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ALBERT MANGGADING HUTAPEA: DIGESTION, DISPOSITION AND METABOLISM OF STEVIOSIDE. THESIS ADVISORS: CHAIVAT TOSKULKAO, D.V.M., Ph.D., PAWINEE PIYACHATURAWAT, Ph.D., VARANUJ CHATSUDTHIPONG, Ph.D., VORANUNT SUPHIPHAT, Ph.D., YUPIN SANVARINDA, Ph.D. 269 P. ISBN 974-662-223-4.

Stevioside is a major sweet constituent of the herb, *Stevia rebaudiana* Bertoni, and has been commonly used as a non-caloric sugar substitute in several countries. As the use of stevioside as a non-caloric sugar substitute continues to increase, its safety should be reviewed seriously. As a part of the study of its safety, *in vivo* studies on the absorption, distribution, metabolism and excretion of stevioside in living organisms were carried out in adult hamsters. The animals were force fed with stevioside at a dose of 1 g/kg BW. Blood samples were collected at various time points between 1 to 120 hours after the feeding. Various tissues collected at 3 hours and at a 24-hour interval at 96-144 hours after the dose. Urine and feces were collected at a regular interval of 24 hours from the first 24 hours until 192 hours after the dose, then analyzed for the presence of stevioside and its metabolites. S-9 fractions of several tissues were incubated with stevioside to examine their capability to metabolize stevioside *in vitro*. The results of the *in vitro* studies showed that human saliva, purified human salivary α-amylase, pepsin, human gastric secretions, pancreatin, pancreatic α-amylase, jejunal brush border membrane of the mouse, rat and hamster did not digest stevioside. Intestinal microflora of rats, hamsters, mice and human feces digested stevioside *in vitro* and produced steviol at the end of the 2- and 4-day incubation. Stevioside was non-detectable in plasma. The peak concentration of metabolites in plasma was at 24 hours postdose, with 15α-hydroxysteviol as the principal metabolite. Liver and kidney were the largest deposit sites for stevioside and its metabolites, and kidney had the highest affinity for these compounds. The principal metabolite deposited in tissue was 15α-hydroxysteviol. Fecal excretion was the main route of elimination. The principal metabolite excreted via feces was 15α-hydroxysteviol whereas the principal metabolite excreted via urine was isosteviol. A total of 64 % of the stevioside administered was eliminated in urine and feces during the first 24 hours, and a total of 76 % during the first 48 hours after the dose. About 94% of the dose was absorbed, probably as stevioside and/or as its metabolite(s), then metabolized by various tissues, and 1% of this amount was excreted as stevioside in urine. The other 6% was excreted as stevioside in feces. The highest *in vitro* metabolizer of stevioside was liver when compared with kidney and small intestine. The principal *in vitro* metabolite produced by each these tissues was 15α-hydroxysteviol. Therefore, the results of these studies suggested that the ingested stevioside was mostly metabolized and was eliminated from the body at a high rate.