## O2 ANTIHYPERGLYCEMIC EFFECTS OF CINNAMIC ACID AND DERIVATIVES : INVOLEMENT OF INSULIN SECRETAGOGUE ACTIVITY

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Diabetes Mellitus and its complications constitute a major health problem in modern societies. It is mainly classified in two types. Type 1 (Insulin Dependent Diabetes Mellitus, IDDM) and Type 2 (Non-Insulin Dependent Diabetes Mellitus, NIDDM). Among the classes of chemical compounds isolated from plants with documented anti-diabetic activity are alkaloids, glycosides, terpenoids, polysaccharide and amino acids. Recent interest in plant phenolic compounds, cinnamic acid and it's derivatives, have shown their potentially anti-hyperglycemic activities such as increasing the glucose utilization in peripheral tissues, inhibiting hepatic gluconeogenesis and stimulatory effect of insulin secretion. Therefore, the purposes of this study were to investigate the effects of cinnamic acid and 6 different kinds of cinnamic acid derivatives, ortho-, meta-, para-hydroxycinnamic acid, and ortho-, meta-, para-methoxycinnamic acid, on antihyperglycemic activity, as well as, the effects of these compounds on insulin secretion from perfused rat pancreas. Male Sprague-Dawley rat weighting 250-380 g were divided into 8 groups. Each group contained 8 rats. Group 1 received an intravenous administration of vehicle. Group 2-8 received cinnamic acid and six different cinnamic acid derivatives (5 mg/kg), respectively. The intravenous glucose tolerance test (IVGT; 0.25 mg/kg) was performed 30 min after intravenous administration of the treatments. Blood plasma samples were collected from femoral vein to determine glucose concentration using Glucose Oxidase Test at 0, 5, 10, 30, 60, 90 and 120 min. In addition, we investigated the effects of cinnamic acid and derivatives, which showed *In vivo* antihyperglymic activity, on insulin secretion from perfused rat pancreas in the presence of both normal and high glucose conditions.

The cinnamic acid, *p*-methoxycinnamic acid (*p*-MCA) and *o*-hydroxycinnamic acid (*o*-HCA) significantly reduced plasma glucose concentration at 5,10,90 and 120 min. In the presence of normal glucose condition, both cinnamic acid and *p*-MCA stimulated insulin secretion by 1.5- and 2-fold of the baseline level, respectively. In addition, they caused a greater potentiation of insulin secretion in 10 mM glucose than in 5 mM glucose, which were 4-fold and 12-fold of the baseline level, respectively. However, the *o*-HCA failed to increase insulin secretion from perfused rat pancreas in either condition. Taken together, our findings suggest that 1) the cinnamic acid, *p*-MCA and *o*-HCA exerted antihyperglycemic activity in vivo 2) the first two agents have insulin secretagouge activity and the higher the glucose concentration, the greater the potentiation in cinnamic acid- and *p*-MCA-induced insulin secretion, which could help explain their activities in vivo and 3) the mechanism underlying *o*-HCA-induced antihyperglycemic activity need to be further investigation.