A PRACTICAL ENTERIC COATING FOR THE RETAIL PHARMACIST.*

BY F. S. BUKEY AND PHYLLIS RHODES.[1]

Several references to the use of gelatin treated with formaldehyde as an enteric coating for pills and capsules are to be found in the literature. The results reported from these researches are varied. Hausmann (1) patented the process of immersing filled capsules in an 0.8 per cent solution of formaldehyde for 18 minutes. Dr. Hans Rumpel (2) patented the process of treating empty capsules with mixtures of formaldehyde and other solvents. He made the claim that the capsules would not harden with age. Smith (3) immersed filled capsules in 10 per cent aqueous solution of formaldehyde for 15 minutes. Ballenger and Elder (4) suggest two methods, one in which the capsule is immersed in 1 part of 40 per cent formaldehyde solution in 40 to 60 parts of water. In the other the capsules are exposed to the vapors of formaldehyde for 6–12 hours. DeLanney (5) reports soaking unfilled capsules in 20 per cent formaldehyde solution for several hours. Scoville (6) immersed filled capsules in a 1 per cent solution of formaldehyde for 30 seconds and suggests that they be stored for two weeks before they are used. In a second paper (7) Scoville states that he uses the same solution concentration and that the capsules will be in good condition for a year. Cooper and Dyer (8) in their textbook, "Dispensing for Pharmaceutical Students," state that filled capsules immersed in *formaldehyde solution B. P. (36 to 38 per cent w/v) for 10 minutes* have an ideal enteric coating. They also claim that the rate of the solution in the pancreatic fluid varies inversely with the length of the formaldehyde treatment. They find that a capsule treated for 5 minutes requires 3 hours for digestion but one treated for 15 minutes digests in 1 hour.

It would seem from the results of the above investigations that almost any concentration of formaldehyde solution could be used in the treatment of enteric coated capsules. It was decided, however, to check some of this work using the X-ray to locate the point of disintegration. Both pills and capsules were used in this study. The pill mass was made of 95 parts barium sulphate, 5 parts althea root and a sufficient quantity of syrup. Methylene blue was also added to some of the masses. The pills were about one-quarter inch in diameter; when dry they were coated with gelatin. The gelatin solution used for the coating was prepared by warming flake gelatin in sufficient water to make a thick solution. It was found that the pill could be removed from the pin used for dipping, without sticking to the fingers, in about two minutes. The small hole left by the pin was sealed by touching this spot with a hot spatula. The gelatin coating was then allowed to harden. Capsules, size O, filled with barium sulphate were used and sealed in the usual manner. The pills and capsules were then ready for immersion in formaldehyde solution.

Each of the subjects in this experiment was given a pill and capsule to be taken at the same time. The first picture was taken one hour after the pills had been swallowed. If the pill and capsule appeared low for the normal position of

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the stomach, two ounces of Bari-o-meal in eight fluidounces of water were given before the next picture. The second picture was usually taken at the end of the second hour. The barium sulphate outlined the stomach so that the exact position of the pill and capsule could be located. The Bari-o-meal masked the pill and capsule in a very few cases.

The results of the experiment are listed according to the concentration of the aqueous formaldehyde solution and the length of the time immersed. The observations and results are listed as follows:

40% Time 10 Minutes.—Two subjects were used. Pictures were taken for 4 hours, with negative results on disintegration. In one case the pill contained methylene blue and in the other case, the capsule. The urine was not colored in either instance.

40%, Time 1 Minute.—Two subjects were used. Pictures were taken for 7 hours. In one case the pill and capsule were in the stomach at the end of 7 hours. In the other case they remained in the stomach 2 hours and disintegrated in the intestine at the end of 5 hours.

40%, Time 15 Seconds.—Two subjects were used. In one case pictures were taken for 5 hours. Pill and capsule remained in the stomach 3 hours, not disintegrated at the end of 5 hours. In the other case pictures were taken for 3 hours. Pill and capsule remained in the stomach 1 hour. At the end of 3 hours the pill was low in the intestine and the capsule had disintegrated.

20%, Time 15 Seconds.—Two subjects were used. Eight pictures were taken. In one case the pill and capsule were in the stomach at the end of 5 hours and were still intact at the end of 8 hours. In the second case the pill was in the stomach at the end of 8 hours; the capsule was in the intestine intact. In both of these cases methylene blue indicated disintegration at a later time.

10%, Time 4 Minutes.—Three subjects were used. Pictures were taken for 8 hours. In each of the three cases the pill and capsule were in the stomach at the end of 8 hours. Methylene blue gave no evidence of later disintegration.

10%, Time 15 Seconds.—Four subjects were used. In one case five pictures were taken. The pill left the stomach in 2.5 hours and disintegrated in the intestine in 2 hours. The capsule remained in the stomach 3 hours and disintegrated in the intestine in 2 hours. In the second case, six pictures were taken. The pill and capsule remained in the stomach 4 hours and disintegrated in the intestine in 2 hours. In the third case seven pictures were taken. Pill and capsule left the stomach in 3 hours. The capsule disintegrated in the intestine in 4 hours but the pill remained intact. In the fourth subject both the pill and capsule were in the stomach at the end of 7 hours.

10%, Time 10 Seconds.—Two subjects were used. In one case six pictures were taken. The pill disintegrated in the intestine in 3 hours and the capsule in 5 hours. In the second subject the fate of the pill was unknown but the capsule disintegrated in the intestine in 5 hours.

10%, Time 5 Seconds.—Two subjects were used in this experiment, both reacted in almost the same manner. Five pictures were taken of each. The pill and capsule remained in the stomach 2 hours and disintegrated in the intestine in 2 hours.

5%, Time 2 Seconds.—Three subjects were used; with the first, five pictures were taken. The capsule was in the stomach at the end of 5 hours and the pill disintegrated there. With the second subject, nine pictures were taken. The capsule was intact in the stomach at the end of 9 hours and the pill disintegrated there in 7 hours. The third subject had two pictures taken. Both the pill and capsule were out of the stomach in 1 hour, and disintegrated in the intestine sometime in the second hour.

The results of these experiments show that the time of disintegration does not vary inversely with the length of immersion, as Cooper and Dyer have stated. They used the artificial pancreatic digestion method of testing and this may be the cause for the results they report.

The above experiments also show that several of the other early investigators were using too strong a solution of formaldehyde, thus producing a pill or capsule

which would pass through the digestive tract without disintegration. A considerable variation was noted in the time that was required for the pill and capsule to leave the stomach. In one subject, it was noted that the pill and capsule would remain in the stomach after a meal had passed through it. This condition seemed to be normal for this individual as the same results were obtained in three different experiments.

A formaldehyde concentration of 10 per cent and an immersion time of 5 seconds was considered to be the best method. This gave a disintegration in the upper intestine, which is usually desirable. If further penetration is desired, the 10- or 15-second immersion would be better.

We do not believe that the gelatin coating, formaldehyde treated, would be ideal for commercial products because of the mechanical difficulties which would develop. The method could be used successfully, however, by the pharmacist who may have an occasional call for a small number of specially prepared capsules. No extra equipment is necessary and the product, when dry, is not unsightly. The pharmacist must be careful that the capsules are well sealed or the contents are in some danger of becoming wet with the formaldehyde solution.

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A PROPOSED FORMULA FOR BELLADONNA OINTMENT.*

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Therapeutically, ointment of belladonna seems to have, for the most part, justified the claims made for it. Pharmaceutically, however, many complaints have been made about the present official formula. Chief among these are:

1. That it stains due to the presence of chlorophyll in the pilular extract.
2. It is difficult to rub the extract smooth previous to incorporation in the base. This may be due, in part, to the character and quality of the extract.
3. The finished product is too sticky.

Believing that it should be possible to prepare a satisfactory belladonna ointment free from the objections enumerated, prompted this study.

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