These disadvantages have been remedied. Although a solution of 5% 4-dimethylaminobenzaldehyde in hydrochloric acid: ethanol (1:1) turns from yellow to brown within a week, replacement of ethanol by methanol provides a solution which is stable for several months. The use of a porcelain tile or tube is avoided by placing a small amount of the suspect material on a filter paper and adding a drop of the reagent. Radial striations of colour develop from the centre of the spot. By chromatographic action the material responding to the reagent is carried away from the bulk of the sample, where dyestuffs and other materials interfere, and is concentrated into striations. It is possible to obtain a response with weak samples of lysergide which have failed to produce a fluorescence with an ultraviolet lamp. The Table summarizes the responses obtained using this technique for some known hallucinogens and structurally related substances.

Although similar colour reactions are observed with hallucinogens derived from lysergic acid and the tryptamines, as well as the natural ergot bases and dihydroergotamine, the test is convenient for non-scientific personnel and is much more restrictive than the observation of ultraviolet-induced fluorescence. When taken with adequate circumstantial evidence there is less likelihood of mistakingly seeking professional confirmation. The filter paper may be retained as a record of the test and can be signed and witnessed. A combination of the two techniques assists the examination of heterogeneous specimens.

Laboratory of the Government Chemist,
Stamford Street,
*London, S.E.*1, *U.K.*

GERALDINE V. ALLISTON
A. F. F. BARTLETT
M. J. de FAUBERT MAUNDER
G. F. PHILLIPS

November 3, 1970

REFERENCES

CLARKE, E. G. C. (1967). *J. forens. Sci. Soc.*, **7** (1), 46–50.
de FAUBERT MAUNDER, M. J. (1969). *Bull. Narcot.*, **21** (4), 37–43.
DECHERT D. D. (1968). *Microgram*, **1** (4), 16–17 (restricted circulation).
GOVERNMENT CHEMIST (1969). Report for 1968, p.47, London: HMSO.

In vitro release of aspirin from various wax-coated formulations

Wax-coating of pharmaceuticals has been reported amongst techniques used for controlling drug releases. We have studied the *in vitro* release of aspirin from various wax-coated formulations in an attempt to explain the differences in release profiles. The waxy materials used were spermaceti, stearic acid, a hydrogenated grade of cottonseed oil and a blend of equal parts of these waxes. Two methods were adopted in the preparation of the formulations; the congealing method (Robinson, Moorestown & Svedres, 1957) and the aqueous dispersion method (Robinson & Becker, 1968). All formulations were prepared to contain 1 part of aspirin and 5 parts of the wax. The release experiments were made using the 23/30 mesh fraction.

The release rates were determined at 37° ± 0·1° in a rotating bottle apparatus similar to that of Souder & Ellenbogen (1958). Acid pepsin and alkaline pancreatin solutions of the B.P. 1963 were used as the dissolution media. After specified time intervals the contents were filtered and an aliquot was assayed for aspirin by spectrophotometric measurement of the salicylic acid (in 0·1N HCl at 305 nm) produced after preliminary hydrolysis with 0·1N NaOH. Blank experiments were made using equivalent amounts of the waxes. Fig. 1 shows the release patterns in both dissolution media. In acid pepsin the release rate followed the sequence: spermaceti > stearic

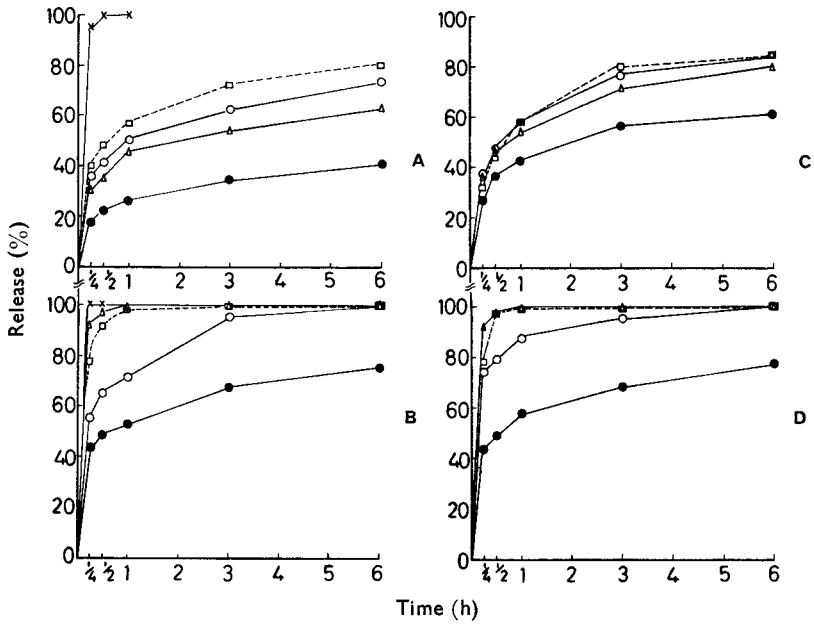

FIG. 1. *In vitro* release of aspirin from formulations prepared by the congealing method (A,B) and the dispersion method (C,D). A,C in acid pepsin solution (pH 1·2). B,D in alkaline pancreatin solution pH 8·3. ●—● hydrogenated cottonseed oil; △—△ stearic acid; ○—○ spermaceti; □—□ mixed waxes (equal parts). Ratio of aspirin to wax 1:5; ×—× plain aspirin crystals.

acid > hydrogenated cottonseed oil. In alkaline pancreatin solution the sequence was: stearic acid > spermaceti > hydrogenated cottonseed oil. In a given time the release in this medium was faster than in acid pepsin solution. The method of preparing the formulations affected the release in a particular medium. The dispersion method gave higher release rates for all the waxes particularly in acid pepsin solution (Fig. 1C). Products prepared using a blend of equal parts of the three waxes gave unexpectedly higher release rates in both dissolution media (Fig. 1). In this respect our results do not agree with those of John & Becker (1968). They found, for a blend of 1:1 combination of two waxes, a release profile intermediate between the two waxes.

It is difficult to attribute the difference in release through waxy matrices as solely due to the chemical composition of the waxes since other factors may also contribute. The relative hydrophilic nature of the waxes has been claimed to affect the release rate (Cusimano & Becker, 1968). We found a correlation between the release rate through a particular wax–aspirin mixture and the melting point of wax. In acid pepsin the release at 37° followed the sequence: spermaceti (m.p. 45–46°) > stearic acid (m.p. 58–60°) > hydrogenated cottonseed oil (m.p. 65–66°). Measurements of the relative softening of the congealed waxes were made at 37° using the penetrometer technique (Martin, 1962). The results (Table 1) showed that the relative softening followed the above sequence. In alkaline pancreatin solution it is probable that the dissolution rate of the waxes has a decisive effect. Experiments were made to compare the dissolution rate of the waxes (using the 25/30 mesh) at 37° in the alkaline pancreatin solution (pH 8·3). The results (Table 2) showed that the dissolution rate followed the sequence: stearic acid > spermaceti > hydrogenated cottonseed oil. This is similar to the sequence found in the release study in alkaline pancreatin solution. The release through the mixed waxes gave unexpectedly high release

Table 1. *Relative softening of the congealed waxes measured by the penetrometer at* 37°. (Penetrometer readings in 0·1 mm. after 5 s)

Wax	m.p. °C	Penetrometer reading*
Spermaceti	45–46	5·3
Stearic acid	58–60	2·4
Hydrogenated cottonseed oil	65–66	1·1
Mixed waxes†	48–50	12·7

* Average of 12 runs (±3%).
† A blend of equal parts of the three waxes.

Table 2. *Dissolution rates of the wax particles* (25/30 *mesh*) *in alkaline pancreatin solution* (pH 8·3) *at* 37° ± 0·1

Wax	% Dissolution* 1 h	3 h	6 h
Spermaceti	7·1	12·6	27·3
Stearic acid	48·3	57·6	62·6
Hydrogenated cottonseed oil	3·9	5·1	8·8

* Average of three experiments (±4%).

probably due to the appreciable softening, which occurred at 37° (Table 1) and the 'distortion' which may occur in the waxy matrix as a result of the dissolution of component(s) of the blend during the release experiment. This would be the case in alkaline pancreatin solution where a relatively high percentage of stearic acid dissolves (Table 2).

Determination of the salicylic acid content (using a modified B.P. method) in the plain aspirin powder used and in the freshly prepared formulations revealed an insignificant increase (within the B.P. limit for salicylic acid in aspirin powder).

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Department of Pharmaceutics,
Faculty of Pharmacy,
University of Alexandria,
Alexandria, Egypt, U.A.R.

SALEH A. H. KHALIL
SAFAA S. ELGAMAL

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REFERENCES

CUSIMANO, A. G. & BECKER, C. H. (1968). *J. pharm. Sci.*, **57**, 1104–1112.
JOHN, P. M. & BECKER, C. H. (1968). *Ibid.*, **57**, 584–589.
MARTIN, A. N. (1962). *Physical Pharmacy*, p. 632, Philadelphia: Lea & Febiger.
ROBINSON, I. C. & BECKER, C. H. (1968). *J. pharm. Sci.*, **57**, 49–53.
ROBINSON, M. J., MOORESTOWN, N. J. & SVEDRES, E. V. (1957). *U.S. Patent*, 2,805,977.
SOUDER, J. C. & ELLENBOGEN, W. C. (1958). *Drug Stand.*, **26**, 77–83.