Thesis Title Nephrotoxicity of stevioside in rats and hamsters

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ABSTRACT

Stevioside, a major sweet constituent in Stevia rebaudiana Bertoni, was subjected to investigation for its effect on kidney and liver. This study was performed to compare the susceptibility of stevioside in three different animal species such as mice, rats and hamsters of both sexes and different routes of administration including intragastric intubation (I.G.), intraperitoneal injection (I.P.) and subcutaneous injection (S.C.). General signs and symptoms were observed and the numbers of dead animals were recorded within a period of 7 days after stevioside administration for estimation of LD_{50} value. Mice were found to be more susceptible to stevioside than rats but less than hamsters in all three routes of administration. When given stevioside via I.P. and S.C. routes, all of three animal species were more susceptible to stevioside than those when given via I.G. routes. The possible causes of death were then investigated by histopathological examinations. Histopathologic changes, mostly seen in kidney, revealed necrosis of epithelial cells and dilatation of convoluted tubules with cell debris and proteinous casts. Therefore, the possible causes of death may be due to acute renal failure although some extent

hepatotoxic can be found. Effects of stevioside on the plasma levels of biochemical parameters and urine volume were then investigated. Various doses of stevioside ranging from 0.5 to 2.05 g/kg BW were given to rats. At 6 hrs after S.C. injection, stevioside significantly increased BUN, creatinine, uric acid, PGPT and PGOT values but markedly depressed plasma albumin and urinary excretion. It is likely that stevioside is capable of inducing nephrotoxicity with evidences of histopathologic changes in kidney. Incidence and severity of nephrotoxicity were progressively increased with the dose of stevioside. Stevioside also exhibited time-related manner when given at the dose of 2.05 g/kg BW (S.C.) for 0, 3, 6, 9 and 12 hrs. However, intragastric administration of stevioside (4.1 g/kg BW) did not significantly cause any changes in kidney and liver functions. Whereas, S.C. and I.G. administration of stevioside induced severe nephrotoxic and some extent hepatotoxic effects in rats and hamsters, respectively. These results indicated that hamsters were more susceptible to stevioside nephrotoxicity than rats. The effects of stevioside on mean arterial blood pressure and urine excretion were slightly decreased but there were no significant changes in creatinine and PAH clearances as indicators of glomerular filtration rate and renal plasma flow, respectively. So, the renal impairment may be occurred in renal tubules rather than glomerulus.