

Studies are now in progress, using the free films concurrently prepared as controls, to evaluate the simulated coatings applied to tablets and to study some of the relations among coating solution, tablet substrate, and dissolution properties. It is felt that this approach will yield greater correlation of data and give a more practical representation of films deposited on commercially coated tablets.

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## Effect of Aspirin and Ethanol on the Gastric Mucosa of the Rat

**Keyphrases** □ Aspirin and ethanol—effect on gastric mucosa, rats □ Ethanol and aspirin—effect on gastric mucosa, rats □ Gastric mucosa irritation—effect of aspirin and ethanol, rats

Sir:

In 1964, Davenport (1) reported gastric mucosal injury in dogs by aspirin. Mucosal injury also was reported in humans (2, 3), dogs (4), cats (5), guinea pigs (6), and albino rats (7, 8). In 1967, Davenport (9) reported that ethanol damaged the canine oxyntic glandular mucosa as observed by changes in Na<sup>+</sup> output. Concentrations of 8.2% or smaller caused no damage, whereas 27% ethanol caused a large positive Na<sup>+</sup> flux, indicating damage to the mucosal barrier. The effect of 14% ethanol was intermediate. Recently, Davenport (10) reported that concurrent exposure to nondamaging concentrations of ethanol potentiated the damaging

effects of aspirin. Our observations with rats are in essential agreement with his findings in dogs.

Twenty-three male Holtzman rats<sup>1</sup> weighing between 160 and 180 g. were fasted for 36 hr., water being allowed *ad libitum*, prior to oral administration of 0.3 ml. of 30% ethanol to each animal. This amount and concentration of ethanol given to the rats would be roughly equivalent to a generous dry Martini taken by a human being on an empty stomach. Two hours after administration of the ethanol solution, the rats were killed. Then their stomachs were removed, opened along the line of lesser curvature, stretched, and pinned on a large rubber stopper, and the mucosal surface was examined for lesions and evidence of hemorrhage.

The severity of the lesions was rated on an 8-point scale (a rating of 1 is normal and 8 is most severe) developed by Morris *et al.* (11). The mean lesion rating of the 23 stomachs was 5.4, a rating that can be described as moderate. The appearance and severity of these lesions were similar to those described earlier for rats given 0.28 mmole/kg. body weight of aspirin in citrate buffer, pH 5.6 (7, 8, 11). Nine additional rats were treated in the same way, except that they were given an oral dose of 0.28 mmole/kg. body weight of aspirin dissolved in 30% ethanol. All nine animals developed severe lesions, which were rated as 8 on the 8-point scale. In all cases the lesions appeared only in the acid-secreting corpus portion of the stomach.

It is clear from these observations that a solution of 30% ethanol in water causes damage to the gastric secretory mucosa of the albino rat as does 27% ethanol to that of the dog (9), and that the injurious effects of aspirin and ethanol are additive in the rat as they are in the dog (10).

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