A STUDY OF THE DISINTEGRATION RATES OF COATED TABLETS

By W. R. Howard

From the Laboratories of Savory and Moore Ltd.

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It is stated in the monographs of the British Pharmaceutical Codex for a number of compressed tablets that they may be coated and that, in such cases, the Disintegration Test of the British Pharmacopœia does not apply. Since for the purpose of control some disintegration test was desired it was decided to investigate the application of the official disintegration test to such tablets and to examine the validity of the exemption.

The investigation was restricted to the coated tablets included in the British Pharmaceutical Codex and the tests were carried out using a simple apparatus essentially the same as that described by Berry and Nutter Smith[1] complying with the requirements of the British Pharmacopœia and allowing 5 tablets to be tested at a time. Since the tablet disintegration test of the British Pharmacopœia is a limit test and the end-points could not be determined with greater accuracy, the disintegration times were recorded to the nearest half-minute and the average times have been rounded off similarly. The duration of the test was arbitrarily limited to 4 hours in view of the likely length of time that the tablets would stay in the stomach, and on practical considerations. Few of the tablets actually broke up under the conditions of the test and a common result was the splitting of the coat giving a tablet exposed at the edge but covered on both faces by a layer of the coat which frequently had a marked protective effect.

Tablets were considered to have disintegrated when at least one of the following criteria was satisfied: 1. The tablet broke into several small pieces; 2. A recognisable residue of the tablet could no longer be seen in the tubes. Tablet cores smaller than one-sixteenth of an inch in diameter were classed as too small for recognition; 3. Where the coat split as described above, the discs of the coat separated and no recognisable residue of the tablet remained.

Even so the determination of the end-points was a matter of difficulty in several cases and it was found necessary to make trials and to observe tablets one at a time in order to reach a reasonable standard of reliability.

Samples of tablets were obtained from several sources at random and it is known that the products of at least 6 makers are included in the series. In view of the mixing action of the tablet coating process it seemed reasonable to regard the samples examined as representative of the bulk. In general a sample of 5 tablets was used for the actual determinations but where the variations were considerable 10 tablets were used in determining averages. Only 5 representative results are shown in Table I for the sake of conciseness.

TABLE I

Tablets		Disintegration Times in Minutes					Averages
Tablets of Aloes...	(a)		more than 240				—
and Nux Vomica	(b)	41	33½	31½	31½	31	33½
Tablets of Aloin :—							
½ grain	(a)		No definite end-point				>150
,, ...	(b)	37	46	50	46	61	48
,, ...	(c)	22	16½	22½	20½	20	20½
1 grain	(a)	9	10½	12	13½	12	11¼
Compound Tablets of Aloin ...	(a)	24½	24½	28	28	23½	26
,, ,, ,, ...	(b)		No definite end-point				about 40
,, ,, ,, ...	(c)	43	31½	30	36	39	36
,, ,, ,, ...	(d)	21½	21	27½	24½	28½	24½
Tablets of Cascara Sagrada :—							
5 grains...	(a)	19½	22½	22	22	22	21½
,, ...	(b)	16	17	17	17	18½	17
2 grains...	(a)	13	13½	10½	10½	12½	12
,, ...	(b)	10½	11	8½	9	10	10
,, ...	(c)	37	42	62	48	58	49
Compound Tablets of Cascara	(a)		more than 240				
Sagrada...	(b)		more than 240				
,, ,, ,,	(c)	58	59	61	58	58	59
Compound Tablets of Colocynth and							
Jalap	(a)	95	107	77	93	107	96
,, ,, ,,	(b)	121	111	106	115	109	112
,, ,, ,,	(c)	222	240	155	230	>240	?
Tablets of Iron Carbonate ...	(a)		Coat apparently not penetrated				
,, ,, ,, ...	(b)		Disintegration stopped at 120–135 minutes				
			Soft core ⅛ in. diameter				
,, ,, ,, ...	(c)	80	61	81	73	62	71
,, ,, ,, ...	(d)	151	>240	240	>240	>240	?
Tablets of Iron Carbonate and Aloin	(a)	125	135	142	135	138	135
Tablets of Iron Carbonate and Arsenic	(a)	208	>240	>240	>240	>240	?
,, ,, ,,	(b)	158	83	125	110	108	117
,, ,, ,,	(c)		more than 240				
Tablets of Ferrous Phosphate with							
Quinine and Strychnine (60 minim)	(a)		more than 240				
,, ,, ,,	(b)	111	134	170	170	180	157
,, ,, ,,	(c)	12½	14	13	14½	14½	13½
,, ,, ,,	(d)	53½	30½	39½	38½	41	40½
Tablets of Ferrous Sulphate, 3 grains	(a)	155	160	102	112	105	127
,, ,, ,,	(b)	23	20	21½	19½	17	19¾
,, ,, ,,	(c)	111	174	126	126	140	135
,, ,, ,,	(d)	14	13	15	14	13½	14
Compound Tablets of Ferrous Sulphate	(a)	9½	11	9	11½	10	10
,, ,, ,,	(b)	20	16	17	17½	19	18
,, ,, ,,	(c)	41	36	36	50½	42	41½
,, ,, ,,	(d)	190	220	190	220	195	203
,, ,, ,,	(e)	21½	11½	8½	10½	14½	13½
Compound Tablets of Hypophosphites	(a)		more than 240				
,, ,, ,,	(b)	18	19½	17	18½	16½	18
,, ,, ,,	(c)	22½	24	25½	29	23	25
,, ,, ,,	(d)	24	27½	26½	25½	30½	27
Compound Tablets of Phenolphthalein	(a)	180	140	145	210	>240	?
,, ,, ,,	(b)	43	43	55	39½	44½	45
,, ,, ,,	(c)	17½	18	16	17	20½	18
Tablets of Phenytoin Sodium, 0·1 gm.	(a)	9½	9½	9½	10	9	9½
,, ,, ,,	(b)	10½	11	11	10	12½	11
,, ,, ,,	(c)	12	13	15	13	13	13
,, ,, ,,	(d)	14½	12½	13	13	13	13
,, ,, ,,	(e)	19½	39	>240	35	24	?

Comments:

Tablets of Aloes and Nux Vomica:

(a) The tablet was only attacked at the edges leaving a large hard core.

Tablets of Aloin. ½-grain:

(a) The inner layers of the coat persisted as an opaque shell.

(b) Disintegration depended on how soon the varnish coat gave way.

(c) No signs of a persistent envelope.

Compound Tablets of Aloin:

(a) The coat separated in large shaped pieces.

(b) A persistent flexible capsule prevented exact observation of the end-point.

(c) The tablet was only exposed at the edges.

(d) The coat usually separated as two flakes.

Tablets of Cascara Sagrada. 2-grains:

(c) This sample appeared to have a more resistant varnish coat.

Compound Tablets of Cascara Sagrada:

Samples (a) and (b) were only attacked round the edges.

Compound Tablets of Colocynth and Jalap:

(a) Slow dispersal of the tablet made the end-point difficult to determine.

(b) The inner layers of the coat tended to separate as two discs.

Tablets of Iron Carbonate:

(a) Disintegration seemed to be prevented by the varnish coat as the tablet slowly dispersed when cut in half.

Tablets of Iron Carbonate and Aloin:

The tablets were only attacked at the edges.

Tablets of Iron Carbonate with Arsenic:

(a) Tablets outlasting the test showed soft but shaped cores.

(b) The variations in disintegration times seemed to be due to a resistant varnish coat.

(c) The tablets were only exposed at the edges.

Tablets of Ferrous Phosphate with Quinine and Strychnine:

(a) An old sample. Cutting the tablet made no difference.

(b) The inner layer of the coat usually split at the edge and separated as two discs.

Tablets of Ferrous Sulphate. 3-grain:

(a) The tablets finally broke up giving a fairly sharp end-point.

(b) The tablets dissolved steadily.

(c) The tablets were only attacked at the edges.

(d) The tablets dispersed steadily.

Compound Tablets of Ferrous Sulphate:

(c) The tablets usually split into two halves each with one coated surface.

(d) Slowness of dispersal did not seem to be entirely due to the coat.

Compound Tablets of Hypophosphites:

(a) The tablets were only exposed at the edges.

(b) A definite envelope was seen to separate.

(c) The tablets were only exposed at the edges.

(d) The coat came off in flakes.

Compound Tablets of Phenolphthalein :

(a) Tablets which exceeded the 4-hour limit were estimated to have lost rather more than half their bulk.

(b) The inner coat broke sharply exposing a negligible residue.

Tablets of Phenytoin Sodium 0·1 gm.:

(a), (b) and (d) There was no sign of a varnish coat.

(c) A stout film, apparently of polish, separated. No definite signs of an inner varnish coat were seen.

(e) The tablets had a stout varnish coat. Varnish also seemed to have penetrated the tablets.

Discussion

Since tablet coating is an art, allied perhaps more to confectionery than pharmacy, appearance and stability of the coat are likely to be factors of some importance from the viewpoint of the tablet maker. Palatability and, in certain cases, the protection of the active ingredients will also play a part. Pharmaceutical requirements include regularity of action and release of the drug at a time appropriate to its action; obviously no coated tablets should be of such a permanent nature as to be passed whole by the patient. The results so far obtained disclose only one sample that might enter into this category, Tablets of Ferrous Phosphate with Quinine and Strychnine B.P.C. (a), and here age may have been an additional factor but this point has not been explored.

It is well known that some drugs, e.g., aloin, are liable to stain the coat unless adequately sealed against the water of the coating solutions and similarly prevented from leaking into the coat during storage. It is, accordingly, the practice to apply a coat or coats of a simple varnish to the tablets, the number depending on the tablet being coated and the judgment of the operator. The results show that it is this varnish coat and not the subsequent layers which has most influence on the disintegration of the tablet since the sugar or pearl coats were usually dispersed in a few minutes but the varnish coats were very persistent in a number of cases. The usual finding in these latter cases being that the coat was penetrated or ruptured round the junction of the edge and the faces of the tablets resulting in a disc on each side of the tablet. This would be expected since even with a deep-cup punch a sharp edge is formed where the curved face meets the straight side of the tablet and this edge would be most difficult to cover with a varnish; even in a fully coated tablet it is very frequently the thinnest part of the coat.

Variations in the varnish coat from undetectable, or possibly non-existent capsules (e.g., Phenytoin Sodium (a)) up to complete persistent capsules (e.g., Tablets of Aloin (a) and Compound Tablets of Aloin (b)) were found among the samples but it was not possible to ascribe variations within the samples with certainty to the varnish coat. Clearly information about the uncoated tablets would also be necessary.

Analysis of the results shows that eleven of the samples gave

disintegration times falling within the 15-minute limit of the Pharmacopœial distintegration test.

TABLE II

Tablet Sample		Average Disintegration Time (minutes)
Aloin, 1 grain...		11½
Cascara Sagrada, 2 grains	(a)	12
" " "	(b)	10
Ferrous Phosphate with Quinine and Strychnine...	(c)	13½
Ferrous Sulphate	(d)	14
Compound Ferrous Sulphate	(a)	10
" " "	(e)	13½
Phenytoin Sodium ... "	(a)	9½
" "	(b)	11
" "	(c)	13
" "	(d)	13

If the limit is raised to 30 minutes the following additional 8 samples would be included.

TABLE III

Tablet Sample		Average Disintegration Time (minutes)
Aloin, ½ grain...	(c)	20½
Compound Aloin	(a)	26
Cascara Sagrada, 5 grains	(a)	21½
" " "	(b)	17
Ferrous Sulphate	(b)	19½
Compound Hypophosphites...	(c)	25
" "	(d)	27
Compound Phenolphthalein...	(c)	18

Thus out of 54 samples examined 11 satisfy the disintegration test and 19 would comply if the time limit were doubled.

The significance of these figures should not be overestimated; consideration of the samples shows that 7 tablets (24 samples) have a purgative action, 6 tablets (21 samples) are preparations of iron and 1 tablet (5 samples) is a hypnotic usually administered for prolonged and continued rather than rapid action.

A short disintegration time is, therefore, not essential, and there might be advantages in a delayed release of the active material in avoiding gastritis. On the other hand, uniformity is desirable and this requires a means of standardisation.

The Pharmacopœial disintegration test has two drawbacks, the test period is likely to be unduly long and no allowance could be made for the possibility of the varnish coats being attacked rapidly *in vivo*. Furthermore the end-points obtained in many cases were not very definite, and practice was necessary in some cases before reliable figures were obtained.

The problem is by no means a simple one and the Codex authorities would seem to be well advised in exempting the coated tablets from the disintegration test.

CONCLUSIONS

1. Examination of 54 samples of B.P.C. coated tablets by the B.P. disintegration test shows that the majority (43 samples) fall outside the limit.

2. The exemption in the B.P.C. of coated tablets from the disintegration test is justified in the light of the evidence presented.

3. A method of standardising the disintegration rates of coated tablets is desirable in view of the variations observed from sample to sample, but further study is necessary before suggestions can be made.

SUMMARY

1. 54 samples of B.P.C. coated tablets have been examined for disintegration by the method of the B.P. with results which support their exemption from the test. The implications of the results are discussed.

2. It is concluded that the present exemption of coated tablets from the official disintegration test is justified and that standardisation is desirable, though further information on the behaviour of coated tablets is a necessary preliminary.

Thanks are due to the Directors of Savory and Moore Ltd. for permission to publish this work.

REFERENCE

1. Berry and Nutter Smith. *Quart. J. Pharm. Pharmacol.*, 1944, **17**, 250.

DISCUSSION

The paper was presented by MR. W. R. HOWARD.

The CHAIRMAN said that the paper brought out the difficult questions of the rates of disintegration and of the assay of sugar-coated tablets. It would be interesting to have the author's opinion of the proposal before the Pharmacopœia Commission that the normal disintegration time of the uncoated tablet should be increased by 45 minutes for the corresponding sugar-coated tablet. He pointed out that only certain tablets needed to be sugar-coated, and the Commission might be advised to specify which should be so coated unless otherwise prescribed. Some of the long disintegration times recorded by the author were not surprising. The publication of a standard for official tablets would do much to reduce the disintegration time of sugar-coated tablets available on the market.

MR. A. W. BULL (Nottingham) stated that some observations had been made on the disintegration rate of various sugar-coated tablets, including samples of various ages. With one exception, disintegration times were under 2 hours. The B.P. disintegration time for the uncoated tablets plus 45 minutes would not be adequate for the samples tested. The rate of disintegration appeared to be affected by the age of the tablet, although the tablets examined were from different batches. New tablets took longer to disintegrate than those which were 4 to 6 weeks old, and after that the disintegration time seemed to increase again. He asked the author whether he had noted any particular aspect of the coating in those cases where there was a particularly long time of disintegration.

MR. H. BURLINSON (Ashton-under-Lyne) agreed that the main difficulty in connection with disintegration rates of sugar-coated tablets was the resinous coating. In his view the time had arrived when manufacturers must change over to more soluble waxes and resins of synthetic or natural origin. He emphasised the importance of low disintegration rates for coated tablets containing substances which were required to produce rapid results.

DR. R. E. STUCKEY (London) confirmed the author's findings, and said that the paper should be read in conjunction with that recently published by Stephenson and Smith (*J. Pharm. Pharmacol.*, 1951, **3**, 547). In most cases the sugar coat comes off readily, but the difficulty was the breaking up of the shellac or resinous coating. He agreed that it was necessary to find a water-soluble coat of a resinous character, but the omnibus formula of adding 45 minutes to the disintegration time of the corresponding uncoated tablet would be difficult to apply. A further difficulty was the fact that compression might have to be increased in order that the tablet would withstand the coating process.

MR. A. R. G. CHAMINGS (Horsham) emphasised the importance of having quick disintegration in all cases where rapid action was required.

MR. D. H. STEPHENSON (Dartford) said that his experience was that sugar-coated tablets disintegrated more rapidly than the paper appeared to indicate. Where its use was essential, less resinous undercoat should be used. He had recommended as the standard for sugar-coated tablets an addition of half an hour to the official disintegration time for the uncoated tablets. The question of coating a tablet must in any case depend upon the nature of the medicament, and each tablet would have to be considered on its own merits. He suggested that 2 hours should be the maximum disintegration time for all tablets.

MR. A. NUTTER SMITH (Nottingham) expressed misgivings about the apparent zeal for disintegration which was so prevalent at the present time. In his view individual disintegration times should be stated for each tablet. The French Codex had a time limit of 2 hours, but the tablet was not required to disintegrate, only to crumble at the slightest pressure. He did not agree with making a hard tablet, neither was it necessary to have a heavy coat of varnish. Thickness of the tablet at the edges and also its shape were important.

DR. E. F. HERSANT (London) referred to the question of the inner coating and said that it did not matter whether it dissolved or disintegrated so long as it fractured so that the material which was enclosed dissolved.

MR. HOWARD, in reply, expressed the opinion that good practice in tablet coating could give short disintegration times. He was unwilling to express any view about the arbitrary addition of 45 minutes until he knew more about the actual behaviour of the tablets themselves in the uncoated form. He could give no information on the age of the samples used in his experiments, as they had been collected at random. The author was in agreement with the work of Stephenson and Smith in regard to the rate of dispersal of the white coat.