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Received December 16, 1971.
Accepted for publication March 9, 1972.
Supported in part by Grant NB-04349 from the U.S. Public Health Service.
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# Technique for Preparing Simulated Coated Dosage Forms and Preliminary Evaluation of Sprayed and Cast Films

**Keyphrases** ☐ Films, sprayed and cast, from the same coating solution—method, apparatus ☐ Simulated coated dosage forms—free films, method and apparatus ☐ Coating solutions—method and apparatus for preparing both cast and sprayed free films

*Sir:*

Numerous investigations have appeared in the literature evaluating polymeric films either on the basis of their performance on coated tablets prepared by conventional spraying techniques or as unsupported free films prepared by casting techniques.

In a publication dealing with free films, Kanig and Goodman (1) pointed out the benefits of studying the properties of free films without introducing the variables arising from the coating technique or the nature of the dosage form.

In contrast, Zatz *et al.* (2) stated that free films only provide a model for evaluating gross properties of applied films, with limited information in other areas, while Banker *et al.* (3) concluded that free film evaluations should not be used as the sole criterion for accepting or rejecting potential film coatings.

**Table I**—Free Film Profiles[a]

| Property | Cast Film | Sprayed Film |
|---|---|---|
| Percent volatiles[b] | 8.12 ± 0.28 | 9.16 ± 0.34 |
| Tear strength, g.[c] | 7.20 ± 0.44 | 5.85 ± 0.32 |
| Thickness range, mm. | 0.048–0.052 | 0.043–0.048 |
| Water vapor permeability[d] | 0.8817 ± 0.0362 | 0.8977 ± 0.0126 |
| Weight/unit area, g.[e] | 0.3968 | 0.3728 |

[a] These numbers represent mean values of at least four determinations. [b] Measured weight loss under vacuum at 40° to constant weight. [c] Elmendorf Tear Tester, modified ASTM, D687. [d] Modified ASTM, E96-66, units = g. cm. cm.$^{-2}$ × 10$^{-6}$/24 hr. *Reference 5.* [e] Area of test strip = 80 cm.$^2$.

These reports suggest the importance of a technique or method that would afford the investigator the opportunity to prepare both cast and sprayed free films from the same coating solution and also permit application to simulated dosage forms during a single experiment. In fact, Allen *et al.* (4) recently pointed out the need for a method of preparing free films which simulate, more realistically, those deposited on dosage forms.

To attempt such studies, we devised an apparatus and developed techniques which afford us the options mentioned. The apparatus consists basically of a Teflon-coated metal plate with holes carefully machined to accommodate accurately tablets so that only the tablet surfaces are exposed to the coating formulation. The plate used was 16.5 cm. wide and 56.0 cm. long, with a thickness of 0.385 cm. It consisted of four pairs of holes, each having a diameter of 3.2 cm., with each pair of holes located 9.0 cm. from the next pair in the direction of casting. The holes were spaced in this manner to allow maximum recovery of unsupported free film samples at the same time coated tablets were prepared. The actual spacings are not critical and were selected to provide film samples of adequate size for selected ASTM test procedures.

The tablets used were 3.2 cm. in diameter and were prepared on a Carver press[1] at a weight of approximately 3.0 g., using 11,000 lb./sq. in. pressure. This combination yielded a thickness optimal for use in the coating plate and subsequent test procedures. At this point in the studies, any clearance variation between tablet and hole did not interfere with preparation or recovery of samples so long as a relatively tight fit was maintained.

Experiments were conducted using a casting knife[2] following a technique similar to that outlined by Munden *et al.* (5) and also using a spray[3] process outlined by Allen *et al.* (4). The Teflon plate can be modified into a rotating device where the spray distance, spray rate, and spray time can be varied as well as the revolutions per minute of the device.

Our first concerns were testing the uniformity and investigating the equivalency of cast and sprayed free films as well as developing control tests for these free films. Typical results of these studies for a film consisting of methylcellulose[4] are summarized in Table I.

[1] Model B, Fred S. Carver Inc., Summit, N. J.
[2] Gardner Laboratory Inc., Bethesda, Md.
[3] E. G. A. Type Spray Gun, DeVilbiss Co., Broomall, Pa.
[4] Methocel HG, Dow Chemical Co., Midland, Mich.

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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Received October 28, 1971.
Accepted for publication March 9, 1972.
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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 $Na^+$ output. Concentrations of 8.2% or smaller caused no damage, whereas 27% ethanol caused a large positive $Na^+$ 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[1] 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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Received November 16, 1970.
Accepted for publication December 1, 1971.
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[1] Holtzman Rat Co., Madison, Wis.