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Guest editorial:

RECENT STUDIES ON ROSMARINIC ACID AND ITS BIOLOGICAL AND PHARMACOLOGICAL ACTIVITIES

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Rosmarinic acid (RA), an ester of caffeic acid and 3,4-dihydrophenyllactic acid (Figure 1), is a naturally occurring phenylpropanoid that is commonly found in species of the Boraginaceae family, the subfamily Nepetoideae of the Lamiaceae family, and in lower plants such as ferns and hornworts (Petersen and Simmonds, 2003). RA was first isolated and purified in 1958 from *Rosmarinus officinalis* by two Italian chemists, Scarpati and Oriente, who then named it according to the plant that they isolated it from (Scarpati and Oriente, 1958). The biosynthesis of RA has been extensively studied, and a biosynthetic pathway was first reported in 1970 by Ellis and Towers. They demonstrated that two aromatic amino acids - L-tyrosine and L-phenylalanine - are the building blocks of rosmarinic acid (Ellis and Towers, 1970).

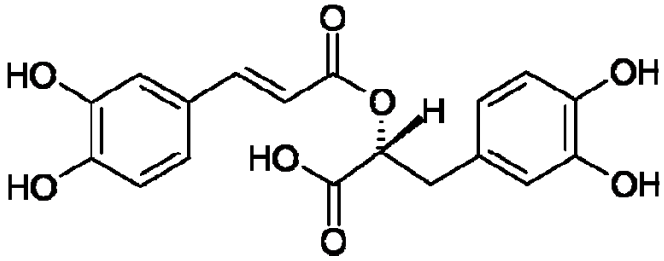

Figure 1: Chemical structure of rosmarinic acid

RA has a range of biological activities, making it an interesting material for the pharmaceutical, food, and cosmetics industries. Here we summarize key messages of recent studies performed on RA and its biological and pharmacological activities (Table 1).

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Table 1: Key messages of recent studies performed on RA and its biological and pharmacological activities

Key message	Reference
RA was shown to ameliorate cisplatin-induced oxidative stress, inflammation, and apoptosis in the kidneys.	Domitrović et al., 2014
RA prevented ischemia/reperfusion injury in the kidneys by decreasing oxidative stress.	Ozturk et al., 2014
RA was found to have protective effects against hyperthermia-induced cellular apoptosis and damage of muscle cells by changing the expression of stress genes and increasing intracellular antioxidant capability.	Chen et al., 2014
RA showed efficacy in ameliorating some aspects of diabetic neuropathy. Therefore, RA is a good candidate for diabetic neuropathy treatment in clinical studies.	Hasanein and Mohammad Zaheri, 2014
The analgesic effects of the acetyl derivative of RA were found to occur via a peripherally mediated mechanism. The acetyl ester derivative of RA is potentially applicable as a new lead compound for the management of pain and inflammation.	Lucarini et al., 2013
RA protected aortic endothelial function and ultrastructure against diabetes-induced damage. Both antioxidant and anti-inflammatory effects of RA seemed to have a role in the mechanism of protection.	Sotnikova et al., 2013
RA inhibited Cd(2+)-mediated cell toxicity, reactive oxygen species generation, interleukin (IL)-6 and IL-1β production, the translocation of the apoptosis-inducing factor into the nucleus, and the activation of caspase-3 in an auditory cell line, HEI-OC1. In addition, RA prevented the destruction of hair cell arrays in the rat organ of corti primary explants in the presence of $Cd(^{2+})$.	Kim et al., 2013
The data demonstrated that RA protects the brain against I/R (ischemia and reperfusion) injury with a favorable therapeutic time-window by alleviating diabetic cerebral I/R injury and attenuating the breakdown of the blood-brain barrier (BBB).	Luan et al., 2013
The authors believed that RA should be viewed as a possible therapeutic agent for the treatment of various inflammatory diseases via inhibition of the HMGB1 (high-mobility group box 1) signaling pathway.	Yang et al., 2013
RA showed chemopreventive potential against 1,2-dimethylhydrazine (DMH)-induced rat colon carcinogenesis and it is a possible chemopreventive agent against colon cancer.	Venkatachalam et al., 2013
Chronic consumption of RA resulted in quantifiable levels of parent compound in the plasma and intestinal tract of the Apc(Min) mouse model of colorectal carcinogenesis, and may slow adenoma development.	Karmokar et al., 2012
The polyphenol RA showed therapeutic potential in a murine model of a respiratory allergy to a clinically relevant human sensitizer allergen.	Costa et al., 2012
RA demonstrated potent anti-inflammatory effects in in vivo models of acute lung injury (ALI) induced by lipopolysaccharide (LPS).	Chu et al., 2012
RA had potent anticancer, anti-lipid peroxidative, and apoptotic effects in DMBA (7,12-dimethylbenz(a)anthracene)-induced skin carcinogenesis.	Sharmila and Manoharan, 2012
RA could decrease the levels of DNA damage induced by ethanol.	De Oliveira et al., 2012
Neuroreparative effects of RA were demonstrated against 6-ODHA (6-hydroxydopamine)-induced degeneration of the nigrostriatal dopaminergic system. They were achieved by decreasing nigral iron levels and regulating the ratio of Bcl-2/Bax gene expression.	Wang et al., 2012

Table 1 (cont.): Key messages of recent studies performed on RA and its biological and pharmacological activities

Key message	Reference
RA suppressed oral carcinogenesis by stimulating the activity of detoxification enzymes, improving the status of lipid peroxidation and antioxidants, and downregulating the expression of p53 and bcl-2 during DMBA (7,12-dimethylbenz(a)anthracene)-induced oral carcinogenesis.	Anusuya and Manoharan, 2011
RA acted as a vasoactive substance and a cardioprotector due to its antioxidant property. Thus, RA may be useful in reducing the cardiovascular risk associated with insulin resistance.	Karthik et al., 2011
Antihemorrhage activity of RA was reported for the first time, and RA was found to greatly contribute to the antihemorrhagic efficiency of *Argusia argentea* against crude snake venoms and hemorrhagic toxins.	Aung et al., 2010
In animal experiments, intraperitoneal administration of 2 mg of rosmarinic acid significantly reduced the weight of tumors and the number of lung nodules compared with those of a control group. Therefore, these results demonstrated that rosmarinic acid can effectively inhibit tumor metastasis in vitro and in vivo.	Xu et al., 2010
In vivo experiments showed the capacity of orally administered RA to inhibit cutaneous alterations caused by UVA exposure (skin photocarcinogenesis). According to this research, RA can be considered a photo-protective agent.	Sánchez-Campillo et al., 2009
Our investigation into the atopic dermatitis-mitigating effect of RA through in vivo experiments demonstrated the possible clinical use of RA as a therapeutic agent for atopic dermatitis.	Lee et al., 2008
The nitration of RA strongly improved the anti-integrase inhibition and the antiviral activity without increasing the cellular toxicity.	Dubois et al., 2008

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