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β-patchoulene improves lipid metabolism to alleviate non-alcoholic fatty liver disease via activating AMPK signaling pathway

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ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) has been a leading cause of chronic metabolic disease, seriously posing healthy burdens to the public, whereas interventions available for it are limited to date. Patchouli oil had been reported to attenuate hepatic steatosis in our previous study. β-patchoulene (β-PAE) is a representative component separated from patchouli oil with multiple activities, but its effect against NAFLD is still unknown. To investigate the effect and potential mechanism of β-PAE on NAFLD, we used high fat diet (HFD) in vivo and free fatty acid (FFA) in vitro to induce hepatic steatosis in rats and L02 cells, respectively. Histological examination was evaluated via Hematoxylin-eosin and oil red O staining. The parameters for hepatic steatosis were estimated via biochemical kits, western blotting and quantitative real-time PCR. Compound C, the inhibitor of AMPK, was applied further to examine the precise mechanism of β-PAE on NAFLD. Our results indicated that β-PAE significantly attenuated HFD-induced weight gain, hepatic injury, lipid deposition in serum and hepatic tissue as well as FFA induced-lipid accumulation. Besides, β-PAE markedly improved the expression of AMP-activated protein kinase (AMPK) and its downstream factors which correlate with hepatic lipid synthesis and oxidation in vivo and in vitro. Nevertheless, Compound C abrogated the benefits derived from β-PAE in L02 cells. In conclusion, these results suggest that β-PAE exerts AMPK agonist-like effect to regulate hepatic lipid synthesis and oxidation, eventually prevent NAFLD progression.

1. Introduction

Non-alcoholic fatty liver disease (NAFLD), the most common type of chronic liver disease associated with caloric excess and disordered metabolism, includes a continuum of complicated pathological processes from simple steatosis to non-alcoholic steatohepatitis, cirrhosis and even hepatocellular carcinoma [1]. Along with the social-economic development, the incidence of metabolic diseases, such as obesity, diabetes and metabolic syndrome, has greatly increased. NAFLD represents the hepatic manifestation of metabolism syndrome whose prevalence is escalating, with an estimated 25 % incidence to date [2].

Affected individuals of NAFLD typically perform aberrant

Abbreviations: β-PAE, β-patchoulene; ACC1, acetyl-CoA carboxylase 1; ACOX1, acyl-CoA oxidase 1; ALT, alanine aminotransferase; AMPK, AMP-activated protein kinase; AST, aspartate transaminase; CPT-1a, carnitine palmitoyltransferase 1a; FASN, fatty acid synthase; FFA, free fatty acid; FGF21, fibroblast growth factor 21; GSH-Px, glutathione peroxidase; HDL-C, high-density lipoprotein-C; HFD, high fat diet; HMG-CR, HMG CoA reductase; LDL-C, low-density lipoprotein-C; MDA, malondialdehyde; NAFLD, non-alcoholic fatty liver disease; NC, normal control; NEFA, nonesterified free fatty acids; OA, sodium oleate; PGC-1α, peroxisome proliferators-activated receptor-γ coactivator-1α; PPARα, peroxisome proliferator activated receptor-α; RSV, rosuvastatin; SCD1, stearoyl-CoA desaturase 1; SIRT1, silent information regulator of transcription 1; SOD, superoxide dismutase; PA, sodium palmitate; SREBP-1c, sterol regulatory element-binding protein 1c; TC, total cholesterol; TG, triglyceride; VE, vitamin E.

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