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Interaction of certain pharmaceutical products with polysorbate 80 in solution

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Very often a surfactant is added to simulated gastric fluid (SGF) without pepsin, to obtain a surface tension comparable to that of human gastric juice (Finholt and Solvang, 1968).

The aim of this study is to verify if, and to what extent, polysorbate 80 (P80) interacts with phenacetin and/or lactose. A possible interaction is examined by measuring liquid penetration rates in powderbeds, and by comparing surface tensions of saturated drug solutions to that of pure SGF.

The solid substances used are phenacetin USP XX (powder grade, Bayer, Leverkusen) and lactose USP XX (200 mesh, DMV, Veghel). Two simulated gastric fluids are used. The first one is composed of 0.1 N HCl with 0.2% NaCl. To the second one, an additional 0.001% of polysorbate 80 (Tween 80) is added.

Liquid penetration rates into powder mixtures of phenacetin with 30 or 50% lactose are measured with the Baumann apparatus (Baumann, 1966). Simulated gastric fluids with and without polysorbate 80 are used as the penetrating liquids. The penetration data are analyzed by the Washburn equation (Washburn, 1921):

$$L^2 = \frac{d \cdot \gamma \cdot \cos\theta \cdot t}{4\eta}$$

where L is the penetration depth, d is the mean pore diameter, γ and η are the surface tension and viscosity of the liquid, θ is the contact angle and t is the time. Contact angles on powder compacts are measured directly on sessile drops, by means of a goniometer microscope (Erma contact angle meter, Tokyo, Japan), and their values are given in Table 1. The penetration plots are shown in Fig. 1. Every point represents the mean of 6 determinations. The slopes of the penetration curves and the contact angles for the different combinations of powders and liquids are given in Table 1. The presence of polysorbate 80 does not seem to influence the penetration rate. Adsorption of Tween 80 at the surface of the phenacetin crystals could be one possible explanation for the lack of difference between the penetration

TABLE 1

INFLUENCE OF THE LIQUID ON CONTACT ANGLES AND PENETRATION RATE

Liquid	Phen. + 30% lactose		Phen. + 50% lactose	
	slope (10^{-6} m^2·s^{-1})	θ	slope (10^{-6} m^2·s^{-1})	θ
SGF + P80	2.82	70.2°	5.30	61.1°
SGF − P80	2.74	71.7°	5.39	63.7°

rates of the two liquids. Another possibility would be the opposite effects of the simultaneous lowering of the contact angle and the surface tension (Doelker et al., 1981). However, in our experiments this seems unlikely, in view of the small differences between the contact angles of SGF with or without surfactant.

The static surface tension is measured at 25°C by the Wilhelmy plate method. The measurements are made after stabilization of the surface tension of the solutions (between 2 and 4 h). To obtain saturated solutions, simulated gastric fluid, with or without polysorbate, is mixed for 24 h at 25°C, with an excess of the solid substance.

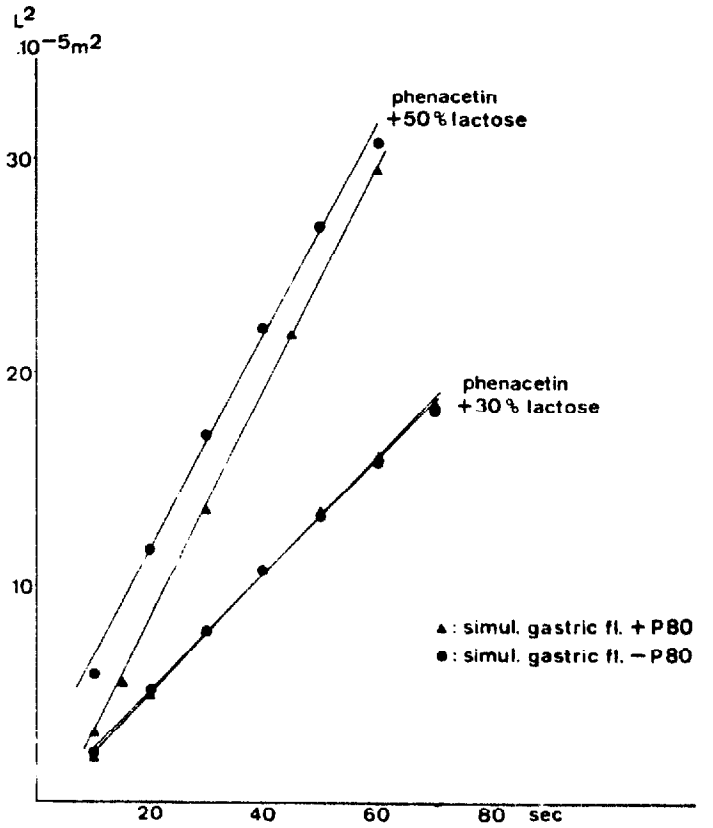

Fig. 1. Influence of polysorbate 80 on liquid penetration into powderbeds of phenacetin and lactose.

TABLE 2

STATIC SURFACE TENSIONS OF SOLUTIONS WITHOUT POLYSORBATE (25°C)

Liquid	Surface tension ($mN \cdot m^{-1}$)
Water	72.0
SGF (−P80) [a]	71.4
SGF (−P80)+lactose	72.5
SGF (−P80)+phenacetin	68.3
SGF (−P80)+phenacetin+lactose	68.2

[a] SGF (−P80) = simulated gastric fluid without polysorbate 80

Surface tension values for solutions without surfactant are shown in Table 2. Lactose has no influence on the surface tension. The addition of phenacetin seems to cause a very slight lowering of the surface tension. Table 3 gives the values for SGF with polysorbate and for the same solution saturated with the drugs. The surface tension lowering properties of P80 are only slightly affected by lactose, but are strongly reduced in the presence of phenacetin. A similar rise in surface tension of surfactant solutions through the addition of phenacetin was observed by Doelker (Doelker et al., 1981).

This reduction of the surface tension lowering properties could be caused by 2 phenomena: (1) an interaction of the surfactant with the dissolved phenacetin; and (2) an adsorption of polysorbate at the surface of the non-dissolved drug.

To determine which of these two phenomena is responsible for the reduction, surface tensions of saturated solutions in SGF without surfactant, but to which polysorbate 80 is added *after* filtration, are measured. The results are given in Table 4. The surface tension values for these solutions are comparable to that of pure SGF with P80.

From these experiments it appears that there is only an interaction between polysorbate 80 and the non-dissolved phenacetin. The surfactant is probably adsorbed at the hydrophobic surface of the phenacetin crystals, which causes a decrease in surfactant concentration in the solution.

The foregoing shows that the adsorption of polysorbate 80 at the surface of

TABLE 3

STATIC SURFACE TENSIONS OF SGF AND OF SGF SATURATED WITH THE DRUGS (25°C)

Liquid	Surface tension ($mN \cdot m^{-1}$)
SGF (+P80) [a]	34.2
SGF (+P80)+lactose	40.6
SGF (+P80)+phenacetin	59.1
SGF (+P80)+phenacetin+lactose	59.2

[a] SGF (+P80) = simulated gastric fluid with polysorbate 80.

TABLE 4

STATIC SURFACE TENSIONS OF SATURATED SOLUTIONS IN SGF TO WHICH P80 WAS ADDED AFTER FILTRATION

Liquid	Surface tension ($mN \cdot m^{-1}$)
SGF (−P80)+lactose: filtr.+P80	33.7
SGF (−P80)+phenacetin: filtr.+P80	38.3
SGF (−P80)+phenac.+lactose: filtr.+P80	32.7

undissolved pharmaceutical products can have an influence on the surface properties of the surfactant solution.

This phenomenon calls for caution in the interpretation of, for example, liquid penetration rates, when surfactant solutions are used as the penetrating fluid, since no certainty exists about the actual values of surface tension and contact angle of the liquid in the pores.

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