Study on the antihyperglycemic activity of triterpenes in banana peel

［課程博士・論文博士共通］

博士学位論文内容要旨
Abstract

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Banana including dessert banana and cooking banana, is the second largest produced fruit after citrus (about 17% of the world's total fruit output). Banana peel as by-product, which is about 35% of the total fresh weight, usually used as organic fertilizer or simply discarded as waste. Many researches have shown that banana peel is an important resource which contain many kinds of nutrients and active components. These active components have been reported to show multiple activities. Diabetes mellitus (DM) which is divided into type 1 (account for 5–10%) and type 2 (account for 90–95%), has been becoming an important global health problem. Under most circumstances, the current antidiabetic medicines are often responsible for various side effects which means that we need to develop less toxic and free from side effects natural compounds. Triterpenes are good candidates that have shown the antihyperglycemic activity with several mechanisms. Banana peels are rich in triterpenes with cycloeucalenone and its isomer, 31-norcyclolaudenone as the major components. The purpose of this research is to develop potential antidiabetic natural compounds and take full advantage of banana peel resource by investigating the antihyperglycemic activity of main triterpenes in banana peel.

In chapter 2, four compounds were purified from banana peel ethyl acetate extract by HPLC based on the proton NMR. Fr. 2-2-1 (compound 1) maybe 31-norcyclolaudenone and its recovery rate is 0.17%. Fr. 2-2-2 (compound 2) maybe cycloeucalenone and its recovery rate is 0.52%. Fr. 3-3-3-2-1 (compound 3) maybe the isomer cycloeucalenol and its recovery rate is 0.005%. Fr. 3-3-3-2-2 (compound 4) maybe cycloeucalenol and its recovery rate is 0.014%.

In chapter 3, the structures of four compounds were analyzed and confirmed by 1D and 2D NMR. Based on the ^{1}H and ^{13}C along with COSY, HMQC, HMBC, DEPT 90, DEPT 135 and comparison with literature data, compound 1 is 31-norcyclolaudenone (isoCE-one), compound 2 is cycloeucalenone (CE-one), compound 3 is isomer of cycloeucalenol (isoCE-ol), compound 4 is cycloeucalenol (CE-ol). These four compounds are similar compounds. The structural differences of four triterpenes are the carbonyl group or hydroxy group at C-3 and the position of double bond (Δ25(27) or Δ24(28)) in the side chain.

In chapter 4, the α-glucosidase and α-amylase inhibitory activity of four triterpenes were measured and compared *in vitro*. And the structure-activity relationships of them were analyzed. In addition, the kinetic analysis of CE-one in α-glucosidase inhibitory assay was elucidated. CE-one and isoCE-one exhibited both α-glucosidase and α-amylase inhibitory activities *in vitro*. And CE-one showed higher α-glucosidase and α-amylase inhibitory activities than that of isoCE-one. On the other hand, CE-ol and isoCE-ol did not show both inhibitory activities. The IC_{50} of CE-one and isoCE-one on α-glucosidase were 31.83±2.46 and 38.85±1.54 μM, respectively. And their IC_{50} on α-amylase were 20.33±0.59 and 27.63±0.83 μM, respectively. The main active sites of CE-one and isoCE-one are the carbonyl group at C-3 and double bond in the side chain. And CE-one induced a parabolic mixed-type inhibition with the K_i value of 73.86 μM in α-glucosidase inhibitory assay.

In chapter 5, the antihyperglycemic activity of CE-one in normal mice and STZ-induced diabetes mice

were investigated. Carbohydrate-loading test (maltose and starch) indicated that CE-one exerted antihyperglycemic activity in normal mice. The 80 mg/kg dose of CE-one showed 26.7% decrease of blood glucose compared with control group at 30 min in oral maltose tolerance test. The 40 and 80 mg/kg dose of CE-one showed 33.4% and 39.2% decrease of blood glucose compared with control group at 30 min in oral starch tolerance test. CE-one showed more effective on the inhibition of α-amylase in normal mice. The results of CE-one in STZ-induced diabetes mice indicated that it can decrease the blood glucose level, food intake, water consumption and liver index. Cycloeucalenone cannot affect the body weight, spleen index, kidneys index, and insulin level of diabetes mice. The mechanisms maybe because of CE-one can improve the condition of liver, such as increase liver glycogen and decease the level of AST and ALT. In addition, CE-one can also decrease the level total cholesterol in plasma while has no effect on triglyceride level.

The results of this study first time showed the antihyperglycemic activity and mechanisms of cycloeucalenone *in vitro and vivo*. This study not only provides the possibility to use cycloeucalenone as potential antidiabetic agent, but also provides an alternative method to recycle banana peel resource.