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PROMSUK JUTABHA : EFFECTS OF STEVIOSIDE AND STEVIOL ON P-AMINOHIPPURATE TRANSPORT BY ISOLATED PERFUSED RABBIT RENAL PROXIMAL TUBULE. THESIS ADVISORS: VARANUJ CHATSUDTHIPONG, Ph.D., CHAIVAT TOSKULKAO, D.V.M., Ph.D., SAMAISUKH SOPHASAN Ph.D., CHUMPOL PHOLPRAMOOL, Ph.D. 199 p. ISBN 974-664-734-2.

Stevioside is a non-caloric natural sweetener which has been used widely as a sugar substitute in many countries. It is a major component isolated from the *Stevia rebaudiana* leaves. There are several reports suggesting stevioside and its major metabolite, steviol, to have some influences on renal function, but little is known about their effects on renal tubular function. Therefore, the present study was designed to explore the direct effect of stevioside and steviol on transepithelial transport of p-aminohippurate (J_{PAH}) in the isolated S_2 segment of rabbit renal proximal tubules by using an *in vitro* microperfusion technique. Addition of stevioside at a concentration of 0.45 mM to either the tubular lumen or bathing medium or both at the same time had no effect on J_{PAH}. Similarly, a concentration of 0.7 mM when present in the lumen had no effect on J_{PAH}. However, this concentration in the bathing medium inhibited PAH transport significantly by approximately 25-30%. The inhibitory effect of stevioside was abolished after it was removed from the bath. To further examine this phenomenon, 0.7 mM stevioside was added to both lumen and bathing medium at the same time; there was no added inhibitory effect from that observed with bath addition alone. Addition of steviol (0.01-0.25 mM) to the bathing medium significantly depressed J_{PAH} (50-90%). The inhibitory effect was of dose-dependent manner and reached maximum at a concentration of 0.05 mM. Steviol at a low concentration (0.01 mM) permanently reduced J_{PAH}, but had no effect when present in the lumen. However, increasing the concentration of steviol in the lumen to 0.05 mM inhibited J_{PAH} by about 70%. The reduction of J_{PAH} after 0.7 mM stevioside or 0.01 and 0.05 mM steviol treatment occurred without the alterations of Na^+-K^+ ATPase activity and cell ATP content. The kinetic studies indicate that both stevioside and steviol inhibit transepithelial transport of PAH by interfering with the basolateral entry step, the rate-limiting step for transepithelial transport at the PAH transporter. The results from the present study suggest that stevioside does not harm the renal tubule, whereas steviol does.