unless some manufacturer begins to separate the 1,2,4 from the 1,2,5 and markets a single salt in place of the mixture or some one actually makes the 1,2,6 compound.

5. That the proportion of the 1,2,4 to the 1,2,5 is approximately 3 to 1.

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A COMPARATIVE STUDY OF ENTERIC COATINGS.[1]

BY F. S. BUKEY AND PHYLLIS RHODES.[2,3]

The authors in a previous study of enteric coatings found a wide variation in the efficiency of the coating materials. It was, therefore, decided to test various types of commercial coatings. Several of the pharmaceutical manufacturers agreed to coöperate in this study by applying their enteric coatings on tablets of barium sulphate.

Five different enteric coatings were submitted by the manufacturers for this study. Among these types were two of keratin, one salol-shellac, one shellac and one composed of a mixture of salol and resins. In every case the products submitted were finished and in external appearance resembled any sugar-coated tablet. The uncoated tablets measured 10.5 mm. in diameter and 4.8 mm. in thickness. In addition to the tablets, one manufacturer supplied enteric and sugar-coated No. 1 capsules filled with barium sulphate.

The subjects for these experiments were picked from the student body and in every case normal individuals in apparent good health. The X-ray was used to determine the exact point of disintegration. In general, the following procedure was used in making this study. Each subject was given a certain number of tablets followed at once with a glass of water containing a teaspoonful of Bari-o-meal. The Bari-o-meal was sufficient to outline the stomach, but did not produce a density great enough to mask the tablets. The first radiograph was usually taken after 30 minutes and others followed at desired intervals until disintegration occurred.

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The results of this study have been tabulated into groups according to the type of coating. The chart gives the number of tablets taken, the time at which they were taken and the point and time of disintegration.

Kind of Coating.	Subject.	Number of Tablets Taken.	Time of Taking.	Point and Time of Disintegration.
Keratin No. 1	No. 1	3	4:30 P.M.	3, stomach, 45 min.
	No. 2	3	4:30 P.M.	3, stomach, 45 min.
	No. 3	3	7:40 P.M.	3, stomach, 60 min.
	No. 4	3	7:40 P.M.	3, stomach, 80 min.
	No. 5	3	7:40 P.M.	3, stomach, 80 min.
	No. 6	3	8:10 P.M.	1, stomach, 45 min. 2, stomach, 60 min.
	No. 7	3	8:10 P.M.	1, stomach, 45 min. 2, stomach, 60 min.
	No. 8	3	8:10 P.M.	2, stomach, 60 min 1, stomach, 80 min.
	No. 9	3	8:10 P.M.	3, stomach, 80 min.
Keratin No. 2	No. 1	4	10:00 A.M.	1, ascending colon, 6 hrs. 30 min. 2, descending colon, 10 hrs. 20 min. 1, pelvic colon, 10 hrs. 20 min.
	No. 2	4	9:00 A.M.	2, ascending colon, 11 hrs. NOTE: Two were in the stomach at the end of 13 hrs., point of disintegration not determined.
	No. 3	4	9:30 A.M.	1, small intestine, 10 hrs. 30 min. 3, small intestine, 12 hrs. 30 min.
	No. 4	4	9:00 A.M.	3, ascending colon, 12 hrs. 1, transverse colon, 24 hrs.
	No. 5	4	1:40 P.M.	1, stomach, 9 hrs. 10 min. 1, pelvic colon, 17 hrs. NOTE: The point of disintegration of 2 tablets was unknown.
	No. 6	4	1:40 P.M.	2, descending colon, 17 hrs. NOTE: The point of disintegration of 2 tablets was unknown.
	No. 7	4	7:00 A.M.	3 were excreted in 29 hrs. NOTE: The point of disintegration of 1 tablet was unknown.
Shellac (3 coats)	No. 1	3	1:30 P.M.	3, stomach, 3 hrs.
	No. 2	3	1:30 P.M.	3, stomach, 3 hrs.
	No. 3	3	6:30 P.M.	3, stomach, 1 hr.
	No. 4	3	1:45 P.M.	3, stomach, 1 hr. 20 min.
	No. 5	3	1:45 P.M.	1, stomach, 1 hr. 25 min. 2, stomach, 2 hrs.
	No. 6	3	1:45 P.M.	1, stomach, 1 hr. 30 min. 2, stomach, 2 hrs. 5 min.
	No. 7	3	2:00 P.M.	3, stomach, 1 hr. 40 min.
	No. 8	3	2:00 P.M.	3, stomach, 1 hr. 20 min.
Salol and gum resin mixture	No. 1	3	11:00 A.M.	1, small intestine, 5 hrs. 10 min. 1, stomach, 7 hrs. 1, small intestine, 7 hrs.
	No. 2	3	12:30 P.M.	1, stomach, 3 hrs. 30 min. 1, stomach, 5 hrs. 30 min. 1, small intestine, 6 hrs. 30 min.

	No. 3	3	12:30 P.M.	1, stomach, 3 hrs. 30 min. 1, stomach, 4 hrs. 30 min. 1, stomach, 6 hrs. 30 min.
	No. 4	3	3:00 P.M.	1, stomach, 4 hrs. 1, small intestine, 4 hrs. NOTE: The point of disintegration of one was not determined. It was still in the stomach at the end of 7 hrs.
	No. 5	3	3:00 P.M.	1, small intestine, 4 hrs. 1, small intestine, 5 hrs. NOTE: The point of disintegration of one was not determined. It was still in the stomach at the end of 7 hrs.
	No. 6	3	11:00 A.M.	1, small intestine, 4 hrs. 30 min. 2, small intestine, 5 hrs. 30 min.
	No. 7	3	11:00 A.M.	1, stomach, 5 hrs. 30 min. NOTE: The point of disintegration of two was not determined. They were still in the stomach at the end of 6 hrs. 30 min.
	No. 8	3	12:30 P.M.	2, stomach, 4 hrs. 1, stomach, 5 hrs.
	No. 9	3	4:00 P.M.	1, small intestine, 4 hrs. 2, small intestine, 5 hrs.
	No. 10	1	4:00 P.M.	1, small intestine, 4 hrs.
	No. 11	3	4:00 P.M.	1, small intestine, 4 hrs. 2, small intestine, 5 hrs.
	No. 12	3	4:00 P.M.	1, small intestine, 5 hrs. 2, small intestine, 6 hrs.
	No. 13	3	5:15 P.M.	1, stomach, 5 hrs. 1, stomach, 6 hrs. NOTE: The point of disintegration of one was unknown. It was still in the small intestine at the end of 7 hrs.
	No. 14	3	5:15 P.M.	1, stomach, 3 hrs. 2, small intestine, 6 hrs.
Salol-shellac	No. 1	2 T 2 C	11:00 A.M.	1 capsule, stomach, 2 hrs. 30 min. 1 capsule, small intestine, 5 hrs. 30 min. 2 tablets, small intestine, 6 hrs. 30 min.
	No. 2	2 T 2 C	11:00 A.M.	1 capsule, small intestine, 2 hrs. 30 min. NOTE: The point of disintegration of one capsule was unknown. 2 tablets, stomach, 5 hrs. 45 min.
	No. 3	2 C 2 T	11:00 A.M.	1 capsule, stomach, 6 hrs. 1 capsule, stomach, 8 hrs. 2 tablets, stomach, 8 hrs.
	No. 4	2 C 2 T	12:45 P.M.	2 capsules, stomach, 5 hrs. 15 min. 2 tablets, small intestine, 8 hrs. 30 min.
	No. 5	2 C 2 T	10:00 A.M.	NOTE: The point of disintegration of 2 capsules was not known. 1 tablet, small intestine, 6 hrs. 1 tablet, small intestine, 7 hrs.
	No. 6	2 C 2 T	11:00 A.M.	2 capsules, small intestine, 3 hrs. 1 tablet, small intestine, 4 hrs. 45 min. 1 tablet, small intestine, 6 hrs.

It is evident from the data obtained that there is about as much variation in the commercial coatings, as in those prepared in the laboratory. On considering the keratin coating No. 1, we find total disintegration in the stomach, the average time being about one hour. These tablets are of no value for enteric medication. From experience we have had with keratin as an enteric coating we concluded that the adverse results were caused by a faulty method of application. The results of the experiments for keratin No. 2, showed that 13 tablets disintegrated in the colon, 4 in the small intestine, and 1 in the stomach. The point of disintegration of 7 was unknown, and 3 were excreted. This coating proved to be 80.95% efficient. In making this calculation for the various coatings, results were disregarded in all cases where the exact point of disintegration was unknown. The results from the keratin No. 2 coating indicate an exceptionally good enteric coating. The experiments for the shellac coating show that these tablets are of no value for enteric medication. The average time for disintegration was between 70 and 100 minutes. Faulty application cannot be claimed for this coating as other tablets purchased on the market disintegrated in about the same average time. In the case of the salol resin mixture, 13 tablets disintegrated in the stomach and 22 tablets in the intestine. Five tablets had not disintegrated when the last picture was taken, and their fate was not determined. This enteric coating was 63.00% efficient. The results of the experiments using salol shellac showed that 8 tablets disintegrated in the small intestine and 4 in the stomach. Four capsules disintegrated in the small intestine and 5 in the stomach. The fate of 3 capsules was not determined. The average time of disintegration for the tablets was 6 hours and of the capsules was 4 hours. The percentage efficiency of the tablets was 66.66% and of the capsules was 44.44%. In this case, it appears that the tablets are a better means of medication than the capsules.

It may be concluded that none of the enteric coatings studied was perfect. The best results would seem to be obtained with keratin when properly applied. However, if one considered the absorption rate of the colon less than that of the small intestine, the salol mixtures would be better. Capsules with the same type of enteric coating as a tablet are not as efficient, due no doubt to mechanical difficulties as the capsules roll thin on the ends during the coating process. Shellac by itself is of no value as an enteric coating.

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ENTERIC COATINGS. I. A LABORATORY METHOD FOR THE STUDY AND CONTROL OF ENTERIC COATINGS.*

BY MILTON WRUBLE.

Several years ago a preliminary report on enteric coatings was made by the writer (1). Since that time the opportunity has presented itself to study the prob-

* The Research Laboratories, The Upjohn Company, Kalamazoo, Michigan. (June 26, 1935.)