LETTERS TO THE EDITOR

Aspirin-induced gastric mucosal damage in rats: cimetidine and deglycyhrrhizinated liquorice together give greater protection than low doses of either drug alone

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The value of some drugs is reduced because they damage the gastric mucosa, so that ways of preventing this are therapeutically desirable. In rats, the histamine H_2 receptor antagonist cimetidine reduced the damage caused by aspirin, but a very high dose was needed to give almost complete protection (Okabe et al 1977). Deglycyrrhizinated liquorice (DGL) also lessened gastric mucosal damage (Rees et al 1979), and we have therefore examined the effect with small doses of both drugs given together.

Using the method described by Rees et al (1979), male Wistar rats weighing 180–230g were fasted from 15.00 h to 11.00 h the next day, but allowed free access to water. They were divided into four groups of equal numbers, usually 4 or 6 per group, and given aspirin 60 mg/rat by stomach tube as a suspension in 2 ml 1% tragacanth. The additional treatments were as follows: (1) 0·5 ml 0·15 M NaCl intraperitoneally. (2) 5 mg kg^{-1} cimetidine in 0·15 M NaCl intraperitoneally. (3) 50 mg DGL mixed with the aspirin + 0·15 M NaCl intraperitoneally. (4) DGL by stomach tube + cimetidine intraperitoneally.

After 4 h at room temperature (23–27°C) the rats were killed by inhalation of chloroform and the stomachs excised. Gastric mucosal damage was assessed using the scoring system described by Rees et al (1979). Protection against gastric mucosal damage by aspirin was greater using cimetidine and DGL than with either drug alone. The median reductions in the mucosal damage scores were 80% for cimetidine + DGL, 25% for cimetidine, and 55% for DGL (Table 1).

Table 1. Gastric mucosal damage scores (Rees et al 1979). All rats received aspirin, and only the additional drugs are shown. Each score is a median, with semi-quartile ranges in parentheses.

Group N	Controls (A) 28	Cimetidine (B) 28	DGL(C) 20	Cimetidine + DGL(D) 27
lesion score	10(6–15)	7·5(4–11)	4·5(1–11)	2(1–6)
% protection		25	55	80

The probability values (1-tailed Mann-Whitney U-test) for differences between the groups were: A vs B, $P = 0.049$; A vs C, $P = 0.0253$; A vs D, $P = 0.00014$; B vs C, $P = 0.17$; B vs D, $P = 0.0031$; C vs D, $P = 0.156$.

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Cimetidine 5 mg kg^{-1} gave slightly less inhibition of aspirin-induced gastric mucosal damage than that obtained with 12·5 mg kg^{-1} cimetidine intraperitoneally in pylorus-ligated rats (Okabe et al 1977). Inhibition of gastric acid secretion through blockade of histamine H_2 receptors probably accounted for at least some of the protective effect of cimetidine. However, we could not determine the effect on acid secretion because the pylorus was not ligated. Presumably cimetidine reduced the amount of acid available for back-diffusion through the mucosa, and lessened the ionization and gastric absorption of aspirin. There is some evidence that the protection by cimetidine can also be independent of inhibition of acid secretion (Kauffman & Grossman 1978) but this is disputed (Robert et al 1979).

DGL 50 mg gave a smaller, but nevertheless significant, reduction of gastric mucosal damage than that obtained by Rees et al (1979) with 100–500 mg DGL. The mechanism of action by DGL is not understood but may involve a prolonged increase in resistance of the mucosa to damage (Tewari & Wilson 1973).

The efficacy of low doses of cimetidine and DGL given together decreases any problems of drug toxicity, and it seems worthwhile to examine such combinations for the reduction of gastric mucosal damage by aspirin and similar drugs, and possibly in the treatment of peptic ulceration.

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