bility of some *n*-alkyl *p*-aminobenzoates in various binary solvent systems consisting of propylene glycol and water are shown in Fig. 1. It can be seen from the data in Fig. 1 that the slopes of the lines (*i.e.*, the value of ϵ) increase with the increasing chain length of the ester. In other words, the more nonpolar the homolog, the greater is its dependence upon the volume fraction of the nonaqueous component.

It has been noted (5–10) that frequently in water and other pure solvents:

$$\log S_n = \log S_{n=0} - \delta n \qquad \text{(Eq. 2)}$$

where S_n is the solubility of the homolog having n carbons in its alkyl chain, and $S_{n=0}$ is the intercept at a real or hypothetical chain length of zero. We have also noted that this relationship can be valid for homologous series in mixed solvents of any composition. As can be seen from the slopes of the lines in Fig. 2, the value of δ for the alkyl *p*-aminobenzoates is highly dependent on the solvent composition. [The breaks in the curves at four carbons were explained previously (7).]

It was postulated by other investigators (10–15) that solubility is determined in part by the combined energy required to create a cavity in the solvent which can accommodate the solute molecule and the energy involved in the insertion of a solute molecule into the cavity. For nonpolar materials, these processes can be highly influenced by the molecular hydrophobic surface area. To be specific, we have observed that the above δ and ϵ values can be related to the interfacial tension between the polar solvent or solvent mixture and a low energy hydrocarbon surface such as hexane, multiplied by the hydrophobic surface area of the homolog that would be exposed to the polar solvent. This work and some of its ramifications will be reported more completely in a forthcoming publication[1].

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Magnesium Lauryl Sulfate—Soluble Lubricant

Keyphrases ☐ Magnesium lauryl sulfate—evaluation as tablet lubricant ☐ Lubricants, tablet—evaluation of magnesium lauryl sulfate ☐ Tablet lubricants—evaluation of magnesium lauryl sulfate

Sir:

Lubricants are usually required in tablet and capsule formulations. Magnesium stearate is the most widely used lubricant, but its waterproofing properties can retard disintegration and dissolution. Thus, surfactants, such as sodium lauryl sulfate, are often added to formulations to counteract the waterproofing action of magnesium stearate (1, 2). We searched for a compound with the lubricating properties of magnesium stearate but without its waterproofing liability. We found one effective in three of four formulations studied.

The criteria against which the lubricants were measured were:

1. Will the formulation run?
2. What is the unit tablet or capsule weight variation from the mean (*i.e.*, the variance)? In each study, we tested for differences in weight variability given by two different batches by forming the ratio of these variances. If the two batches give weight distributions having equal variances, this ratio has the F distribution and one can test the hypothesis of uniform variance. In the first study, a tablet granulation with terra alba (89.9%), α-cellulose (4.8%), acacia (1.2%), and sucrose (4.1%) was used. Starch (5%) and the lubricant (Table I) were added with adequate mixing, and the granulations were

Table I—Tablets

	Lubricant	Mean Tablet Weight[a], mg.	*CV*, %
0.5%	Magnesium lauryl sulfate	1191.9	1.80
0.25%	Magnesium lauryl sulfate	1238.5	1.77
0.125%	Magnesium lauryl sulfate	Would not compress	
0.5%	Magnesium stearate	1191.2	1.84
0.25%	Magnesium stearate	1229.0	1.88
0.125%	Magnesium stearate	1200.5	2.10
0.0625%	Magnesium stearate	Would not compress	
0.5%	Sodium lauryl sulfate	1233.5	2.59
0.25%	Sodium lauryl sulfate	1246.1	2.65
0.0125%	Sodium lauryl sulfate	Would not compress	
0.5%	Talc	Would not compress	
0.5%	Polyethylene glycol 6000	Would not compress	
0.5%	Dioctyl sodium sulfosuccinate (85%) and sodium benzoate (15%)	Would not compress	
None		Would not compress	

[a] Twenty tablets were taken at regular intervals during a run, and 20 tablets were taken at random from a completed batch. Statistical evaluation of tablet weight variation data showed that sequential weight data and random weight data had roughly equal variability; variance estimates from the two sets were, accordingly, pooled.

Table II—Capsules

Lubricant, mg./capsule	Mean Capsule Weight, mg.[a]	Disintegration Time, min.[b]	Dissolution, % in 10 min.[b]	*CV*, %
1.0 Magnesium lauryl sulfate	472.0	4	97	2.4
0.5 Magnesium lauryl sulfate	489.7	4	—	3.6
0.25 Magnesium lauryl sulfate	473.7	4	—	5.1
1.0 Magnesium stearate	468	>270	15	2.2
0.5 Magnesium stearate	491.7	120	—	3.6
0.25 Magnesium stearate	469.3	50	—	3.0
None	471.0	7	—	3.9
2.5 Sodium lauryl sulfate	477.9	4	—	5.5

[a] Twenty capsules were taken at regular intervals at each of two stations, and 20 capsules were taken at random from a completed batch. Variance estimates from the sets of 20 capsules tended to be quite homogeneous and were, accordingly, pooled for each lubricant–amount combination. [b] NF XIII Method II with six capsules in 600 ml. of 0.3% HCl was used for disintegration and dissolution.

compressed on a tablet machine[1] equipped with capsule shape punches.

Table I shows that: (*a*) magnesium lauryl sulfate and magnesium stearate were equivalent because there were no significant tablet weight variability differences between any pair of the five combinations; (*b*) variability for either concentration of sodium lauryl sulfate was significantly higher than for all amounts of the magnesium salts, except in one case where 0.5% sodium lauryl sulfate was more variable than 0.125% magnesium stearate, but the difference was not significant at the 0.05 level; (*c*) weight variation varied inversely with lubricant content; and (*d*) several other agents were not effective lubricants at the 0.5% concentration.

A similar granulation was run on the rotary tablet machine[2] equipped with 0.79 × 0.79-cm. (0.31 × 0.31-in.) punches. Statistical analyses showed: (*a*) magnesium lauryl sulfate (0.25%) was equivalent in variability to magnesium stearate (0.5%); (*b*) magnesium lauryl sulfate (0.25%) was significantly less variable than sodium lauryl sulfate (0.5%); and (*c*) magnesium stearate (0.5%) was significantly less variable than sodium lauryl sulfate (0.5%).

Lubricant performance in the rotary tablet machine was also evaluated in a direct compression mix containing lactose[3] and starch. The results were: (*a*) magnesium stearate (0.5%) was significantly less variable than magnesium lauryl sulfate (2.0%); (*b*) magnesium lauryl sulfate (2.0%) was significantly less variable than sodium lauryl sulfate (2%); and (*c*) magnesium stearate (0.5%) was significantly less variable than sodium lauryl sulfate (2%).

Relative lubricating properties of magnesium lauryl sulfate and magnesium stearate were also determined by comparing capsule weight variations of mixes filled on an automatic capsule-filling machine[4]. Each capsule contained lithium carbonate (300 mg.), spray-dried lactose (90 mg.), and lubricant.

Table II shows that: (*a*) magnesium lauryl sulfate and magnesium stearate were equivalent at 1.0 and 0.5 mg./capsule concentrations; (*b*) magnesium stearate gave less weight variability than magnesium lauryl sulfate at 0.25 mg./capsule concentration; and (*c*) weight variation varied inversely with lubricant content. Note in Table II that the capsules with 1 mg. magnesium lauryl sulfate disintegrated rapidly and the contents dissolved rapidly ($T_{50\%}$ dissolved = 2.7 min.) but the capsules with 1 mg. magnesium stearate did not ($T_{50\%}$ dissolved = 48 min.).

In three of four formulations, magnesium lauryl sulfate was equivalent to magnesium stearate as a lubricant. It was better than sodium lauryl sulfate. Thus, these data indicate that magnesium lauryl sulfate possesses the lubricating properties of magnesium stearate but without its waterproofing liability.

While the safety of magnesium lauryl sulfate for use in pharmaceuticals remains to be established, we anticipate that it is as safe as sodium lauryl sulfate. Full details will be published later.

[1] Stokes model F.
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[3] Fast-Flo.
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Solid-State Ophthalmic Dosage Systems in Effecting Prolonged Release of Pilocarpine in the Cul-De-Sac

Keyphrases □ Ophthalmic prolonged-acting dosage forms—pilocarpine alginate flakes, cul-de-sac deposition, compared to pilocarpine hydrochloride solutions □ Miosis—prolonged-acting pilocarpine alginate flakes □ Timed-release dosage forms, ophthalmic—pilocarpine alginate flakes, compared to pilocarpine hydrochloride solutions

Sir:

In the area of oral prolonged-acting pharmaceuticals, polyuronic acids have been described (1–3) as suitable carriers for the preparation of slightly soluble salt complexes. In this respect, we previously cited (4) the advantages to solid dose cul-de-sac deposition over that of conventional liquid installation for prolonging the duration of a desired pupillary response.