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Nerolidol effects on mitochondrial and cellular energetics

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Abstract

In the present work, we evaluated the potential toxic effects of nerolidol, a sesquiterpenoid common in plants essential oils, both on mitochondrial and cellular energetics. Samples of enriched natural extracts of nerolidol (a racemic mixture of *cis* and *trans* isomers) were tested on rat liver mitochondria and a decrease in phosphorylative system was observed but not in the mitochondrial respiratory chain activity, which reflects a direct effect on F1-ATPase. Hence, respiratory control ratio was also decreased. Cellular ATP/ADP levels were significantly decreased in a concentration-dependent manner, possibly due to the direct effect of nerolidol on F_0F_1-ATPsynthase. Nerolidol stimulates respiratory activity probably due to an unspecific effect, since it does not show any protonophoric effect. Furthermore, we observed that mitochondrial permeability transition was delayed in the presence of nerolidol, possibly due to its antioxidant activity and because this compound decreases mitochondrial transmembrane electric potential. Our results also show that, in human hepatocellular liver carcinoma cell line (HepG2), nerolidol both induces cell death and arrests cell growth, probably related with the observed lower bioenergetic efficiency.

Highlights

▸ Toxicological evaluation of a sesquiterpene commonly present in plant essential oils. ▸ Nerolidol interfere with the mitochondrial membrane in an unspecific way. ▸ Nerolidol inhibit F_0F_1-ATPsynthase in a

concentration dependent manner. ▶ Hepatic cell cytotoxicity a putative effect from a decrease in ATP/ADP levels.

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Keywords

Nerolidol; Sesquiterpenoid; Mitochondria; FOF1-ATPsynthase; Cell death

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...It is known that the hydrophobicity of EOs components enables them to partition in the lipids of the bacterial cell membrane, disturbing the structures and rendering them more permeable. This loss of differential permeability is considered the cause of cell death of microorganisms since it leads to extensive loss of cell contents or to the exit of critical molecules and ions (Ferreira et al., 2012; Oliveira et al., 2011; Simões et al., 2008). In specific case of the tested EOs, the antibacterial activity is probably due to the presence of carvacrol because of its high abundance in S. montana EOs and its high specific activity as compared to other EO components, considered one of the main active components of EOs (Friedman, 2014; Veldhuizen et al., 2006)....

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...The major components were the sesquiterpenes (E)–nerolidol (56.04%) and α-cadinol (3.46%), monoterpenes α–pinene and β–pinene (4.16% and 3.39%, respectively), linalool (5.98%) and terpinolene (4.41%), amongst others. According to the results presented in Table 1, the principal component of the EOCA was (E)-nerolidol, which is a sesquiterpene alcohol, naturally occurring in EO of various plants, possessing floral aroma (Ferreira et al., 2012; McGinty, Letizia, & Api, 2008). Frequently incorporated to cosmetics (as shampoos or perfumes) and non-cosmetic products (as detergents and cleaning products) (McGinty et al., 2008), nerolidol is also widely used in the food industry as flavor enhancer since it was approved as to be safe by the Food and Drug Administration (FDA) of the USA....

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