AMP-activated Protein Kinase is responsible for Steatogenic Effects of Food Additive α-Terpineol

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α-Terpineol is a colorless monoterpenoid alcohol with slightly sweet odor that is found in the oils of many herbs and widely used in cosmetic products as a fragrance material. The oils from *Melaleuca alternifolia*, *Salvia officinalis* and *Carthamus tinctorius* contain α-terpineol, the content of which account for about 3-4%. These oils have been used as a flavor in food, antibacterial agent and essential oil. Council of Europe and US FDA approved α- and β-terpineol as synthetic flavoring substances that are permitted for direct addition to food for human consumption. The present study reports that α-terpineol induces fatty liver via AMP-activated protein kinase (AMPK)-mTOR-sterol regulatory element-binding protein-1 (SREBP-1) pathway. Treatment of hepatocytes with α-terpineol increased neutral lipid accumulation significantly. α-Terpineol suppressed AMPK phosphorylation and increased p70S6 kinase (p70S6K) phosphorylation and SREBP-1 activation. It also increased the luciferase activity in LXRE-tk-Luc and SRE-tk-Luc transfected cells. Inhibition of mTOR signaling by co-treatment with rapamycin or co-transfection with dominant negative p70S6K completely blocked the α-terpineol effects. Oral administration of mice with α-terpineol for 2 weeks decreased AMPK phosphorylation and increased SREBP-1 activation in the liver, which were followed by hepatic lipid accumulation. On the other hand, co-treatment with rapamycin reversed α-terpineol-induced SREBP-1 activation and fatty liver in mice. These data provide evidence that α-terpineol causes fatty liver mediated by the AMPK/mTOR/SREBP-1 pathway.