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The effect of particulate dispersing agents on the antifoaming properties of dimethicone 1000 in antiflatulent products

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The effect of finely divided silica on the antifoaming properties of polydimethylsiloxanes (dimethicone 1000) when formulated in a typical antiflatulent tablet has been examined. A dynamic froth test has been used to show that removal of extractable dimethicone by ether extraction of the tablet powder markedly reduces the antifoaming properties of the powder, despite retention of a small percentage of the polydimethylsiloxane dispersed on the surface of the silica and aluminium hydroxide gel content of the tablet. A series of static froth tests similarly demonstrate that tablet formulations from which silica is omitted also possess significant antifoaming properties.

The intrinsic antifoaming properties of polydimethylsiloxanes such as dimethicone 1000 which find application in their use in large-scale fermentation as antifoam and in medicine as antiflatulents are limited by their high viscosity and hydrophobic properties. As a result they fail to disperse and remain as large viscous droplets in aqueous media. However, if they are dispersed as particles smaller than 2 μm in diameter they are effective defoamers at concentrations of only few parts per million (Osipon, 1962). Various devices are adopted to enhance their antifoam properties by adsorption onto solid surfaces in forms for rapid dispersion throughout the foam. Some antifoams are produced by dispersing silica in the polydimethylsiloxane, e.g. silica in dimethicone suspension, B.Vet.C., or by chemical reaction between polydimethylsiloxane and the surface hydroxyl groups of silica particles, at elevated temperatures, e.g. 175–300° (Sullivan, 1968). An alternative method is to use hydrophobic silica as the dispersing agent, produced by reacting hydrophilic silica with dimethylchlorosilane (Klein & Maluzi, 1970). Whichever the method adopted, the fundamental concept is the creation of a much enlarged interface between the silicone and the foam awaiting dispersal. In parallel with other well established surface-active effects, it could therefore be argued on theoretical grounds that this effect would be maximized by the use of antifoam and solid in ratios such that a monomolecular film is just achieved over the entire solid surface. Nevertheless, silica in dimethicone suspension, B.Vet.C., which contains 6–8% of finely divided silica of specific surface *ca* 400 m^2g^{-1}, contains silicone far in excess of that required to produce a monomolecular film. Indeed, calculations show that approximately equal proportions of the two components will achieve the required monomolecular layer.

The experiments herein described were designed to establish the extent to which added silica and other powders contribute to the antifoaming properties of dimethicone in a typical antiflatulent tablet formulation.

MATERIALS AND METHODS

Materials

Asilone tablets* (Berk Pharmaceuticals Ltd.). Chewable tablets drawn from commercial batches, of nominal weight 2·5 g containing dimethicone, B.P.C., 250 mg, aluminium hydroxide gel dried, B.P., 500 mg, silica (Aerosil 200) 15 mg $\pm$ 2 mg in a flavoured base consisting of sucrose, acacia and sorbitol. Talc was present as a lubricant. Wet granulation was used to prepare tablet granules for tableting.

Granules. A series of specially prepared granules conforming to the Asilone tablet specifications with the following additions and omissions:

Aa, silica omitted; Bb, silica added before wet granulation; Cc, silica added to dry granules; Dd, silica and dimethicone omitted; Ee, dimethicone omitted, silica added before wet granulation; Ff, dimethicone omitted, silica added to granules which had been dried ready for tableting; Gg, control: granules conforming to Asilone tablet formula, prepared with a pre-mix of dimethicone 1000 and 4·5 to 7% silica.

Sodium lauryl sulphate. B.D.H. Laboratory Reagent 30176, containing not less than 99% sodium lauryl sulphate.

Methods

Dimethicone content

Method 1. A group of tablets was weighed and powdered, and the average weight calculated. The powder was continuously extracted with chloroform in a Soxhlet apparatus, the chloroform was removed by distillation, the residue dried at 110° in a current of nitrogen, until the odour of peppermint had disappeared, and weighed.

Method 2. A group of tablets was treated as in method 1 using ether as solvent.

Method 3. A group of tablets was weighed and powdered, and the average weight calculated. The powdered tablets were treated with water (3–4 ml) followed by hydrochloric acid (15 ml) and, after thorough dispersion of the powders, the mixture was extracted quantitatively with ether in the normal manner. The extract was washed successively with water, 0·1 N NaOH and water, and filtered through cotton wool and anhydrous sodium sulphate to yield a colourless bright filtrate. Ether was evaporated and the residue dried to constant weight.

Recovery and characterization of dimethicone

About eighty tablets were powdered and extracted with ether in a Soxhlet. The ether extract was washed with dilute HCl, water, 0·1 N NaOH and water. The residue obtained after evaporation of the ether was dried at 100° in a vacuum (2 h) and 115° in a vacuum (4 h). It appeared as a faintly coloured, very slightly opalescent viscous liquid, still smelling faintly of peppermint. The residual traces of peppermint were removed on allowing the liquid to stand in an open vessel in a desiccator over paraffin wax for several weeks. The infrared spectrum of the residual liquid was recorded on a Perkin-Elmer 157 instrument, and its weight ml^{-2} and viscosity measured.

Dynamic froth test

Cetomacrogol solution (10%, 2 ml) was added to 400 ml of either 0·1 N HCl or saturated sodium bicarbonate solution at room temperature (20°) in an 800 ml beaker.

The solution was stirred with a magnetic stirrer and aerated through a small,

* Registered Trade-mark.

sintered glass disc to form a head of froth which reached almost to the top of the vessel. A powdered Asilone tablet (2·5 g) was mixed with 5 ml of water, the suspension added all at once to the froth, and at the same time a stop watch was started. The time was taken to the disappearance of the froth from all the surface of the liquid except that of the vortex produced by the magnetic stirrer. The experiment was repeated with powdered Asilone tablets (2·5 g) from which dimethicone had been extracted with ether and with chloroform, respectively.

Control experiments, in which a suspension of calcium carbonate (2·5 g) in water (5 ml) was added to a froth prepared similarly from cetomacrogol solution (10%, 2 ml) in 400 ml of water, showed that the effect of adding other powders was negligible.

Static froth test

Preliminary experiments were conducted with a variety of foaming agents, e.g. sodium lauryl sulphate, Tween 20, liquid extract of quillaia, pepsin, serum albumin (bovine and human). Of these, sodium lauryl sulphate produced the most copious and stable foam that was most suitable for following the rate of foam destruction.

The following procedure was based on the method of Rezak (1966). 100 ml of sodium lauryl sulphate 0·25% in water was shaken in a 250 ml graduated cylinder (total capacity *ca* 300 ml) until the volume of froth plus liquid was 250 ml. The granules (1 g) were added to the cylinder which was inverted five times to disperse the granules. The volume of foam was noted at 15 s intervals. By standardizing the procedure reproducible results were obtained.

RESULTS

Dimethicone content

With method 1 and batches A B C D, containing between 243–251 mg of dimethicone per tablet, a mean of 98·9 (100·5 — 97·5) % was obtained. With method 2 and batch E (230 and 234 mg dimethicone per tablet) the % labelled strength found was 92·0 and 93·8 (2 samples). With method 3 and batch F (237 and 235 mg dimethicone per tablet) the % labelled strength found was 94·6 and 94.1 (2 samples).

Characterization of recovered dimethicone

(*a*) *Infrared spectrum.* The infrared spectrum of the recovered dimethicone exhibits maxima only at the same wavelengths as and having similar intensities to those in the spectra of authentic samples of dimethicone 1000 confirming that the material is unchanged dimethicone.

(*b*) *Weight per ml at 20°.* Found: 0·968. B.P.C. specification 0·965 to 0·980.

(*c*) *Viscosity* at 25° was measured with reference to redistilled glycerol as standard: found, 1009 centistokes, B.P.C. specification 950 to 1050 centistokes. Authentic dimethicone 1000 (Berk Pharmaceuticals Ltd.) 1039 centistokes; Authentic dimethicone 1000 (Sigma Chemical Co. Ltd.) 1022 centistokes.

Froth tests

The results of the dynamic test are given in Table 1 and of the static test in Fig. 1.

DISCUSSION

There is no chemical reaction in the generally accepted sense of the term between dimethicone 1000 and silica—merely strong intermolecular hydrogen bonding between

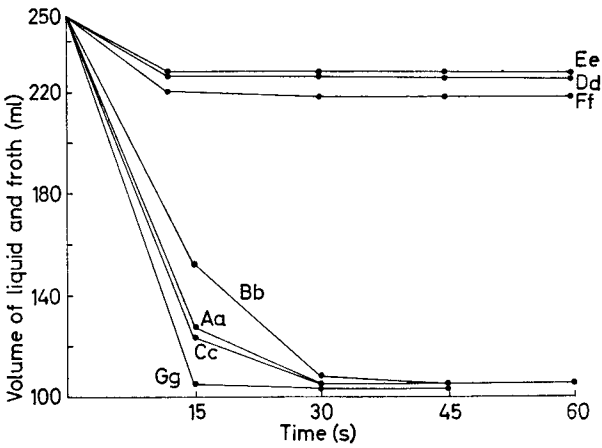

FIG. 1. Defoaming of sodium lauryl sulphate solutions by granules. The results of the static froth test. Mean values for granules Aa–Gg.

the silica surface and the silicone polymer. This is demonstrated by the enhanced hydrogen bonded hydroxyl absorption at 3450 cm^{-1} and the corresponding fall in free hydroxyl absorption at 3700 cm^{-1} on the silica surface, on admixture with silicone (Buist, Burton & Elvidge, 1973), which is reversed by washing with suitable solvents. That such interaction is by no means essential for the production of significant antifoaming properties of the particular antiflatulent tablets examined is demonstrated by experiments in which the silica is omitted (sample Aa).

From Fig. 1 it can be seen that the granules not containing dimethicone (Dd, Ee, Ff) have negligible defoaming action. The slight initial decrease of foam after 15 s is probably no greater than that produced by any inert powder being added to a foam. The granules corresponding to the standard Asilone formula (Gg) were the most effective defoamer after 15 s, but from 30 s onwards there was little difference between these and the granules when silica was absent (Aa) or when it was added separately to the granule formulation.

The tablets contain a substantial excess of dimethicone over that required to produce a monomolecular film on the silica and alumina present. Despite the fact that neither sucrose nor sorbitol react or even hydrogen bond with dimethicone (Buist & others, 1973), dynamic antifoaming experiments show that the extractable

Table 1. *Dynamic froth test.*

Froth	Preparation	Froth reduction Time (s)	Extent
Cetomacrogol–0·1N HCl	Asilone tablet (as formulated)	17	complete
	Asilone tablet (ether extracted)	60	80%
	Asilone tablet ($CHCl_3$ extracted)	60	80%
Cetomacrogol–satd $NaHCO_3$	Asilone tablet (as formulated)	20	complete
	Asilone tablet (ether extracted)		10–0%
Cetomacrogol–water	Calcium carbonate B.P.		0

dimethicone appears to exert a significant antifoam effect substantially greater than that produced by the residual polymer hydrogen bonded to silica. Recovery experiments using both chloroform and ether as extraction solvents established by means of infrared spectroscopy, refractive index, weight per ml and viscosity measurements that recovered dimethicone conform to the specification of dimethicone B.P.C. 1000. It is shown also that chloroform extraction leads to the recovery of dimethicone from at least four batches in amounts which are in reasonable conformity with the labelled strength. However, whilst it is accepted that this does not establish the actual amounts of dimethicone present in each batch, it is evident from the consistently lower recoveries with ether from similar, but not identical, batches that the ether-extracted powdered tablets used in the dynamic froth test retain some dimethicone. This is confirmed by the hydrophobic properties of the powder. The average difference in recoveries from chloroform and ether extraction is equivalent to 5·3% of the labelled strength of dimethicone (250 mg), i.e. about 13·3 mg per tablet, an amount which is no greater than that required to form a monomolecular film on the constituent silica and alumina particles.

Because dimethicone is retained after ether extraction, the dynamic froth test provides a direct comparison between the tablet as formulated and tablets from which the bulk of the dimethicone (*ca* 95%) has been removed. In the latter only residual dimethicone remains dispersed on the surface of the constituent silica and alumina particles. The marked difference in antifoaming properties in acid solution shown by the powdered tablets before and after ether extraction demonstrates that the unbound extractable dimethicone is primarily responsible for the antifoaming properties of the tablets. Thus powder from unextracted tablets is rapid in action and completely destroys the foam. On the other hand, adsorbed dimethicone in the ether-extracted tablets, whether on the surface of the silica, alumina, or both, plays only a minor role in establishing the antifoaming characteristics, since ether-extracted powder is much slower to take effect, and much less effective in that it is incapable of completely destroying the foam. This is confirmed by examination of chloroform-extracted powder, which yielded results similar to those obtained using ether as solvent.

Thus, in the formulation of antiflatulent tablets of the Asilone type it is not essential to use a pre-mix of dimethicone and silica, e.g. Silica in dimethicone suspension B.Vet.C., as the method of incorporating silica makes little difference and the antifoaming capability lies predominantly in the bulk dimethicone phase. Aluminium hydroxide and possibly the talc appears to be responsible for dispersing the dimethicone resulting in an effective defoaming product, even in the absence of silica.

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