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Letter to the editor:

A RECENT OVERVIEW ON THE BIOLOGICAL AND PHARMACOLOGICAL ACTIVITIES OF FERULIC ACID

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Dear Editor,

Ferulic acid (FA) is an important phenolic acid that is commonly present in the leaves, fruits, and seeds of most plants. Certain types of grasses, including rice, wheat, and oats, are highly concentrated sources of FA. The name, ferulic, originates from the genus, *Ferula*, referring to giant fennel (*Ferula communis*). The International Union of Pure and Applied Chemistry (IUPAC) name for FA is (*E*)-3-(4-hydroxy-3-methoxy-phenyl) prop-2-enoic acid (Srinivasan et al., 2007; Bento-Silva et al., 2018). In plants, FA is biosynthesized from caffeic acid by the enzyme caffeate O-methyltransferase. FA, along with dihydroferulic acid, acts as a component of lignocellulose, which crosslinks lignins and polysaccharides, thereby conferring rigidity to the cell walls (de Oliveira et al., 2015).

FA has been recognized as an important chemical structure serving several biological activities, including antioxidant, anti-inflammatory, antiviral, antiallergic, antimicrobial, antithrombotic, anticarcinogenic, and hepatoprotective actions, directly or indirectly (Kumar and Pruthi, 2014; Mancuso and Santangelo, 2014). The FA enrichment in different food items could reduce oxidative damage and amyloid pathology, especially for Alzheimer disease (Nabavi et al., 2015; Sgarbossa et al., 2015). In this review, we summarize the recent findings on the biological and pharmacological activities of FA (Table 1).

Table 1: Recent studies on the biological and pharmacological activities of ferulic acid

Key findings	**Reference**
In a recent study, it was reported that FA improves hepatic fibrosis through the nhibition of the transforming growth factor (TGF)-β1/*Smad* pathway *in vitro* and *in vivo*. These findings revealed that FA can potentially be used to protect against liver fibrosis.	Mu et al., 2018
FA enhances the antibacterial activity of quinolone-based antibiotics against *Acinetobacter baumannii* by enhancing reactive oxygen species (ROS) generation, energy metabolism, and the activity of the electron transport chain with a concomitant decrease in glutathione	Ibitoye and Ajiboye, 2018
Chen et al. reported that FA can potentially treat various disorders, including NG-nitro-l-arginine methyl ester (L-NAME) induced preeclampsia in rats by decreasing placental inflammation and apoptosis.	Chen et al., 2018
Research findings revealed that FA fights against kidney ischemia reperfusion injury by decreasing apoptosis, increasing adenosine generation, reducing inflammation, and upregulating CD39 and CD73 expression.	Zhou et al., 2018
Supplementation of FA in other foods or ingredients enriches the development of the reproductive tract and ovarian activity of pre-pubertal hair breed ewe lambs during the natural anestrous season. An enhancement in the functionality of the glucose-insulin system could be a cause of this beneficial effect of FA.	Macías-Cruz et al., 2018
FA and sugarcane aqueous extract (SCAE) can protect against toxic conditions. All of these effects are not necessarily related to SCAE, because FA requires the skn-1 pathway to exert its protective manner in *Caenorhabditis elegans*.	Colonnello et al., 2018
FA intervention significantly ameliorates human umbilical vein endothelial cells (HUVEC) radiation injury through the thrombomodulin pathway. Therefore, FA could be effectively used as a potential agent to attenuate radiation-induced damage.	Shao et al., 2018
FA performs better than caffeic acid as an inhibitor of melanin production; the differences in the inhibitory efficacy of these two substances might be attributed to the difference in their tyrosine-binding activity. This study reveals that both substances effectively inhibited the CK2 (casein kinase 2)-mediated phosphorylation of tyrosinase.	Maruyama et al., 2018
FA and fish oil (FO) demonstrate anti-inflammatory and renoprotective effects through their peroxisome proliferator-activated receptor gamma (PPAR-γ) agonistic activity. Both FA and FO are natural products, and they both can offer a safe intervention strategy after exposure to nephrotoxins.	El-Ashmawy et al., 2018
FA is considered as a remedy for the plaques related to collagen deposition, because it is a potential inhibitor of collagen fibrillation and its propagation.	Jayamani et al., 2018
FA has protective effects against lipopolysaccharide (LPS)-induced acute kidney injury (AKI) in mice, which might suggest a chemopotential role treating AKI in humans.	Mir et al., 2018
FA, along with caspofungin, has synergistic effects against *Candida albicans*. These two compounds help to combine the existing anticandidal drug with phytochemicals to increase the efficacy of the anticandidal drug.	Canturk, 2018
FA and quercetin exhibit excellent bioavailability and bioactivity against some metabolic syndromes, like inflammatory bowel diseases and obesity.	Zhang et al., 2018
The new poly(ether ester urethane)urea elastomer (PEEUU) adapted with FA could act as a promising candidate for the vascular application of enhancing blood compatibility and vascular cell-compatibility.	Asadpour et al., 2018
FA mixed with nanostructured lipid carriers (NLCs) improves the pharmacological profile of FA and activates the phosphatidylinositol 3-kinase (PI3K) pathway, which has a therapeutic value against cerebral stroke.	Hassanzadeh et al., 2018

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Key findings	Reference
FA stimulates the synthesis of procollagen and hyaluronic acid, the inhibition of metalloproteinase, and the reduction in matrix metalloproteinase (MMP)-1 and MMP-9 expression in CCD-986sk cells stimulated with ultraviolet B (UV-B). FA can potentially be used as functional food for whitening and anti-wrinkle activities.	Park et al., 2018
FA combined with-vinylguaiacol forms a chemical starting structure for the development of new small molecules that protects against epidermal growth factor receptor (EGFR).	Sudhagar et al., 2018
FA has endothelium-independent vascular relaxant responses in different types of arteries. The molecular mechanism of FA-induced vasorelaxation involves the inhibition of a calcium channel and calcium desensitization.	Zhou et al., 2017
FA has beneficial effects on diabetes-induced cognition lesions, which was revealed by the regulation of the protein tyrosine phosphatase 1B (PTP1B) and insulin signaling pathways. PTP1B inhibition may be an approach to remedy abnormal signaling linked to diabetes-induced cognitive impairment.	Wang et al., 2017
FA shows potential therapeutic efficacy in enhancing survival and differentiation of neural stem cells (NSCs) to protect against gentamicin-induced neuronal hearing loss.	Gu et al., 2017
FA shows antiepileptogenic effects and protects against oxidative stress and cognitive impairment induced by pentylenetetrazol kindling by acting as a promising adjuvant for antiepileptic drugs.	Hassanzadeh et al., 2017
FA acts as an anti-inflammatory and antioxidant agent on macrophages due to its free radical scavenging activity in a cell free system. Consuming FA in a diet can defend the host from the development and/or progression of inflammation.	Szulc-Kielbik et al., 2017
In rice bran, FA represents an active component that enhances the expression of mitochondrial biogenesis and dynamics markers. In a vascular damage mouse model, FA decreases oxidative stress in endothelial cells and human mononuclear cells.	Perez-Ternero et al., 2017
FA could be considered as a novel agent to increase the management of depression, because it repairs stress caused by the hypothalamic-pituitary-adrenal-axis dysfunction.	Zeni et al., 2017
FA treatment significantly protects against oxidative stress, shows positive antioxidative activity, and improves histological parameters to normal, exhibiting the nephroprotective and antioxidant effects of this phenolic compound.	Bami et al., 2017
FA enhances the obesogenic status induced by a high-fat diet (HFD), and the integral effects of FA on a biological system were elucidated.	Salazar-López et al., 2017
FA reduces preeclampsia symptoms in a rat preeclampsia model, exhibiting its potential value in treating preeclampsia.	Gong et al., 2017
FA diminishes the increase in gene expression and assembly of proteins related to the emission of three types of Aβ peptides in H_2O_2-stimulated human lens epithelial (HLE) cells. These findings provide evidence of the antioxidative functions of FA in lens epithelial cells.	Nagai et al., 2017
The oxygen-carrying capacity of a hemoglobin site specifically adapted with ferulic acid (FA-Hb) was similar to endogenous Hb, but the rate of autoxidation of FA-Hb was much lower than Hb in various systems.	Qi et al., 2017
Pretreated with 0.1 mM of FA impairs the methylglyoxal (MG)-induced decrease of cell viability and protects against MG-induced cell apoptosis in pancreatic β-cells. These findings suggest that FA is capable of protecting β-cells from MG-induced cell damage in diabetes.	Sompong et al., 2017
FA shows protective effects against ultraviolet A (UVA)-induced cell damage through antioxidant and stress-inducible cellular action in human dermal fibroblasts (HDFs).	Hahn et al., 2016
FA significantly improved the intracellular concentration of δ-tocotrienol (T3), enhancing the bioavailability of δ-T3, and thus increasing the inhibitory power of δ-T3 on telomerase. For the above mentioned activities, FA could be a promising candidate to target δ-T3 and augment the anti-cancer activity.	Eitsuka et al., 2016

Key findings	**Reference**
FA could effectively act against acetaminophen-induced liver injury by down-regulating the expression of CYP 2E1 and the inhibition of Toll-like receptor (TLR) 4-mediated inflammatory responses.	Yuan et al., 2016
FA could inhibit the interferon-γ (IFN-γ)-induced inflammatory response by reducing the release of pro-inflammatory cytokines to improve trinitrobenzenesulfonic acid-induced colitis.	Sadar et al., 2016
FA protects the initiation of apoptotic signaling in the spleen by obstructing the free radical chain reaction and by scavenging superfluous ROS. FA can prevent the spleen from ionizing radiation.	Das et al., 2016
FA has a potential therapeutic response exhibiting antioxidant and hypoglycemic effects, which might help in circumventing stress-mediated diabetic cardiomyopathy in rats.	Chowdhury et al., 2016
FA is a promising candidate to treat developmental lead neurotoxicity. These hopeful findings will initiate future investigations evaluating the FA-mediated potentiation of neurite outgrowth following lead exposure *in vivo*.	Yu et al., 2016
Trans-FA at concentrations between 0.06 to 0.6 mM shows anti-proliferation and anti-migration effects in the human lung cancer cell line, H1299.	Fong et al., 2016
FA prevents osteoclast fusion by reducing the expression of dendritic cell-specific transmembrane protein (DC-STAMP) and enhancing apoptosis in mature osteoclasts through the caspase-3 pathway.	Sagar et al., 2016
FA-loaded hydrogel (thermosensitive) could salvage Cisd2-deficient (Cisd2(-/-)) cardiomyocytes (CM) from oxidative stress-induced damage and could acted as a potential therapeutic in the future treatment of cardiovascular diseases (CVD).	Cheng et al., 2016
The anti-hyperalgesia response of FA, which might be related to its antioxidant and anti-inflammatory activity, in rats with chronic constriction injury (CCI) could be effective as an adjuvant to conventional medicines. FA is also related to the protection of neuropathic pain.	Aswar and Patil, 2016
A study by Yang et al. shows that FA significantly inhibits important diseases, such as d-galactose(d-gal)-induced AchE (acetylcholinesterase) activity, neuroinflammation and neurodegeneration, and oxidative stress, thus consequently ameliorates memory impairment.	Yang et al., 2016
FA is a promising hepatoprotective agent against formaldehyde toxicity, because it exhibits positive effects on oxidative stress parameters.	Gerin et al., 2016

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Conflict of interest

The authors declare no conflict of interest.

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