. **Fig. 4** shows the conversion of ferulic acid into vanillin. The conversion of vanillin from ferulic acid is a two-step process. Feruloyl CoA synthetase and enoyl CoA hydratase/aldolase convert the ferulic acid into vanillin. CoA thioester activates the ferulic acid, which is catalyzed by the *fcs* gene. Ferulyl CoA is hydrated by *ech* gene and cleaved to vanillin and acetyl CoA[4].

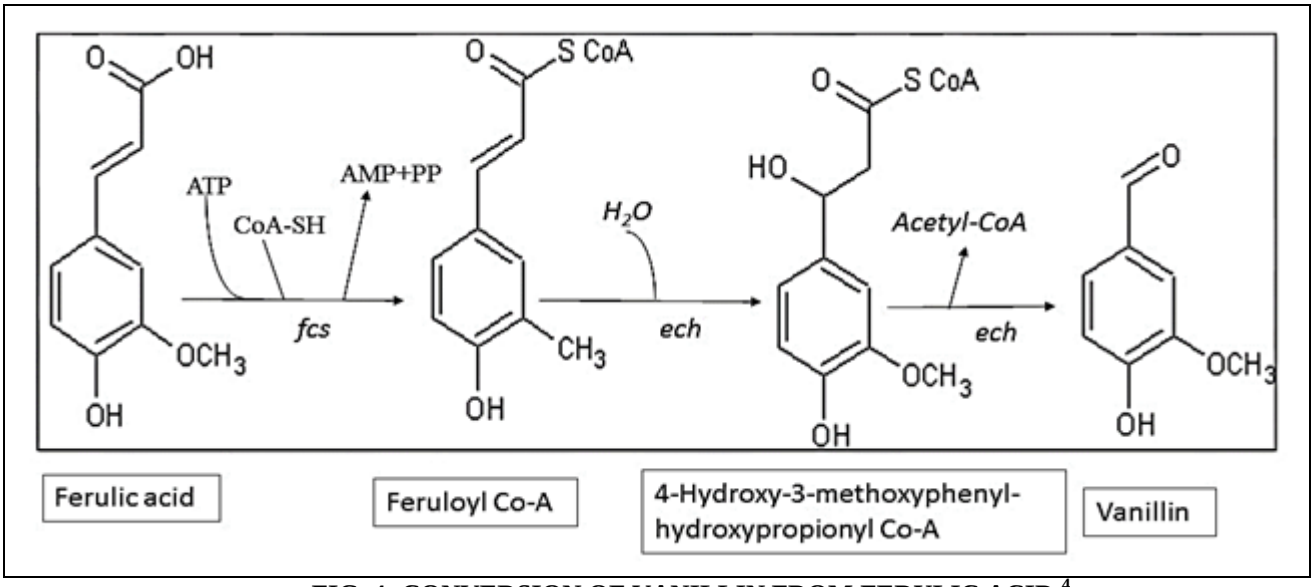


FIG. 4: CONVERSION OF VANILLIN FROM FERULIC ACID [4]

CONCLUSION AND FUTURE PROSPECTS: The present review summarizes the evidence and information on the availability, synthesis, structure, and metabolism of ferulic acid. FA exhibits a wide range of therapeutic properties like antibiotic, antimicrobial, anti-inflammatory and antioxidant properties. The review also explains its use in food and cosmetic industries as well as an alternative for the production of vanillin. FA is still not fully exploited. Additional studies focusing on the application are essential for the development of new drugs. Food supplementation and cosmetic

formulation are strongly encouraged as FA has a strong market of about 55 million dollars by 2025.

ACKNOWLEDGEMENT: Not applicable

CONFLICTS OF INTEREST: Authors declares no conflict of interest

REFERENCES:

1. Wu H, Li H, Xue Y, Luo G, Gan L, Liu J and Mao L: High efficiency co-production of ferulic acid and xylooligosaccharides from wheat bran by recombinant xylanase and feruloyl esterase. Biochemical Engineering Journal 2017; 120: 41-48.
2. Lomascolo A, Stentelaire C, Asther M and Lesage-Meessen L: Basidiomycetes as new biotechnological tools to generate natural aromatic flavours for the food industry. Trends in biotechnology 1999; 17: 282-89.
3. Ma Y, Chen K, Lv L, Wu S and Guo Z: Ferulic acid ameliorates nonalcoholic fatty liver disease and modulates the gut microbiota composition in high-fat diet fed ApoE−/− mice. Biomedicine and Pharmacotherapy 2019; 113108753.
4. Yoon S, Li C, Kim J, Lee S, Yoon J, Seo W and Kim S: Production of vanillin from ferulic acid using recombinant strains of *Escherichia coli* Production of vanillin by metabolically engineered Escherichia coli. Biotechnology Letters 2014; 27: 1829-32.
5. Boz H: Ferulic Acid in Cereals – a Review: Czech Journal of Food Science 2015; 1: 1-7.
6. Kumar N and Pruthi V: Potential applications of ferulic acid from natural sources. Biotechnology Reports 2014; 4: 86-93.
7. Kim JK, Park SU: A recent overview on the biological and pharmacological activities of ferulic acid. EXCLI journal 2019; 18: 32-8.
8. Bento-Silva A, Patto MC and do Rosário Bronze M: Relevance, structure and analysis of ferulic acid in maize cell walls. Food Chemistry 2018; 246: 360-78.
9. Liu S, Bischoff KM, Anderson AM and Rich JO: Novel feruloyl esterase from Lactobacillus fermentum NRRL B-1932 and analysis of the recombinant enzyme produced in *Escherichia coli*. Applied and Environmental Microbiology 2016; 82: 5068-76.
10. Dilokpimol A, Mäkelä MR, Mansouri S, Belova O, Waterstraat M, Bunzel M and Hildén KS: Expanding the feruloyl esterase gene family of Aspergillus niger by characterization of a feruloyl esterase, FaeC. New Biotechnology 2017; 37: 200-09.
11. Zhao Z and Moghadasian MH: Chemistry, natural sources, dietary intake and pharmacokinetic properties of ferulic acid : A review. Food Chemistry 2008; 109: 691-702.
12. Antonopoulou I, Leonov L, Jütten P, Cerullo G, Faraco V, Papadopoulou A and Ralli M: Optimized synthesis of novel prenyl ferulate performed by feruloyl esterases from *Myceliophthora thermophila* in microemulsions. Applied Microbiology and Biotechnology 2017; 101: 3213-26.
13. Ghosh S, Chowdhury S, Sarkar P, Sil PC: Ameliorative role of ferulic acid against diabetes associated oxidative stress induced spleen damage. Food and Chemical Toxicology 2018; 118: 272-86.
14. Wang R, Yang J, Jang JM, Liu J, Zhang Y, Liu L, Yuan H: Efficient ferulic acid and xylo-oligosaccharides production by a novel multi-modular bifunctional xylanase/feruloyl esterase using agricultural residues as substrates. Bioresource Technology 2020; 297: 122487
15. Deng H, Jia P, Jiang J, Bai Y, Fan TP, Zheng X and Cai Y: Expression and characterisation of feruloyl esterases from *Lactobacillus fermentum* JN248 and release of ferulic acid from wheat bran. International Journal of Biological Macromolecules 2019; 138: 272-77.
16. Tian W, Chen G, Gui Y, Zhang G and Li Y: Rapid quantification of total phenolics and ferulic acid in whole wheat using UV–Vis spectrophotometry. Food Control 2021; 123: 107691.
17. Celebioglu A and Uyar T: Development of ferulic acid/cyclodextrin inclusion complex nanofibers for fast-dissolving drug delivery system. International Journal of Pharmaceutics 2020; 584: 119395.
18. Paciello F, Fetoni AR, Mezzogori D, Rolesi R, Di Pino A, Paludetti G, Grassi C, Troiani D: The dual role of curcumin and ferulic acid in counteracting chemo-resistance and cisplatin-induced ototoxicity. Scientific Reports 2020; 10(1): 1-7.
19. Zheng YZ, Zhou Y, Guo R, Fu ZM and Chen DF: Structure-antioxidant activity relationship of ferulic acid derivatives: Effect of ester groups at the end of the carbon side chain. LWT 2020; 120: 108932.
20. Sibhatu HK, Jabasingh SA, Yimam A and Ahmed S: Ferulic acid production from brewery spent grains, an agro-industrial waste. LWT 2021; 135: 110009.
21. Buranov AU and Mazza G: Extraction and purification of ferulic acid from flax shives, wheat and corn bran by alkaline hydrolysis and pressurised solvents. Food Chemistry 2009; 115: 1542-48.
22. Gao, Le, Wang M, Chen S and Zhang D: Biochemical Characterization of a novel feruloyl esterase from *Penicillium Piceum* and its application in biomass bioconversion. Journal of Molecular Catalysis B: Enzymatic 2016; 133: 388-94.
23. Zwane EN, Rose SH, Zyl WH. and Rumbold K: Overexpression of *Aspergillus tubingensis* faeA in protease-deficient *Aspergillus niger* enables ferulic acid production from plant material. Journal of Industrial Microbiology and Biotechnology 2014; 41: 1027-34.
24. Gopalan, Nishant, Nampoothiri KM, Szakacs G, Parameswaran B and Pandey A: Solid-state fermentation for the production of biomass valorizing feruloyl esterase. Biocatalysis and Agricultural Biotechnology 2016; 7: 7-13.
25. Gopalan N and Nampoothiri KM: Biorefining of wheat bran for the purification of ferulic acid. Biocatalysis and Agricultural Biotechnology 2018; 15: 304-10.
26. Alvarado E, Isabel M and Mateos-díaz JC: Type C feruloyl esterase from *Aspergillus ochraceus*: a butanol specific biocatalyst for the synthesis of hydroxycinnamates in a ternary solvent system. Electronic Journal of Biotechnology 2018; 1-9.
27. Xu D, Ding Z, Bai J, Ke W, Zhang Y, Li F and Guo X: Evaluation of the effect of feruloyl esterase-producing Lactobacillus plantarum and cellulase pretreatments on lignocellulosic degradation and cellulose conversion of co-ensiled corn stalk and potato pulp. Bioresource Technology 2020; 310: 123476.
28. Singh S, Nigam VK and Sachan A: Parametric optimization of ferulic acid esterase production from Mucor Hiemalis Ncim837. International Journal of Pharmacy and Pharmaceutical Sciences 2015; 7: 1-4.
29. Faulds, B and Williamson G: The Purification and Characterization of 4-Hydroxy-3-439 Methoxycinnamic (Ferulic) Acid Esterase from *Streptomyces*

olitrochromogenes. Journal of General Microbiology 2017; 1991: 2339-45.
30. Xu, Zhenshang, Wang T and Zhang S: Extracellular Secretion of Feruloyl Esterase 608 Derived from Lactobacillus Crispatus in Escherichia Coli and Its Application for Ferulic Acid Production. Bioresource Technology 2019; 288(72): 121526.
31. Oliveira DM, Mota TR, Salatta FV, de Almeida GH, Olher VG, Oliveira MA, Marchiosi R, Ferrarese-Filho O and Dos Santos WD: Feruloyl esterase activity and its role in regulating the feruloylation of maize cell walls. Plant Physiology and Biochemistry. 2020; 156: 49-54.
32. Fan G, Zhu Y, Fu Z, Sun B, Teng C, Yang R and Li X: Optimization of fermentation conditions for the production of recombinant feruloyl esterase from Burkholderia pyrrocinia B1213. 3 Biotech 2020; 5: 1-5.
33. Mkabayi L, Malgas S, Wilhelmi BS and Pletschke BI: Evaluating Feruloyl Esterase-Xylanase Synergism for Hydroxycinnamic Acid and Xylo-Oligosaccharide Production from Untreated, Hydrothermally Pre-Treated and Dilute-Acid Pre-Treated Corn Cobs. Agronomy 2020; 5: 688.
34. Alam M: Anti-hypertensive effect of cereal antioxidant ferulic acid and its mechanism of action. Frontiers in Nutrition 2019; 6: 121.
35. Umre R, Ganeshpurkar A, Ganeshpurkar A, Pandey S, Pandey V, Shrivastava A and Dubey N: *In vitro, in vivo* and *in silico* antiulcer activity of ferulic acid. Future Journal of Pharmaceutical Sciences 2018; 4(2): 248-53.
36. Peres DD, Sarruf FD, de Oliveira CA, Velasco MV and Baby AR: Ferulic acid photoprotective properties in association with UV filters: Multifunctional sunscreen with improved SPF and UVA-PF. Journal of Photochemistry and Photobiology B: Biology 2018; 185: 46-9.
37. Fang K, He W, Jiang Y, Li K and Li J: Preparation, characterization and physicochemical properties of cassava starch-ferulic acid complexes by mechanical activation. International Journal of Biological Macromolecules. 2020; 160: 482-8.
38. Karunaratne R and Zhu F: Physicochemical interactions of maize starch with ferulic acid. Food Chemistry 2016; 199: 372-9.
39. Hingse SS, Digole SB and Annapure US: Method development for simultaneous detection of ferulic acid and vanillin using high-performance thin layer chromatography. Journal of Analytical Science and Technology 2014; 5: 1-9.
40. De Oliveira Silva E and Batista R: Ferulic acid and naturally occurring compounds bearing a feruloyl moiety: a review on their structures, occurrence, and potential health benefits. Comprehensive Reviews in Food Science and Food Safety 2017; 16: 580-616.
41. Graf E: Antioxidant potential of ferulic acid. Free Radical Biology and Medicine 1992; 13: 435-48.
42. Doss HM, Samarpita S, Ganesan R and Rasool M: Ferulic acid, a dietary polyphenol suppresses osteoclast differentiation and bone erosion via the inhibition of RANKL dependent NF-κB signalling pathway. Life Sciences 2018; 207: 284-95.
43. Toda S, Kimura M and Ohnishi M: Effects of phenolcarboxylic acids on superoxide anion and lipid peroxidation induced by superoxide anion. Planta Medica 1991; 57: 8-10.
44. Ou S and Kwok KC: Ferulic acid: Pharmaceutical functions, preparation and applications in foods. Journal of the Science of Food and Agriculture 2004; 84: 1261-69.
45. Srinivasan M, Sudheer AR and Menon VP: Ferulic acid: therapeutic potential through its antioxidant property. Journal of Clinical Biochemistry and Nutrition 2007; 40: 92-100.
46. Bezerra GSN, Pereira MAV, Ostrosky EA, Barbosa EG, de Moura MDFV, Ferrari M, Aragao CFS and Gomes APB: Compatibility study between ferulic acid and excipients used in cosmetic formulations by TG/DTG, DSC and FTIR. Journal of Thermal Analysis and Calorimetry 2017; 127: 1683-91.
47. Chaudhary A, Jaswal VS, Choudhary S, Sharma A, Beniwal V, Tuli HS and Sharma S: Ferulic Acid: A Promising therapeutic phytochemical and recent patents advances. Recent Patents on Inflammation & Allergy Drug Discovery 2019; 13: 115-23.
48. Mastrocola R, Restivo F, Vercellinatto I, Danni O, Brignardello E, Aragno M, and Bocccuzzi G: Oxidative and nitrosative stress in brain mitochondria of diabitic rate. Journal of Endocrinology 2005; 187: 37-44.
49. Hou T, Zhang L and Yang X: Ferulic acid, a natural polyphenol, protects against osteoporosis by activating SIRT1 and NF-κB in neonatal rats with glucocorticoid-induced osteoporosis. Biomedicine & Pharmacotherapy 2019; 120: 109205.
50. Panwar R, Raghuwanshi N, Srivastava AK, Sharma AK and Pruthi V: *In-vivo* sustained release of nanoencapsulated ferulic acid and its impact in induced diabetes. Materials Science and Engineering: C. 2018; 92: 381-92.
51. Batista R: Uses and potential applications of ferulic acid. Warren, B., Ed 2014; 39-70.
52. Nankar R, Prabhakar PK and Doble M: Hybrid drug combination: Combination of ferulic acid and metformin as anti- diabetic therap. Phytomedicine 2017; 37: 10-13.
53. Mori H, Kawabata K, Yoshimi N, Tanaka T, Murakami T, Okada T and Murai H: Chemopreventive effects of ferulic acid on oral and rice germ on large bowel carcinogenesis. Anticancer Research 1999; 19(5): 3775-80.
54. Fang L, Chen M, Liu Z, Fang X, Gou S and Chen L: Ferulic acid-carbazole hybrid compounds; combinetion of cholinesterase inhibition, antioxidant and neuroprotection as multifunctional anti-Alzheimer agents. Bioorganic and Medicinal Chemistry 2016; 24(4): 886-93.
55. Alazzouni AS, Dkhil MA, Gadelmawla MH, Gabri MS, Farag AH and Hassan BN: Ferulic acid as anticarcinogenic agent against 1, 2-dimethylhydrazine induced colon cancer in rats. Journal of King Saud University-Science 2021; 33(2): 101354.
56. Cheng WJ, Zhang PP, Luo QQ, Deng SM and Jia AQ: The chemosensitizer ferulic acid enhances epirubicin-induced apoptosis in MDA-MB-231 cells. Journal of Functional Foods 2020; 73: 104130.
57. Daglia M: Polyphenols as antimicrobial agents. Current Opinion in Biotechnology 2012; 23: 174-81.
58. Grimaudo MA, Amato G, Carbone C, Diaz-Rodriguez P, Musumeci T, Concheiro A, Alvarez-Lorenzo C and Puglisi G: Micelle-nanogel platform for ferulic acid ocular delivery. International Journal of Pharmaceutics 2020; 576: 118986.
59. Ibitoye OB and Ajiboye TO: Ferulic acid potentiates the antibacterial activity of quinolone-based antibiotics against *Acinetobacter baumannii*. Microbial Pathogenesis 2019; 126: 393-98.
60. Borges A, Ferreira C, Saavedra M J and Simoes M: Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria. Microbial Drug Resistance 2013; 19: 256-65.

61. Harris V, Ford CM, Jiranek V and Grbin PR: Dekkera and Brettanomyces growth and utilisation of hydroxycinnamic acids in synthetic media. Applied Microbiology and Biotechnology 2008; 78: 997-1006.
62. Walsh LJ: Mast cell and oral inflammation. Critical Reviews in Oral Biology and Medicine 2003; 14: 188-98.
63. Tetsuka T, Baier LD and Morrison AR: Antioxidant inhibit interleukin-1 induced cyclooxygenase and nitric oxide synthase expression in rat mesangial cells. Evidence for post transcriptional regulation. Journal of Biological Chemistry 1996; 271: 1168-69.
64. Cho J and Park E: Ferulic acid maintains the self-renewal capacity of embryo stem cells and adipose-derived mesenchymal stem cells in high fat diet-induced obese mice. The Journal of Nutritional Biochemistry 2020; 77: 108327.
65. Oresajo C, Stephens T, Hino PD, Law RM, Yatskayer M, Foltis P, Pillai S and Pinnell SR: Protective effects of a topical antioxidant mixture containing vitamin C, ferulic acid, and phloretin against ultraviolet-induced photo-damage in human skin. Journal of Cosmetic Dermatology 2008; 7: 290-97.
66. Murray JC, Burch JA, Streilein RD, Iannacchione MA, Hall RP and Pinnell SR: A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. Journal of the American Academy of Dermatology 2008; 59: 418-25.
67. Zdunska K, Dana A, Kolodziejczak A and Rotsztejn H: Antioxidant properties of ferulic acid and its possible application. Skin Pharmacology and Physiology 2018; 31: 332-36.
68. Kaur B and Chakraborty D: Biotechnological and molecular approaches for vanillin production: a review. Applied Biochemistry and Biotechnology 2013; 169: 1353-72.

How to cite this article:
Diarsa M and Gupte A: Ferulic acid: a natural essential compound having potential industrial and medicinal properties. Int J Pharm Sci & Res 2022; 13(2): 603-11. doi: 10.13040/IJPSR.0975-8232.13(2).603-11.