THE LACK OF EFFECT OF SODIUM SALICYLATE ON THE IN-SITU ABSORPTION OF A MINI-SOMATOSTATIN ANALOGUE IN THE RAT

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An octapeptide analogue of somatostatin, CGP 15425, is poorly absorbed from the gastrointestinal tract in the rat, resulting in extremely low blood levels which are difficult to measure. However, this peptide undergoes concentration in the bile which facilitates its measurement, and biliary excretion has been shown to be a reliable index of the absorption of the compound (Bell et al 1984). Sodium salicylate and other related compounds have been shown to enhance the absorption of many drugs including larger polypeptides such as gastrin from the intestine and rectum (Yoshioka et al 1982).

The effect of sodium salicylate on the absorption of the octapeptide ^{3}H-CGP 15425 (provided by Ciba-Geigy) has been studied in a closed in situ loop of rat intestine. Luminal disappearance was studied in three groups of rats (180-200g wt, n=6 per group), which were anaesthetised with sodium pentobarbitone i.p. One group of rats received the octapeptide at a concentration of 1 mg/ml in Kreb's buffer (1 ml) into a closed duodenal loop. The second and third groups received the same dose of octapeptide with 2% and 5% sodium salicylate w/v respectively. ^{14}C - PEG 4000 was added to all solutions to correct for changes in luminal volume. Samples were taken from the loops and counted for ^{3}H and ^{14}C activity at regular intervals up to 1 hour. Integrity of the peptide in all the samples was analysed by HPLC using electrochemical detection. It was noted that there was a similar luminal loss of peptide in both the salicylate-treated animals and control animals, amounting approximately 30% of the dose. In a further experiment, the procedure was repeated in rats with a biliary cannula in situ. The results are shown in Table 1.

Table 1. Biliary recovery of CGP 15425 in the presence of salicylate

Collection Period	Salicylate concentration (% w/v)			
min	0%	1%	2%	5%
0 - 15 min	0.4 ± 0.3	0.4 ± 0.4	0.3 ± 0.2	0.3 ± 0.2
15 - 30 min	0.5 ± 0.5	0.5 ± 0.4	0.5 ± 0.2	0.6 ± 0.3
30 - 45 min	0.4 ± 0.3	0.4 ± 0.3	0.5 ± 0.2	0.6 ± 0.2
45 - 60 min	0.3 ± 0.2	0.4 ± 0.3	0.5 ± 0.2	0.8 ± 0.3
Total	1.6 ± 1.0	1.7 ± 1.1	1.8 ± 0.6	2.3 ± 0.8

Combustion of the tissues showed that approximately 25% of the peptide or its metabolites remained associated with the gut wall without undergoing further absorption, the remaining 75% being unabsorbed during the period of the experiment. Thus sodium salicylate did not promote the absorption of the peptide from the gut, presumably due to the strong binding of the material to the epithelium.

Bell, J. M. et al (1984) J. Pharm. Pharmacol. 36: Suppl. 88P.
Yoshioka, S. et al (1982) J. Pharm. Sci. 71: 593-4.