RANITIDINE: AN IMPROVED H_2-RECEPTOR ANTAGONIST FOR THE TREATMENT OF PEPTIC ULCER

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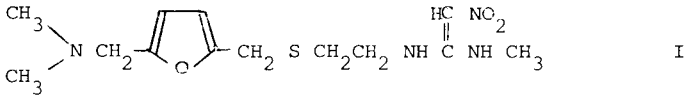
The most important consequence resulting from the sub-classification of histamine receptors into two distinct types,H_1-and H_2-receptors, has been the development of H_2-antagonists for the treatment of peptic ulcer. Such antagonists, like histamine itself, possess an imidazole ring or a closely related heterocycle such as thiazole. Identification of H_2-antagonist activity in substituted furan structures has revealed the possibility of obtaining an improved H_2-antagonist regarding potency and specificity of action and the data presented below has led us to the conclusion that ranitidine (I) is just such a drug.



I

In vitro studies have characterised ranitidine as a selective H_2-receptor antagonist (Daly et al 1980) while in vivo studies have shown that ranitidine potently inhibits gastric acid secretion, in this test it is 5-10 times more potent than cimetidine. Measurement of mucosal blood flow by the ^{3}H-aniline clearance method has shown that inhibition of acid secretion by ranitidine is not a consequence of reduced mucosal blood flow (Table 1).

Table 1. Effects of ranitidine administered orally on gastric acid secretion and blood flow in the conscious Heidenhain pouch dog.

Secretagogue	Ranitidine mg kg^{-1}	Percentage change in Acid secretion (A)	Mucosal blood flow (MBF)	Ratio of MBF/A
Histamine	0.05	-44	-16	+50
Pentagastrin	0.25	-64	-46	+49
Bethanechol	0.15	-51	-14	+66

Leslie & Walker (1977) and Delle Fave et al (1977) have shown that cimetidine possesses anti-androgenic activity in rat,dog and man. Table 2 shows that ranitidine, even in excessive doses, is free from such an action.

Table 2. Seminal vesicle and prostate weights (g) of animals treated daily with oral ranitidine

Ranitidine mg $kg^{-1}day^{-1}$	Rat+ Prostate	Seminal vesicle	Dog* Prostate
Control	0.57	1.34	11.5
25	0.60	1.45	7.9
50	0.66	1.64	NT
75	NT	NT	12.8
100	0.60	1.64	NT
225	NT	NT	9.3

+Rats treated for 10 weeks. *Dogs treated for 54 weeks. NT not tested.

Ranitidine is a potent inhibitor of gastric acid secretion which results from a selective blocking action at H_2-receptors and not from a reduction in mucosal blood flow. Unlike cimetidine, ranitidine has no anti-androgenic activity.

Daly,M.J. et al (1980) Br.J.Pharmac. In press
Delle Fave,G.F. et al (1977) Lancet: 1319
Lesley,G.B.Walker,T.F. (1977) In Proc.2nd Int.Symposium on H_2-receptors antagonists. Excerpta Medica: Amsterdam