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Recent Biological Activity of Ferulic Acid

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ABSTRACT

A common ingredient in fruits, drinks, and food products is 4-hydroxycinnamic acid, which is the source of ferulic acid (FA). Scientific evidence has shown that it has anti-inflammatory, antioxidant, and antimicrobial properties. Its clinical use, for example, is limited to low bioavailability and is therefore only useful in treating neurological illnesses such as Alzheimer's disease, rapid elimination from the gastrointestinal tract after oral treatment, and inadequate translocation across biological barriers, such as the blood-brain barrier (BBB). Consequently, novel nanotechnological strategies are created to control FA's intracellular transit. This review summarizes twenty years of research on FA's biological properties.

KEYWORDS: ferulic acid; antioxidants; neuroprotective action; anticancer.

1. INTRODUCTION

Ferulic acid is usually cross-linked with lignin and polysaccharides to form feruloylated oligosaccharides, a part of plant cell walls; it is rarely seen free. The FA molecule has the structure [(*E*)-3-(4-hydroxy-3-methoxy-phenyl) prop-2-enoic acid)] ($C_{10}H_{10}O_4$), as seen in Fig. 1[1]. FA was extracted from *Ferula foetida*. The plant's botanical name served as the basis for the compound's name [2]. As a phenolic acid, ferulic acid (FA) is found across the kingdom of plants, especially in the Gramineae and Ranunculaceae family umbrellas, wherein plants like Angelica [3].

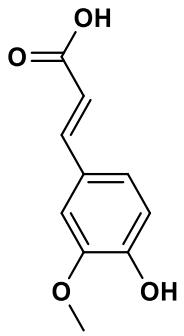

Fig. 1. Ferulic acid's chemical composition.

Among the many natural substances derived from plants are phenolic compounds. Flavonoids and phenolic acids are two examples of antioxidant chemicals that have health-promoting qualities, such as anti-cancer and anti-inflammatory effects [4]. To expand their use

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in medicine, new techniques for their functionalization are being explored [5]. Borage seeds include ferulic acid (FA) and polyphenolic components like quercetin, galanin, and naringenin, among other things. The HT-29 human colon cancer cells exhibit strong antiproliferative activity in response to seed extracts from different species of Borago. Additionally, it is a part of wheat bran and is present in esters that contain sugars such as arabinose. Conversely, it is found in Nitraria sibirica, among other places, as glucosides. Whole-grain barley types were shown to have improved phenolic acid extractability when boiled. Juglans regia, a Persian walnut, also contains free FA, even in the form of esters. Moreover, it is the primary component of foxtail [6].

Additionally, padina tetrachromatic, a marine brown seaweed, was shown to have it. It has the potential to be utilized in the creation of functional foods with antioxidant and antidiabetic properties, as well as in the oleoresin derived from the Curcuma plant, a waste product of the food industry. Furthermore, pectin and propolis made from sugar beet (Beta vulgaris) pulp that is extracted using subcritical water contains FA [7]. Ferulic acid is useful in treating bacterial and viral infections, diabetes, cardiovascular disorders, inflammation, and neurodegenerative diseases from a therapeutic perspective. As a result, it influences the shapes and features of digestive enzymes, including pepsin. It might be important in producing food items with particular medical use [8]. This article's goal is to give a thorough analysis of the biological activity of FA to assess recent developments in therapeutic approaches, with an emphasis on comprehending the underlying mechanisms**.**

2. METHODOLOGY

The search approach was to discover research that explains the underlying biological principles, investigate novel therapy approaches, and evaluate the efficacy of FA treatment modalities. Our FA evaluation included a detailed examination of existing data and a selection of key studies that addressed diverse molecular, clinical, and treatment features. In the context of FA biological activity, a literature search ensures the inclusion of relevant studies while minimizing selection bias. This section describes the search approach used to collect literature on the biological action of FAs.

2.1. Article Selection Process and Selection Criteria

To get the scientific material needed, the search approach involves using numerous electronic databases. The following databases were used: PubMed, Web of Science, Scopus, Cochrane Library, Medline, Google Scholar. The search criteria included ferulic acid, ferulic acid derivatives, anticancer, antioxidant, and inflammatory response. The search results were refined using Boolean operators (AND, OR, NOT) to ensure that all relevant studies were included. The search was limited to items published between 2005 and 2024. The titles and abstracts of the identified publications were evaluated for their relevance to the issue. The whole text of 56 possibly relevant papers was reviewed to ensure that they matched the inclusion criteria. The review comprised 34 articles.

2.2. Inclusion Criteria

- Studies published in peer-reviewed journals;
- Articles in English;
- Research on FA activity;

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- Studies discussing current and emerging treatment strategies;
- Reviews, meta-analyses, research articles, and clinical trials.

2.3. Exclusion Criteria

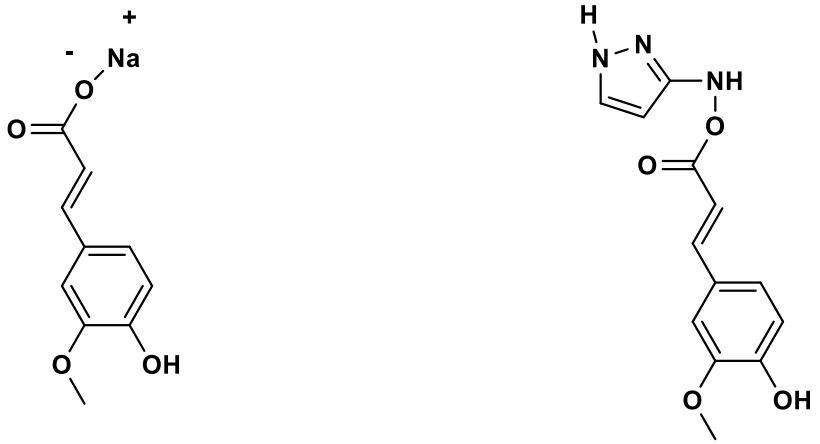
- Non-peer-reviewed articles;
- Studies not focused on biological activity;
- Studies focused on antimicrobial activity
- Articles in languages other than English;
- Publications older than 20 years, unless they were pivotal and landmark works.

2.4. Synthesis of Findings

The extracted data were synthesized to provide a comprehensive overview of the biological activity of FA.

3. THE FA DERIVATIVES

Numerous related investigations on derivatives of FA have been published in recent years. After chemical modification, the derivatives of FA exhibited decreased toxicity, better stability, and comparable or stronger antioxidant activity than ferulic acid. Potassium ferulate was found (SF; 25–200 mg/L) (Fig. 2A) in vitro tests using the sodium salt of FA revealed no toxicity. It can protect human corneal endothelial cells (HCE) from the oxidative damage caused by lidocaine (LD; 2 g/L) [9]. According to Wang *et al.*'s study, (3-(4-hydroxy-3-methoxyphenyl)-N-(1H-pyrazol-3-yl) acrylamide), a novel derivative of FA (Fig. 2B), might lessen cardiac I/R injury by limiting the excessive generation of intracellular ROS and reducing the succinate dehydrogenase (SDH) activity. Use of FA and NCX 2057 [3-((4-hydroxy-3-methoxyphenyl)-2-propenoic acid 4nitrooxy) butyl ester, a new FA derivative that generates NO], respectively, was associated with a lower risk of developing chronic neuritis [9].



(A) (B)

Fig. 2: The derivatives of ferulic acid.

According to Wenk et al., the NO-releasing derivative exhibited a stronger inhibitory effect on the activation of microglia, which may attenuate the pathogenic process linked to AD. Sing et al. developed a variety of FA-o-alkylamine derivatives, which exhibited good inhibitory

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efficacy against butyrylcholinesterase (BuChE). In addition to the strong antioxidant properties, all of them could correct the memory loss caused by scopolamine and exhibited no acute toxicity to mice at dosages of up to 1000 mg/kg [10]. FA and amino acid ethyl ester hydrochloride were used to create four different types of FA derivatives: feruloyl methionine ethyl ester (I), feruloyl isoleucine ethyl ester (II), feruloyl threonine ethyl ester (III), and feruloyl phenylalanine ethyl ester (IV). These compounds scavenged free radicals more quickly than FA monomer derivatives and were less irritating. A group of FA-carbazole hybrid compounds was synthesized and produced by Lei et al. These compounds demonstrated antioxidant activity equivalent to that of FA and outperformed the mixture of FA and carbazole monomer in terms of neuroprotective effect [11].

4. FERULIC ACID NATURAL SOURCES

FA has a high bioavailability; it protects the liver, heart, and nerves, avoids thrombosis, and prevents cancer. It also possesses antibacterial, antifungal, antiviral, antioxidant, and anti-inflammatory properties. Cereals, fruits, vegetables, beans, peanuts, and coffee all contain FA [12]. The data on FA available in numerous published sources is compiled in Table 1.

Table 1: The several sources of FA content [2]

Source	Ferulic acid (mg/0.1kg)
Popcorn	313
Rice	24
Soya bean	12
Grapefruit	10.7-11.6
Orange	9.2-9.9
Coffee	9.1-14.3
Peanut	8.7
White wheat bread	8.2
Spinach	7.4
Red cabbages	6.3-6.5
Banana	5.4
Broccoli	4.1
Carrot	1.2-2.8
Green bean	1.2
Avocado	1.1
Tomato	0.29-6
Apples	0.27-0.85

5. MAIN BIOLOGICAL ACTIVITIES OF FA

5.1. FA as an Antioxidant

The production of reactive oxygen species (ROS) is essential for metabolism and cellular equilibrium. Though oxygen is essential for organism existence, infections and external stimuli cause oxidative stress, which is disturbed in the cell, producing hydroxyl radicals and superoxide anions, two types of free radicals, and hydrogen peroxide. Oxidative stress reduction is crucial because it plays a role in differentiation, proliferation, and the activation of pathways responsible for stress response [13,14]. Alzheimer's illness, cancer, heart disease, and type 2 diabetes are just a few of the diseases that ROS has been shown to hasten the

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advancement of them. To combat free radicals, FA donates hydrogen atoms from the group's phenolic hydroxyl. Strong anti-inflammatory activity of FA was observed in rat paw edema models and other comparable systems. FA's antioxidant properties are due to its resonance stabilization. Furthermore, FA's reactive oxygen species have a scavenging equivalent effect from that of superoxide dismutase [2,13]. Ferulic acid exhibits a complicated antioxidant activity mechanism that primarily involves inhibiting the generation of ROS or nitrogen while also neutralizing (sweeping) free radicals. Additionally, metal ions like Cu(II) or Fe(II) are chelated by this acid. Ferulic acid not only increases the activity of scavenger enzymes and scavenges free radicals but also inhibits the enzymes that create free radicals. Its chemical structure directly affects it [15].

The main mechanisms underlying its antioxidizing abilities include the scavenging of free radicals, the binding of transition metals like iron and copper, and the inhibition of lipid peroxidation. Ferulic acid exhibits antioxidative activity through the formation of stable phenoxyl radicals, which are produced when an antioxidant molecule reacts with a radical molecule. This contributes to the difficulty of starting a complicated chain reaction that produces free radicals. Additionally, this substance can give straight atoms to the radicals in the form of hydrogen. This is especially crucial for preventing unwanted autoxidation activities from affecting the lipid acids that make up cell membranes. Ferulic acids and related compounds can bind transition metals, such as copper and iron, acting as secondary antioxidants. This halts the peroxidation of cell membranes by preventing the formation of dangerous hydroxyl radicals [16]. Moreover, normal physiological activities in humans, like cell respiration, can produce free radicals. Xanthine oxidase and COX-2 are two of the enzymes that catalyze these processes. It has been proposed that blocking this enzyme could stop oxidative stress-related alterations, like photophobia. The literature indicates that FA and its derivatives are highly effective in decreasing the activities of xanthine oxidase and cyclooxygenase. Ferulic acid is consequently thought to lessen the quantity of ROS generated by the enzyme-catalyzed transition [17]. FA's antioxidant properties reduce the harmful effects of lead acetate, a substance found in cosmetics, hair dye, and plant protection products. Ferulic acid can prevent non-alcoholic fatty liver disease (NAFLD) in rats on a high-fat diet by reducing triglyceride and cholesterol levels in the liver. The substance blocks AML-12 hepatocytes from producing reactive oxygen species (ROS) and activating proinflammatory cytokines like IL-6 and IL-1β. It makes sense to produce innovative functional food forms boosted with ferulic acid for metabolic illnesses. The in vivo investigation demonstrated that FA enhances gut microbiota, which in turn enhances heart functioning. Additionally, in ferric-induced pancreatic oxidative damage, it modulates dysregulated redox equilibrium [18,19].

5.2. Angiogenesis Effect

Based on current understanding, ferulic acid is thought to influence the behaviour of the primary factors involved in blood vessel development, specifically platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and hypoxia-inducible factor 1 (HIF-1) [16]. Lin et al. have demonstrated that FA raises the quantity of hypoxia-induced HIF-1, resulting in hypoxia-responsive responses, and encouraging the human umbilical vein endothelium to generate VEGF and PDGF. FA, according to the scientists, is a chemical that effectively stimulates the development of new vasculature, as demonstrated by experiments conducted both in vitro and in vivo [20].

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5.3. Regeneration and Wound Healing Effect

FA has been shown in an investigation involving diabetic rats to hasten wound healing and regeneration. After four days, the percentage of rats with wound contractions who received FA ointment was 27%, compared to just 14% in the group of rats that did not receive it. Rats given FA treatment showed nearly full recovery after 16 days (96%). After 16 days, 83% of the wounds in the control group that used an ointment containing 1% soframycin, a typical treatment for wounds that are difficult to heal, had healed. In comparison to the control group, the FA group experienced a quicker initiation of granulomas and a faster rate of epithelialization [21].

In a related study, Ghaisas et al. found that the skin of diabetic rats given FA showed higher levels of hydroxylysine and hydroxyproline, potential amino acids regarding wound healing and collagen synthesis. This was additional wound shrinking faster and the epithelialization increasing. Furthermore, studies have demonstrated that applying FA ointment throughout the healing process raises glutathione, catalase, and superoxide dismutase (SOD) levels while decreasing lipid peroxidation. The phenomenon, according to the investigators, also considerably quickens the wound's shrinking [22].

5.4. FA Antidiabetic Effect

FA, a common natural product that has minimal side effects, has hypoglycemic effects by inhibiting the malfunctioning of multiple target cells in the treatment of diabetes mellitus (DM). FA can help treat hepatic glucose production disorders caused by insulin resistance by enhancing glucokinase (GK), glutathione peroxidase (GPx), SOD, and catalase (CAT) while lowering glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK) activity. FA lowers diabetes-related β-cell dysfunction and excess free radical formation by neutralizing free radicals, lowering lipid peroxidation, and boosting insulin secretion. It also inhibits excess triglyceride (TG) or free fatty acid (FFA) production [23]. Furthermore, FA has a variety of consequences on the complications of DM. FA improves diabetic nephropathy (DN) by elevating the activity of SOD, CAT, and GPx, reduces diabetic neuropathy (DPN) by reducing the inflammatory response, reduces diabetic hypertension (DHP) by promoting NO production, controls diabetic retinopathy (DR) by inhibiting the activation of glycation end products (AGE) receptors and the protein kinase B (Akt) signaling pathway, promotes angiogenesis during wound healing, and treats diabetic cardiomyopathy (DCM) by suppressing ROS production [24].

The NF-κB signaling pathway, which is regulated by FA administration, has a role in the pathophysiology of diabetic complications such as DN, DPN, and DHP. It also regulates the inflammatory response of β-cells, which contributes to β-cell death. Similarly, the phosphoinositide-3 kinase (PI3K)/Akt (PI3K/Akt) pathway is recognized to be a significant effector of insulin metabolism, playing a key role in the development of DN and DCM. FA may play a role in managing DM and its complications through the nuclear factor kappa-B (NF-κB) and PI3K/Akt pathways [23]. Daryagasht et al. reported that liver function and histological examinations indicated that FA protected liver architecture in the sodium arsenite (SA)-treated groups. Furthermore, FA improved antioxidant defense while decreasing lipid peroxidation and tumor necrosis factor-alpha levels in SA-treated animals. FA at 30 and 100 mg/kg reduced SA-induced decreases in peroxisome proliferator-activated receptors (PPAR-

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γ) and glucose transporter 2 (GLUT2) protein expression in mice's liver. In conclusion, FA protected SA-induced glucose intolerance and hepatotoxicity by lowering oxidative stress, inflammation, and hepatic upregulation of PPAR-γ and GLUT2 proteins [25].

5.5. FA Hepatoprotective Effect

Recent research indicated that the CIS-intoxicated group showed increased oxidative stress, a significant reduction in anti-oxidative responses, and a large rise in serum aminotransferase activity. COX-2 and IL-1β transcript levels, as well as caspase-3 enzyme activity, increased, whereas NF-gB-p65 and caspase-1 transcript levels decreased, indicating an overall inflammatory tendency and an increase in apoptotic shift. Co-administration of FA and/or therapy with LDR has reduced the hepatotoxic effect of CIS. Histopathological examination of liver tissues indicated that these adjuvant therapies reduce CIS toxicity. To summarize, it is plausible to infer that the hepatoprotective effects of co-administration of FA and/or LDR against CIS-induced hepatotoxicity are attributable to the possession of anti-apoptosis, anti-oxidative, and anti-inflammatory potency [26].

5.6. FA Antiapoptotic Effect

Nakayama et al. demonstrated that FA is a chemical that suppresses apoptosis produced by hydrogen peroxide (H2O2) or actinomycin D (ActD) in rat pheochromocytoma PC12 cells. We also discovered that FA inhibits H2O2-induced reactive oxygen species (ROS) generation in PC12 cells, acting as an antioxidant. We then used antibody arrays for phosphokinase and apoptosis-related proteins to investigate FA-mediated signaling responses in rat pheochromocytoma, PC12 cells. In PC12 cells, the FA signaling pathway includes the deactivation of pro-apoptotic proteins SMAC/Diablo and Bad. Furthermore, FA reduces H2O2-induced cell damage by inhibiting ERK phosphorylation. Importantly, we discovered that FA restored the production of brain-derived neurotrophic factor (BDNF), a major neuroprotective effector, in H2O2-treated PC12. FA may boost BDNF by modulating the expression of microRNA-10b in response to H2O2 stimulation. Taken together, FA has wide biological effects as a neuroprotective modulator in PC12 cells, regulating the expression of phosphokinases, apoptosis-related proteins, and microRNAs in response to oxidative stress [27].

5.7. Ferulic Acid as an Anticancer Agent

Free radicals have an important role in carcinogenesis. Antioxidants found in food are thought to be possible blockers of free radicals, which stop cells from growing. FA's anti-carcinogenic activity is associated with its capacity to scavenge ROS and activate cytoprotective enzymes. FA reduced lipid peroxidation, DNA single-strand break, protein deactivation, and biological membrane damage [2,28].

FA also has strong antioxidant properties against free radicals because it has lost an atom of hydrogen from its phenolic hydroxyl group [13]. FA's capacity to activate cytoprotective enzymes against ROS is what gives it its anticancer effect [28]. Earlier in vitro and in vivo experimental models have demonstrated that FA can control cellular development and expansion in addition to lowering cytotoxicity by scavenging free radicals, underscoring the role of FA in cancer treatment [29]. Another pathway for FA's anticarcinogenic impact appears to be the activation of detoxifying enzymes; it dramatically increases the activity of

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UDP-glucuronosyltransferases (UGTs) in the liver. As a result, there is higher detoxification of carcinogenic chemicals, which contributes to intestinal prevention and treatment of cancer. [2]. FA also prevents CRC cells from growing. Furthermore, an in vivo test conducted on rats verified that it impeded the growth of colon cancer. In breast cancer cell lines, polyphenols, notably FA, have been found to exhibit tumour-suppressive characteristics. Boosting the body's natural defenses against cancer chemo and radiotherapy is said to decrease their detrimental effects.[2,13,30].

The medicinal potential of FA-enhanced cell replication, apoptosis resistance, reduced DNA and cell proteins-induced damage by free radicals, and unique stimulation of proinflammatory pathways such as cyclooxygenases (COX) and nitric oxide synthase (NOS) all contribute to the pathogenesis of cancer. Each one of these occurrences contributes to carcinogenesis in and of itself, but it also amplifies the dangers of the others, hastening their progression as a result [31]. FA may play a role in cancer treatment as an adjuvant agent due to its capacity to control cell proliferation and development, scavenge free radicals, promote cell protection enzymes, and minimize cytotoxic reactions in experimental conditions [29].

Antitumor action on Caco-2 colon cancer cells over 24 hours was achieved by increasing the expression of multiple genes for centrosome assembly proteins (RABGAP1 and CEP2), as well as the gene for the S phase checkpoint protein, and downregulating CCNB1, CCNA2, ODC1, and MYC expression levels. These selective effects interrupted cell cycle progression in the S-phase. [32].Lung cancer is caused by the creation of free radicals in a range of cell types, including leucocytes, as a result of nicotine. Lactic dehydrogenase and alkaline phosphatase, two plasma markers of cellular damage, were decreased in nicotine-treated rats when FA (10–40 mg/kg orally administered for 22 weeks) was given to them.[29]. An additional target for the anticancer action of FA drugs is COX, which has two major isoforms, COX-1 and COX-2, which are both obligatory and inducible. For example, COX-2 is elevated in several malignancies, and NSAIDs that inhibit COX activities have been potential anticancer medicines.[29,33]. Using FA as an additive to radiotherapy or chemotherapy has been suggested by preclinical studies. FA increased the cytotoxicity of 5-fluorouracil and platinum-based therapies in HeLa and K562 cell lines (carboplatin and cisplatin) [34].

Additionally, FA alone (1–40 mg/ml) or in conjunction with 2-deoxy-glucose accelerated the radiation-induced death of HeLa and large-cell lung carcinoma NCI-H460 cells. This was a complex process, including changes in the stress response and the expression of pro-apoptotic pathways such as those associated with caspase-3, Bax, p21m p53, nuclear factor-kB (NF-kB), and Bax [35]. Squamous cell carcinoma as well as dysplasia in the mouth were reduced by 32 weeks in rats fed on FA (500 mg/kg feed) after seven weeks [29]. Alazzouni et al. assessed the potential effect of FA in the treatment of colon cancer; they reported a significant improvement proved by histopathological examination, immunostaining and gene expression. Rats in the colon cancer group exhibited a considerable intensity decrease ($p < 0.01$) of P53 and Caspase 3 immune reactivity compared to the control group, while there was a substantial rise ($p < 0.01$) in Ki67 and CK20 immune staining. These findings were based on quantitative measurements of positive responses to these markers. In 1,2-dimethylhydrazine-induced colon cancer, FA was able to considerably ($p < 0.01$) enhance the change in immunostaining [36]. Gadelmawla et al. assessed the potential effect of the combination of 5-fluorouracil and FA in colorectal cancer therapy. In comparison to the control

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group, the 1,2-dimethylhydrazine-induced colon cancer group showed a notable increase in Ki67 expression (p 0.01) and a notable decrease in Caspase-3 and P53 expression (p 0.007). The combined FA-5FU group showed a substantial rise in P53 and Caspase-3 (p 0.003 and p 0.01, respectively) in comparison to the colon cancer caused by DMH [37].

A recent investigation assumed that their findings revealed that while lipidic and polymeric nanocapsules (NCs) had similar beneficial qualities, the latter had a higher cumulative percentage released of FA and were smaller in size. With both cell lines, the lipidic nanocapsules outperformed the medication in terms of anticancer activity; apoptosis was the predominant mode of cell death. The in vivo investigation shows FA lipid NCs show notable anti-inflammatory and antioxidant properties. Additionally, they regulated the apoptotic/anti-apoptotic gene BAX/Bcl-2 and reduced IGF II, cyclin D1, and VEGF, demonstrating their potential to be both apoptotic and anti-angiogenic. The histological analysis supported this conclusion [38].

Esmat et al. reported that the hepatotoxic effect of cisplatin (CIS) has been lessened by the co-management of FA and/or treatment with low-dose γ-irradiation (LDR). The analysis of the liver tissues supported this adjuvant therapy's ameliorative effect against CIS toxicity. It is conceivable to propose that the anti-inflammatory, anti-oxidative, and anti-apoptotic properties of FA and/or LDR are responsible for the hepatoprotective benefits of combined administration against CIS-induced liver damage [26]. FA has a potent antioxidant effect on free radicals by removing a hydrogen atom from the phenolic hydroxyl group [13]. FA's capacity to activate cytoprotective enzymes against ROS is the source of its anticancer action [28]. Previous investigations have demonstrated that FA can control cellular growth and proliferation in addition to the fact that it can lower cytotoxicity by scavenging free radicals, underscoring the role of FA in cancer therapy [29].

6. CONCLUSIONS

The review gives brief details about the structure, derivatives, natural sources, and biological activity of FA. Due to conjugation in its side chain and nucleus, FA has a strong antioxidant capability, which is responsible for the majority of its biological activity. These studies provide strong evidence that consuming FA regularly can significantly lower the chance of certain diseases linked to oxidative stress, including cancer.

CONFLICT OF INTEREST

The authors declare no competing interests.

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REFERENCES

[1] Shi Y, Shi L, Liu Q, Wang W, Liu Y. Molecular mechanism and research progress on pharmacology of ferulic acid in liver diseases. Front Pharmacol. 2023;14:1207999.
[2] Kumar N, Pruthi V. Potential applications of ferulic acid from natural sources. Biotechnology Reports. 2014;4:86–93.

Online ISSN: 3009-7800
Print ISSN: 3009-6324

[3] Wu H, Huang Q, Chao S, Yu J, Xu S, Wang F, et al. Determination of Ferulic Acid in Angelica sinensis by Temperature-Controlled Hydrophobic Ionic Liquids-Based Ultrasound/Heating-Assisted Extraction Coupled with High Performance Liquid Chromatography. Molecules [Internet]. 2020 [cited 2024 May 18];25:3356. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7436256/
[4] Panek-Krzyśko A, Stompor-Gorący M. The pro-health benefits of morusin administration—An update review. Nutrients. 2021;13:3043.
[5] Stompor M, Świtalska M, Wietrzyk J. The influence of a single and double biotinylation of xanthohumol on its anticancer activity. Acta Biochimica Polonica. 2019;66:559–65.
[6] [6] Zhang M, Xu Y, Xiang J, Zheng B, Yuan Y, Luo D, et al. Comparative evaluation on phenolic profiles, antioxidant properties and α-glucosidase inhibitory effects of different milling fractions of foxtail millet. Journal of Cereal Science. 2021;99:103217.
[7] Özkök A, Keskin M, Tanuğur Samancı AE, Yorulmaz Önder E, Takma Ç. Determination of antioxidant activity and phenolic compounds for basic standardization of Turkish propolis. Applied Biological Chemistry. 2021;64:1–10.
[8] Zhu S, Bai X, Zhu J, Li W, Wang B. Multi-spectral techniques and molecular docking to investigation of the interaction between ferulic acid and pepsin. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2021;251:119442.
[9] Wang F, Peng Q, Liu J, Alolga RN, Zhou W. A novel ferulic acid derivative attenuates myocardial cell hypoxia reoxygenation injury through a succinate dehydrogenase dependent antioxidant mechanism. European Journal of Pharmacology. 2019;856:172417.
[10] He S, Guo Y, Zhao J, Xu X, Song J, Wang N, et al. Ferulic acid protects against heat stress-induced intestinal epithelial barrier dysfunction in IEC-6 cells via the PI3K/Akt-mediated Nrf2/HO-1 signaling pathway. International Journal of Hyperthermia. 2018;35:112–21.
[11] Fang L, Chen M, Liu Z, Fang X, Gou S, Chen L. Ferulic acid–carbazole hybrid compounds: combination of cholinesterase inhibition, antioxidant and neuroprotection as multifunctional anti-Alzheimer agents. Bioorganic & Medicinal Chemistry. 2016;24:886–93.
[12] 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.
[13] Palani Swamy S kumaran, Govindaswamy V. Therapeutical properties of ferulic acid and bioavailability enhancement through feruloyl esterase. Journal of Functional Foods. 2015;17:657–66.
[14] Abdel-Wahhab KG, Ashry M, Hassan LK, Gadelmawla MHA, Elqattan GM, El-Fakharany EM, et al. Nano-chitosan/bovine lactoperoxidase and lactoferrin formulation modulates the hepatic deterioration induced by 7,12-dimethylbenz[a]anthracene. Comp Clin Pathol. 2023;32:981–91.
[15] Moldovan M, Lahmar A, Bogdan C, Părăuan S, Tomuţă I, Crişan M. Formulation and evaluation of a water-in-oil cream containing herbal active ingredients and ferulic acid. Clujul Med. 2017;90:212–9.
[16] Zduńska K, Dana A, Kolodziejczak A, Rotsztejn H. Antioxidant Properties of Ferulic Acid and Its Possible Application. Skin Pharmacol Physiol. 2018;31:332–6.

Online ISSN: 3009-7800
Print ISSN: 3009-6324

[17] Nile SH, Ko EY, Kim DH, Keum Y-S. Screening of ferulic acid related compounds as inhibitors of xanthine oxidase and cyclooxygenase-2 with anti-inflammatory activity. Revista Brasileira de Farmacognosia. 2016;26:50–5.
[18] Liu Z, Ma Z, Zhang H, Summah BS, Liu H, An D, et al. Ferulic acid increases intestinal Lactobacillus and improves cardiac function in TAC mice. Biomedicine & Pharmacotherapy. 2019;120:109482.
[19] Salau VF, Erukainure OL, Koorbanally NA, Islam MS. Ferulic acid promotes muscle glucose uptake and modulate dysregulated redox balance and metabolic pathways in ferric-induced pancreatic oxidative injury. Journal of food biochemistry. 2022;46:e13641.
[20] Lin C-M, Chiu J-H, Wu I-H, Wang B-W, Pan C-M, Chen Y-H. Ferulic acid augments angiogenesis via VEGF, PDGF and HIF-1 alpha. J Nutr Biochem. 2010;21:627–33.
[21] Dwivedi S, Singh D, Deshmukh P, Soni R, Trivedi R. Healing Potential of Ferulic Acid on Dermal Wound in Diabetic Animals [Internet]. 2015 [cited 2022 Aug 3]. Available from: https://www.semanticscholar.org/paper/Healing-Potential-of-Ferulic-Acid-on-Dermal-Wound-Dwivedi-Singh/18b6111a3d306bfd15474bd22e6e4367e89df796
[22] Ghaisas MM, Kshirsagar SB, Sahane RS. Evaluation of wound healing activity of ferulic acid in diabetic rats. Int Wound J. 2014;11:523–32.
[23] Li X, Wu J, Xu F, Chu C, Li X, Shi X, et al. Use of Ferulic Acid in the Management of Diabetes Mellitus and Its Complications. Molecules. 2022;27:6010.
[24] Dhaliwal J, Dhaliwal N, Akhtar A, Kuhad A, Chopra K. Beneficial effects of ferulic acid alone and in combination with insulin in streptozotocin induced diabetic neuropathy in Sprague Dawley rats. Life Sci. 2020;255:117856.
[25] Daryagasht M, Moosavi M, Khorsandi L, Azadnasab R, Khodayar MJ. Hepatoprotective and anti-hyperglycemic effects of ferulic acid in arsenic-exposed mice. Food and Chemical Toxicology. 2023;178:113924.
[26] Esmat MA, Osman A, Hassan RE, Hagag SA, El-Maghraby TK. Hepatoprotective effect of ferulic acid and/or low doses of γ-irradiation against cisplatin-induced liver injury in rats. Hum Exp Toxicol. 2022;41:9603271221136205.
[27] Nakayama H, Nakahara M, Matsugi E, Soda M, Hattori T, Hara K, et al. Protective Effect of Ferulic Acid against Hydrogen Peroxide Induced Apoptosis in PC12 Cells. Molecules. 2021;26:90.
[28] Barone E, Calabrese V, Mancuso C. Ferulic acid and its therapeutic potential as a hormetin for age-related diseases. Biogerontology. 2009;10:97–108.
[29] Mancuso C, Santangelo R. Ferulic acid: Pharmacological and toxicological aspects. Food and Chemical Toxicology. 2014;65:185–95.
[30] Jose Merlin JP, Venkadesh B, Hussain R, Rajan SS. Biochemical estimations of multidrug resistance (ferulic acid and paclitaxel) in non-small cells lung carcinoma cells in vitro. Biomedicine & Aging Pathology. 2013;3:47–50.
[31] Kundu J, Surh Y. Inflammation: Gearing the journey to cancer. Mutation Research/Reviews in Mutation Research. 2008;659:15–30.
[32] Janicke B, Hegardt C, Krogh M, Önning G, Åkesson B, Cirenajwis HM, et al. The Antiproliferative Effect of Dietary Fiber Phenolic Compounds Ferulic Acid and p -Coumaric Acid on the Cell Cycle of Caco-2 Cells. Nutrition and Cancer. 2011;63:611–22.

Online ISSN: 3009-7800
Print ISSN: 3009-6324

[33] Cuzick J, Otto F, Baron JA, Brown PH, Burn J, Greenwald P, et al. Aspirin and non-steroidal anti-inflammatory drugs for cancer prevention: an international consensus statement. The Lancet Oncology. 2009;10:501–7.
[34] Hemaiswarya S, Doble M. Combination of phenylpropanoids with 5-fluorouracil as anti-cancer agents against human cervical cancer (HeLa) cell line. Phytomedicine. 2013;20:151–8.
[35] Bandugula VR, N. RP. 2-Deoxy-d-glucose and ferulic acid modulates radiation response signaling in non-small cell lung cancer cells. Tumor Biol. 2013;34:251–9.
[36] Alazzouni AS, Dkhil MA, Gadelmawla MH, Gabri MS, Farag AH, Hassan BN. Ferulic acid as anticarcinogenic agent against 1, 2-dimethylhydrazine induced colon cancer in rats. Journal of King Saud University-Science. 2021;33:101354.
[37] Gadelmawla MHA, Alazzouni AS, Farag AH, Gabri MS, Hassan BN. Enhanced effects of ferulic acid against the harmful side effects of chemotherapy in colon cancer: docking and in vivo study. JoBAZ [Internet]. 2022 [cited 2024 May 18];83:28. Available from: https://doi.org/10.1186/s41936-022-00293-8
[38] El-Gogary RI, Nasr M, Rahsed LA, Hamzawy MA. Ferulic acid nanocapsules as a promising treatment modality for colorectal cancer: Preparation and in vitro/in vivo appraisal. Life Sciences [Internet]. 2022 [cited 2024 May 18];298:120500. Available from: https://www.sciencedirect.com/science/article/pii/S0024320522002004

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APPENDIX A: LIST OF ABBREVIATIONS

Abbreviation	Meaning
ActD	actinomycin D
AD	Alzheimer disease
AGE	glycation end products
Akt	protein kinase B
BDNF	brain-derived neurotrophic factor
BuChe	Butyrylcholinesterase
Caco-2	Colon carcinoma cell line
CAT	Catalase
CIS	Cisplatin
COX-2	Cyclooxegenase-2
CRC	Colorectal cancer
DCM	diabetic cardiomyopathy
DHP	diabetic hypertension
DM	Diabetes mellitus
DN	diabetic nephropathy
DPN	diabetic neuropathy
DR	Diabetic retinopathy
FA	Ferulic acid
FFA	free fatty acid
G6Pase	glucose-6-phosphatase
GK	Glucokinase
GLUT2	glucose transporter 2
GPx	glutathione peroxidase
H_2O_2	Hydrogen peroxide
HCE	human corneal endothelial cells
HIF-1	hypoxia-inducible factor 1
HT-29	human colorectal adenocarcinoma cell line with epithelial morphology
LDR	low-dose γ-irradiation
NAFLD	non-alcoholic fatty liver disease
NCs	polymeric nanocapsules
NF-κB	nuclear factor kappa-B
NOS	Nitric oxide synthase
NSAID	Non-steroid anti-inflammatory drug
PDGF	platelet-derived growth factor
PEPCK	phosphoenolpyruvate carboxykinase
PPAR-γ	peroxisome proliferator-activated receptors
ROS	reactive oxygen species
SA	Sodium arsenite
SOD	Superoxide dismutase
TG	Triglyceride
UGT	UDP-glucuronosyltransferases
VEGF	vascular endothelial growth factor

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