

Serotonin (5-HT) and Chloride Secretion in the Rabbit Small Intestine *In-vitro*

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Serotonin contributes to the diarrheal response associated with several diseases by increasing anion and fluid secretion by intestinal epithelial cells. In segments of stripped rabbit ileum, mounted in Ussing chambers, 5-HT causes an increase in short circuit current (ΔI_{sc} ; $\mu A/1.12cm^2$) by stimulating electrogenic Cl^- secretion ($EC_{50} \sim 30\mu M$). This response is unaffected by pretreatment with tetrodotoxin (TTX; $1\mu M$) and yohimbine ($1\mu M$). In addition, neither atropine ($1\mu M$), EGTA ($2.5mM$), nor indomethacin ($10\mu M$) affected the I_{sc} response in the presence of TTX and yohimbine. Three serotonin analogs have been identified that also cause an increase in I_{sc} under these conditions: alpha-methyl serotonin (αCH_3 -5-HT), 5-carboxamidotryptamine (CT), and 5-methoxytryptamine (MOT). Following stimulation with two maximal concentrations of 5-HT ($300\mu M$), there is no further ΔI_{sc} upon addition of αCH_3 -5-HT ($300\mu M$). However, when αCH_3 -5-HT is added first (two times, at a maximal concentration of $300\mu M$), a significant response is still seen upon addition of $300\mu M$ 5-HT. This suggests that there are at least two 5-HT receptor subtypes in crypt cells of the rabbit ileum, and that αCH_3 -5-HT is an agonist at only one of these. Confirmation of this has come from adenylyl cyclase (AC) studies using membranes prepared from isolated ileal crypt cells. Serotonin ($200\mu M$) and αCH_3 -5-HT ($200\mu M$) both significantly stimulate AC activity above basal levels, $32 \pm 6\%$ and $41 \pm 7\%$ respectively, whereas MOT and CT (both at $200\mu M$) do not. Although MOT and CT cause a significant ΔI_{sc} in Ussing chamber studies, the second messenger system(s) have not yet been identified. The characteristics of the αCH_3 -5-HT sensitive receptor are most consistent with the 5-HT₄ subtype.