O3 ANTIHYPERGLYCEMIC EFFECTS AND MECHANISMS OF ACTION OF *COSCINIUM FENESTRATUM* EXTRACT IN NORMAL RATS

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Diabetes mellitus is one of the most serious health problems among people in the world. The prevalence of diabetes worldwide at least 171 million people in 2000 and reach to 366 million people in 2030. In Thailand, the total number of people with diabetes rise from 1.536 million in 2000 to 2.739 million in 2030. Several drugs have been used for treating diabetes, however, they also have limited efficacy and are associated with side effects, including weight gain, hypoglycemia, gastrointestinal disturbances, lactic acidosis and edema.

Recently, the natural products are the one of available sources for finding novel molecules to drug development. "Hamm"or *Coscinium fenestratum (Gaertn.) Colebr.* has been widely used in the North-Eastern part of Thailand. It has been known as a Laos traditional medicine and used for antihypertensive, antihyperglycemic, antihypercholesteremic and detoxifying agents. Since, the request to use this plant is increasing, therefore, the study of pharmacological effects of Hamm become necessary. The objective of this study was to investigate 1) the effects of *Coscinium fenestratum* extract (CFE) on blood glucose level in normal rats 2) the stimulatory effects on insulin secretion from perfused rat pancreas and 3) the inhibitory effect of α-glucosidase (AGH) from rat intestinal acetone powder.

We performed oral glucose tolerance test (OGTT) in normal rats to investigate the effects of CFE on blood glucose concentration. Three different kinds of sugar, including glucose, maltose, and sucrose were used as substrates. The rats in each group of sugar were divided into 3 subgroups contained 8 animals each. Group 1 was fed with sterile water at 0.5 ml/rats. Group 2 was received oral administration of CFE at 500 mg/kg, and group 3 was received glibenclamide at 5 mg/kg (for glucose group) or acarbose at 3 mg/kg (for maltose and sucrose groups), respectively as positive control. After 5 min of administration, each group was treated with 3 g/kg of glucose, maltose or sucrose solutions, respectively. Blood samples were collected from tail vein for glucose concentration determination using Glucose Oxidase Test at 0, 15, 30, 60 and 120 min. In order to clarify the mechanisms underlying CFE-induced hypoglycemic effect, we investigated the direct effect of CFE (10 μg/ml) on insulin secretion using *In Situ* pancreatic perfusion and inhibition of postprandial blood glucose rise through α-glucosidase enzyme from rat intestine.

The CFE significantly decreased plasma glucose concentrations at 30 and 60 min after the oral administration of all three kinds of sugar, suggesting that the antihyperglycemic effect of CFE was achieved by inhibition of maltase, sucrase and glucose transport inhibition. It also stimulated insulin secretion from perfused rat pancreas by 2.72 folds compared with basal control group. This effect was apparent within 5 min of administration and was persistent during 30 min of administration. In addition, from AGH inhibitory assay, CFE inhibited maltase and sucrase from rat intestine with IC_{50} = 5.92 ± 0.48 mg/ml and 7.71 ± 1.23 mg/ml, respectively. Taken

together, we concluded that *Coscinium fenestratum* extract exerted antihyperglycemic activity via two possible pathways, which were stimulation of insulin secretion and inhibition of α-glucosidase, the brush border enzyme in proximal small intestine, thus, leading to increase glucose uptake into the cells and delay carbohydrate absorption from intestinal mucosa into blood stream.