LETTERS TO THE EDITOR

A Simple Device for Testing the Spreadability of Pharmaceutical Suspensions for External Use

SIR,—In the course of my investigations into various aspects of pharmaceutical suspensions with emphasis upon the application of statistical methods[1,2], a simple device called a grindometer generally used to evaluate the fineness of printing inks[3,4] proved after careful experimentation and a statistical treatment of experimental data, to be useful when measuring the spreadability of pharmaceutical suspensions destined for external use. From my experience, the underlying principle of the grindometer, the testing of dispersibility, can also be applied to powdered medicinal substances.

The grindometer used in my work consists of a mild steel block; in the upper surface there is machined an incline, the bottom and sides of which are highly

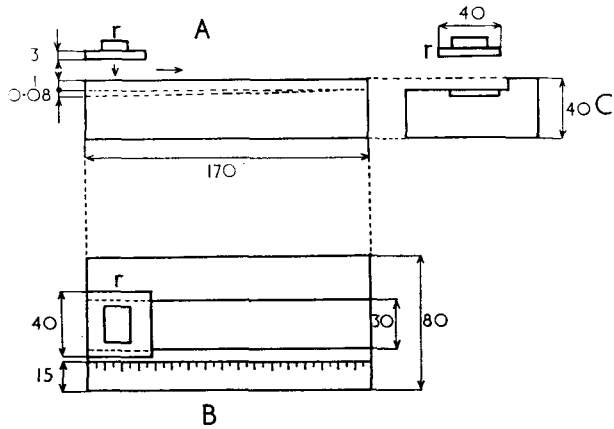

FIG. 1. Schematic sketch of the grindometer. A = front view; B = top view; C = side view; r = rubbing spatula. All dimensions are in millimetres.

polished. An empirical scale projects above the upper surface and is marked along the incline. A separate part of the device is a rubbing spatula. The dimensions are indicated in Figure 1.

In use a sample of 0·2 ml. of the suspension is placed on the incline at the lower end of the grindometer. After 10 seconds the rubbing spatula is placed on the sample and after a further 10 seconds it is moved without applying pressure to it; a smooth linear movement is achieved by resting the rubbing spatula against the projection of the scale during the movement. The value on the scale up to which the coherent layer of the sample then extends is recorded.

Preliminary results have been obtained on the influence of Tween 80 on the spreadability of a test composition. Tween 80, 1 per cent, was added to a suspension the composition of which was as follows: zinc oxide 15 per cent, talc 15 per cent, glycerol 10 per cent, Adulsion ST "Kalle" ("a form of methyl cellulose and carboxymethyl cellulose") 2 per cent, and water 57 per cent. Since it was expected that the addition of Tween 80 would cause an improvement in spreadability and since each experimental value was known before the next experiment was carried out, the results were treated by the pertinent method of sequential analysis[5,6].

As far as the mode of sequential analysis which I have used is concerned, the following data were known or fixed before the start of the actual experiments testing the influence of the addition of Tween 80 to the above-mentioned suspension: mean value of spreadability of the suspension without Tween 80 = 4·7; difference in spreadabilities of suspensions with and without Tween 80 which it is important to detect = 1·0; standard deviation = 0·6; risk of asserting a

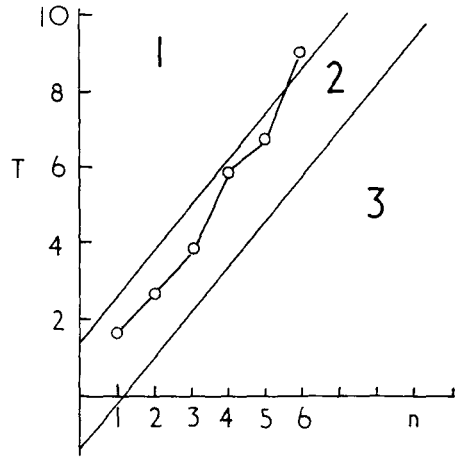

FIG. 2. Sequential test for measuring the improvement in spreadability caused by the addition of 1 per cent Tween 80 to a suspension. n = number of experiments; T = cumulative total of coded values (coded value = actual value − 4·0) of spreadability. Zone 1 = real improvement in spreadability; zone 2 = the experiments to be continued; zone 3 = no improvement in spreadability.

significant difference when none exists = 0·02; risk of failing to detect a significant difference = 0·02. These values served as fundamentals for constructing a graph (Fig. 2) which illustrated the relation between the cumulative value of spreadability of the suspension with Tween 80 (T) and the number of experiments (*n*). The graph was divided into three zones each of which indicates a proper decision to be taken when T is in or enters this zone: zone 1: there is a real improvement in spreadability caused by the addition of Tween 80; zone 2: the experiments are to be continued since the available data are insufficient; zone 3: there is no significant difference in spreadabilities of the suspensions with and without Tween 80. Thus the testing was to be terminated when T entered zone 1 or zone 3.

As is obvious from Figure 2, the decision that the spreadability of the suspension with Tween 80 is better than of that without Tween 80 was taken after the sixth experiment.

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The Critical Micelle Concentration of Polyethyleneglycolmonocetylether

SIR,—The recent paper of Elworthy[1] reporting the determination of the critical micelle concentration (CMC) of a commercial sample of cetomacrogol of molecular weight 1210 has prompted us to report values we have obtained for two commercial samples of polyethyleneglycolmonocetylether; one designated A complied with the B.P.C. 1959 requirements for Cetomacrogol 1000 and the other designated B failed to comply by virtue of 0·1 per cent excess

TABLE I

VALUES FOR THE CRITICAL MICELLE CONCENTRATION OF POLYETHYLENEGLYCOLMONOCETYLETHERS

Method of determination		Critical concentration per cent	
		Batch A	Batch B
Surface tension	1	0·00135	0·00082
	2	0·00119	0·00105
Light absorption ..	1	0·00132	0·00085
	2	0·00145	0·00093

water. In our experiments CMC values were obtained by observing changes in surface tension with concentration as measured by the Du Nouy tensiometer. Determinations were also made with the iodine method of Ross and Oliver[2], using a Unicam SP500 spectrophotometer. Our results are summarised in Table I.

Carless and Nixon[3] report values of 10^{-6} to 10^{-7} M with the Du Nouy tensiometer for the CMC of a sample of cetomacrogol which according to their data contained more ethylene oxide residues than that required by the B.P.C. 1954. As these workers assumed a molecular weight of 1300, their values for the CMC may be expressed as 0·00013 to 0·000013 per cent.

Working with specially prepared samples of polyoxyethylene alcohols, Cohen[4] concluded from surface tension measurements, that for a given alcohol, the CMC was independent of the number of ethylene oxide units. This is to be contrasted with the findings of Becher[5], whose work indicates that for a given alcohol, the CMC varies as the number of ethylene oxide units is increased. The value for the CMC obtained by Cohen[4] for the reaction products of ethylene oxide with cetyl alcohol, was $\frac{M}{50{,}000}$, which for $C_{16}H_{33}O[CH_2CH_2O]_{20}H$, gives a value of 0·00225 per cent.

We have, therefore, values of 0·007[1], 0·001–0·0009 and 0·0001 to 0·00001[3] per cent for the CMC of commercial samples and 0·00225 per cent for a pure sample of this class of compound.