Anti-steatotic effects of eugenol in rats treated with high fat diet and low dose of streptozotocin

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Eugenol (4-allyl-2-methoxyphenol) is a naturally occurring phenolic compound extracted from clove oil (*Eugenia caryophyllata*), basil, and nutmeg. It possesses several biological activities and it has been widely used as a fragrant and favoring agent in a variety of food and cosmetic products. Although protective effects of eugenol on oxidative stress and inflammation have been well-studied, literature data about pharmacological effects on metabolic diseases are very few (*Jo et al., 2014*). The aim of this study was to evaluate the effect of eugenol in a non alcooholic fatty liver disease rat model induced with a high fat/cholesterol diet with a low dose of streptozotocin (HDF/ STZ rats) (*Srinivasan* et al., 2005, *Vornoli et al., 2014; Pozzo et al., submitted*).

HFD/STZ rats, compared to control ones, showed a significant increase of blood parameters (glucose, cholesterol, ALT, ALT and triglycerides) and expression of genes involved lipid metabolism (LXRα, SREBP1c), fibrosis, inflammation, mitochondrial oxidative stress (IL6, TNFa, TGFb e UCP2), β-oxidation and clearance of cholesterol (PPARα, CPT1a, CYP7A1).

Results indicate that eugenol caused a decreasing trend of blood glucose, cholesterol, ALT, and triglycerides in rats with respect to HFD/STZ ones according to *Srinivasan et al*. (2005).

The significant decrease in liver lipids content, with respect to HFD/STZ rats, suggested a lipid-lowering property of the substance; a decreasing trend observed for the hepatic levels of carbonilated proteins confirmed the expected antioxidant properties of the analyzed aromatic compound.

To understand the molecular mechanisms through which it occurs, we evaluated at a transcriptional level the effect of eugenol on expression of genes mentioned above.

Eugenol significantly decreased LXRα expression, the LXRα-dependent CYP7A1, PPARα and SREBP-1c compared to HFD/STZ rats. Consequently, eugenol seems to prevent high levels of intra-hepatic cholesterol and the dysregulation of the *de novo* synthesis of fatty acids, which we observed in HFD/STZ rats.

Furthermore, eugenol-treated rats, compared to steatotic ones, showed a significant down regulation of marker genes of inflammation (TNFα, IL6), fibrosis (TGFβ), oxidative stress at mitochondrial level (UCP2), and CHOP, a marker of endoplasmatic reticulum stress.

Regarding other parameters evaluated eugenol did not influenced CYPs protein expression levels and activity, and the reduced expression of genes involved in the cholesterol biosynthesis (SREBP-2-regulated HMG-CoA reductase and LDLr) observed in HFD/STZ rats.

Results demonstrated the clear anti-steatotic effects of eugenol on HFD/STZ rats, also confirming the effectiveness of the substance as anti-inflammatory and anti-oxidative stress compound.

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