

Thesis Title Acute Toxicity and Carcinogenicity
 Study of Steviol in Hamsters

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ABSTRACT

Stevioside, a diterpene glycoside, is the principle sweet constituent in Stevia rebaudiana Bertoni, leaves. Steviol, an acidic aglycone, is a product of enzymatic hydrolysis of stevioside. They were subjected to investigate for their acute toxicity in various animal species including hamster, rat and mouse and chronic/carcinogenicity study in hamsters. Acute toxicity was performed to compare the susceptibility of steviol and stevioside given via intragastric intubation(I.G.) in both sexes of three differences animal species such as hamster, rat and mouse. General signs and symptoms were observed and the numbers of dead animals were recorded within a period of 14 days after stevioside or steviol administration for estimation of LD₅₀ values. Hamsters were found to be more susceptible to steviol than rats and mice. Orally LD₅₀ values of steviol in hamsters were 5.20

and 6.10 g/kg BW for male and female, respectively. In rats and mice, orally LD₅₀ values of steviol were more than 15 g/kg BW in both sexes. Stevioside at the dose level as high as 15 g/kg BW could not induce any lethality to all three animal species when given by the same route. The possible causes of death were then investigated by histopathological examination. Histopathological changes, mostly seen in kidney particularly in the proximal convoluted tubules showed hydropic degeneration of epithelial cell and found hyaline cast in the lumen of both proximal and distal convoluted tubules. Therefore, the possible cause of death may be due to acute renal failure although some extent hepatotoxic can be found. Effects of steviol on the serum biochemical parameters were also investigated. At the dose level of 5 g/kg BW were given to male hamsters. After treatment, BUN and creatinine significantly increased with time but AST and ALT activities were slightly increased. It is likely that steviol is capable of inducing nephrotoxicity with evidence of histopathologic changes in kidney.

Long term consumption of steviol was also investigated in hamsters to prove its chronic toxicity and carcinogenicity. Groups of 55 male and 55 female Syrian Golden hamsters were given diet containing steviol at 0, 100 and 500 mg/kg diet for 18 months (but this thesis cover only in the first year). After 6 and 12 months, five hamsters from each group were selected for urinalysis, hematological, biochemical examinations and autopsy.

Growth, relative food consumption and utilization, general appearance and mortality were similar in treated and control groups. No treatment-related changes were observed in hematological, urinary or clinical biochemical values at any stage of the study. The incidence and severity of non-neoplastic and neoplastic changes were unrelated to the level of steviol in diet.