

Anti-Obesity Effects of Pteryxin in *Peucedanum japonicum* Thunb Leaves through Different Pathways of Adipogenesis In-Vitro

Authors : Ruwani N. Nugara, Masashi Inafuku, Kensaku Takara, Hironori Iwasaki, Hirotsuke Oku

Abstract : Pteryxin from the partially purified hexane phase (HP) of *Peucedanum japonicum* Thunb (PJT) was identified as the active compound related to anti-obesity. Thus, in this study we investigated the mechanisms related to anti-obesity activity in-vitro. The HP was fractionated, and effect on the triglyceride (TG) content was evaluated in 3T3-L1 and HepG2 cells. Comprehensive spectroscopic analyses were used to identify the structure of the active compound. The dose dependent effect of active constituent on the TG content, and the gene expressions related to adipogenesis, fatty acid catabolism, energy expenditure, lipolysis and lipogenesis (20 µg/mL) were examined in-vitro. Furthermore, higher dosage of pteryxin (50µg/mL) was tested against 20µg/mL in 3T3-L1 adipocytes. The mRNA were subjected to SOLiD next generation sequencer and the obtained data were analyzed by Ingenuity Pathway Analysis (IPA). The active constituent was identified as pteryxin, a known compound in PJT. However, its biological activities against obesity have not been reported previously. Pteryxin dose dependently suppressed TG content in both 3T3-L1 adipocytes and HepG2 hepatocytes ($P < 0.05$). Sterol regulatory element-binding protein-1 (SREBP1 c), Fatty acid synthase (FASN), and acetyl-CoA carboxylase-1 (ACC1) were downregulated in pteryxin-treated adipocytes (by 18.0, 36.1 and 38.2%; $P < 0.05$, respectively) and hepatocytes (by 72.3, 62.9 and 38.8%, respectively; $P < 0.05$) indicating its suppressive effects on fatty acid synthesis. The hormone-sensitive lipase (HSL), a lipid catabolising gene was upregulated (by 15.1%; $P < 0.05$) in pteryxin-treated adipocytes suggesting improved lipolysis. Concordantly, the adipocyte size marker gene, paternally expressed gene1/mesoderm specific transcript (MEST) was downregulated (by 42.8%; $P < 0.05$), further accelerating the lipolytic activity. The upregulated trend of uncoupling protein 2 (UCP2; by 77.5%; $P < 0.05$) reflected the improved energy expenditure due to pteryxin. The 50µg/mL dosage of pteryxin completely suppressed PPAR γ , MEST, SREBP 1C, HSL, Adiponectin, Fatty Acid Binding Protein (FABP) 4, and UCP's in 3T3-L1 adipocytes. The IPA suggested that pteryxin at 20µg/mL and 50µg/mL suppress obesity in two different pathways, whereas the WNT signaling pathway play a key role in the higher dose of pteryxin in preadipocyte stage. Pteryxin in PJT play the key role in regulating lipid metabolism related gene network and improving energy production in vitro. Thus, the results suggests pteryxin as a new natural compound to be used as an anti-obesity drug in pharmaceutical industry.

Keywords : obesity, *peucedanum japonicum thunb*, pteryxin, food science

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