

EFFECTS OF HUYOU (*CITRUS CHANGSHANENSIS*) FRUIT EXTRACTS ON GLUCOSE CONSUMPTION IN HUMAN HEPG2 CELLS AND THEIR HYPOLIPIDEMIC ACTIVITY IN C57BL/6 MICE

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Huyou (*Citrus changshanensis*) fruit is high in nutritional and medicinal value. The present study was designed to study the effect of different Huyou fruit tissues on glucose consumption in HepG2 cells and their hypolipidemic activity in C57BL/6 mice. Results showed that the ethanol extracts of all the four parts of Huyou fruit, *i.e.* flavedo, albedo, segment membrane (SM) and juice sacs (JS), exhibited increased effects on glucose consumption in HepG2 cells in a dose-dependent manner (from 0.2 µg/mL to 25 µg/mL). Naringin and neohesperidin were characterized in the fruit extracts by HPLC, where the highest contents of both compounds were found in the albedo. Efficient simultaneous purification of naringin and neohesperidin from Huyou albedo was established by the combination of D101 macroporous resin and High-Speed Counter-Current Chromatography (HSCCC). Further experiment on HepG2 cells treated with naringin (from 0.2 µg/mL to 5 µg/mL) and neohesperidin (from 0.2 µg/mL to 5 µg/mL) showed increased consumption of glucose, and the combination treatment of both compounds (from 0.5 µg/mL) resulted in synergistic effect. Western blot analysis suggested that the enhancement effect of naringin and neohesperidin on glucose consumption was associated with the phosphorylation of AMP-activated protein kinase (AMPK), which was similar to metformin, a common hypoglycaemic drug. In addition, in a preliminary animal study, the SM (50 mg/kg BW) and albedo (50 mg/kg BW) extracts showed hypoglycaemic and hypolipidemic activity in high fat fed C57BL/6 mice. During the 11-week animal study, the SM extracts treated mice resulted in significantly lower body weight (BW, 26.40±0.67 g, epididymal adipose tissue index (EAT, 0.79±0.06 %), perineal adipose tissue index (PAT, 0.14±0.02 %), blood glucose (BG, 7.3±0.78 mmol/L), serum triglyceride (TG, 0.66±0.05 mmol/L) and glycosylated serum protein (GSP, 1.84±0.05 mmol/L), compared with the control (29.13±0.55 g, 1.44±0.11 %, 0.32±0.06 %, 10.5±0.58 mmol/L, 0.92±0.05 mmol/L and 2.01±0.06 mmol/L for BW, EAT, PAT, BG, TG, and GSP, respectively), while their oral glucose tolerance was significantly increased. Our results showed that the metabolites of Huyou fruit may have the potential efficacy for prevention of diabetes and/or obesity.

Keywords: *Citrus changshanensis*, Fruit extract, Glucose consumption, Hypolipidemic activity