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SPERM MORPHOLOGY

ARTHIT CHAIROUNGDUAN: DOMINANT LETHAL STUDY OF
STEVIOSIDE AND STEVIOL IN MALE HAMSTERS. THESIS ADVISOR:
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Stevioside, a glycoside isolated from *Stevia rebaudiana*, is 300 times sweeter than sucrose and is widely used as a sweetener. Stevioside offers advantages over other non-caloric sucrose substitutes by being heat-stable, resistant to acid by hydrolysis, and nonfermentable. Stevioside is composed of steviol, diterpenic carboxylic alcohol, and three glucose molecules. Stevioside has been subjected to various assessments for safety and no serious toxic effects have been reported, whereas steviol alone showed dose-related positive responses in the forward mutation assay using *Salmonella typhimurium* TM677. To further assess the genotoxicity of stevioside and steviol, we examined their possible mutagenicity, using two short-term *in vivo* mutagenicity tests, dominant lethal mutation assay and sperm head abnormality. Male hamsters were given with stevioside by gastric tube at dose levels of 0, 500, 1000, 2500 mg/kg BW/day and steviol at dose levels of 0, 100, 250, 400 mg/kg BW/day on 5 consecutive days, for 8 weeks. Each male was caged with an untreated female (1Male:1Female) for 2 weeks. Females were dissected at mid-term of gestation for the examination of uterine contents including total, live and dead implants. In addition, motility, population size and morphology were measured in sperm obtained from the cauda epididymides. In the dominant lethal test (DLT), the total number of implants, live implants, dead implants and fertility were not affected by stevioside or steviol treatment at any dose level. The percentage of abnormal sperm, sperm count and sperm motility were not significantly different between groups. Parental growth rates were reduced in hamsters treated with steviol at doses of 400 and 500 mg/kg BW/day. Relative kidney weight was significantly decreased in stevioside-treated hamsters only at a dose of 2500 mg/kg BW/day whereas relative kidney weight from hamsters treated with steviol at a dose of 400 mg/kg BW/day was unchanged. Histopathological changes of kidney including hyaline material filling in some distal tubular lumens and some necrosis in proximal tubules, were observed in both groups. However, in all cases histopathology examination results of testes and cauda epididymides were normal. Of the hamsters treated with a high dose of steviol (500 mg/kg BW/day), seven hamsters died during treatment and two died during the mating period. Histopathological examination of this group showed kidney damage and reduction of spermatozoa in seminiferous tubules. In summary, stevioside and steviol (at dose level 400 mg/kg BW/day) did not affect germ cells in the *in vivo* mutagenicity testing, either with DLT assay or sperm head abnormality.