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The Efficacy of Thymbra spicata Ethanolic Extract and its Main Component Carvacrol on In vitro Model of Metabolically-Associated Dysfunctions

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Abstract : Thymbra spicata is a thyme-like plant belonging to the Lamiaceae family that shows a global distribution, especially in the eastern Mediterranean region. Leaves of T. spicata contain large amounts of phenols such as phenolic acids (rosmarinic acid), phenolic monoterpenes (carvacrol), and flavonoids. In Lebanon, T. spicata is currently used as a culinary herb in salad and infusion, as well as for traditional medicinal purposes. Carvacrol (5-isopropyl-2-methyl phenol), the most abundant polyphenol in the organic extract and essential oils, has a great array of pharmacological properties. In fact, carvacrol is largely employed as a food additive and neutraceutical agent. Our aim is to investigate the beneficial effects of T. spicata ethanolic extract (TE) and its main component, carvacrol, using in vitro models of hepatic steatosis and endothelial dysfunction. As a further point, we focused on investigating if and how the binding of carvacrol to albumin, the physiological transporter for drugs in the blood, might be altered by the presence of high levels of fatty acids (FAs), thus impairing the carvacrol bio-distribution in vivo. For that reason, hepatic FaO cells treated with exogenous FAs such as oleate and palmitate mimic hepatosteatosis; endothelial HECV cells exposed to hydrogen peroxide are a model of endothelial dysfunction. In these models, we measured lipid accumulation, free radical production, lipoperoxidation, and nitric oxide release before and after treatment with carvacrol. The carvacrol binding to albumin with/without high levels of long-chain FAs was assessed by absorption and emission spectroscopies. Our findings show that both TE and carvacrol (i) counteracted lipid accumulation in hepatocytes by decreasing the intracellular and extracellular lipid contents in steatotic FaO cells; (ii) decreased oxidative stress in endothelial cells by significantly reducing lipoperoxidation and free radical production, as well as, attenuating the nitric oxide release; (ii) high levels of circulating FAs reduced the binding of carvacrol to albumin. The beneficial effects of TE and carvacrol on both hepatic and endothelial cells point to a nutraceutical potential. However, high levels of circulating FAs, such as those occurring in metabolic disorders, might hinder the carvacrol transport, bio-distribution, and pharmacodynamics.

Keywords : carvacrol, endothelial dysfunction, fatty acids, non-alcoholic fatty liver diseases, serum albumin
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