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Influence of drug amount and dioctyl sodium sulfosuccinate on dissolution of propyphenazone tablets

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A number of researchers have reported the results of investigating the influence of the amount of slightly soluble drugs on the disintegration and dissolution rate, but the drug content of these tablets seldom exceeded 30%, and even more rarely 50% (Rudnic et al. 1980, Graf et al. 1981; Kitamori and Makino 1982). The aim of this work was to investigate the influence of different, even large amounts of propyphenazone on tablet disintegration and drug dissolution rate in the presence of surfactant.

Two kinds of tablets were prepared: tablets I containing 10–85% w/w propyphenazone (Hofmann–la Roche) and 0.5% dioctyl sodium sulfosuccinate (DSS; American Cyanamid Company) calculated on the total mass of tablet, and tablets II prepared with 1% DSS. Tablets were made by a wet granulation procedure. Dry Kollidon 25 (BASF) was used as the tablet binder in a concentration of 4%, calculated on the mass of active substance. The powder was wetted by concentrated ethanol in which the surfactant was dissolved. Avicel PH 101 (Select Chemie), Kollidon CL (BASF) and magnesium stearate (Ph-Jug.IV) were added to the finished granulate, which was compressed on an Erweka Excenter Tablet Press of EKO type, with flat-faced punches of 9 mm diameter. The pressure was regulated by the input depth of upper punch, so that the resulting hardness of tablets was 5–7 kg/cm^2. Tablet disintegration time was determined on an Erweka apparatus of ZT type, in distilled water at 37 °C. For measuring tablet hardness the Erweka tester was used. Friability was tested on the Roche Friabilator. The content of propyphenazone was determined spectrophotometrically on a Specord M 40 Karl Zeiss Jena spectrophotometer at 237 nm in 7.7 M sulphuric acid (protonated ionic form). The composition and characteristics of the two tablet groups I and II are presented in Table 1.

Decreasing the amount of sightly soluble active substance increased the disintegration rate of propyphenazone tablets I and II. With the increase of propyphenazone content in tablet, the aggregation level of drug particles increased as well, the tablet became more hydrophobic, water diffusion rate decreased, and the disintegrating power of the system declined. DSS as a surfactant shortened the disintegration time, when present in higher concentrations; this was particularly noticeable with higher propyphenazone contents.

The results were compared using a *t*-test which

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TABLE 1

The composition and characteristics of tablets

Propyphenazone per tablet (%)	Avicel PH 101 per tablet (mg) I and II	Disintegration (s) mean ± S.D. ($n = 6$)		Hardness (kg/cm^2) mean ± S.D. ($n = 10$)		Friability (%) mean ± S.D. ($n = 5$)	
		I	II	I	II	I	II
10	186.4	5 ± 0.83	instant	5.43 ± 0.73	5.31 ± 0.49	0.05 ± 0.007	0.03 ± 0.01
20	162.4	10 ± 1.44	10 ± 0.73	5.00 ± 0.70	5.40 ± 0.56	0.11 ± 0.027	0.07 ± 0.015
30	138.4	15 ± 1.67	12.5 ± 0.88	5.21 ± 0.70	5.00 ± 0.77	0.30 ± 0.06	0.11 ± 0.023
50	90.4	19.33 ± 0.58	15.83 ± 1.09	5.00 ± 0.94	5.00 ± 0.56	0.27 ± 0.05	0.10 ± 0.025
70	42.4	174 ± 0.28	123 ± 0.11	5.28 ± 0.85	5.00 ± 0.56	0.15 ± 0.022	0.20 ± 0.027
85	6.4	766 ± 0.35	383.3 ± 1.79	5.38 ± 0.82	5.44 ± 1.02	1.10 ± 0.025	0.65 ± 0.04

Each 240 mg tablet also contained: 10 mg corn starch, 8 mg Kollidon K-25, 8 mg Kollidon chloride and 2.4 mg magnesium stearate. Tablets I contained 0.5% DSS, and tablets II 1% DSS.

showed statistically significant difference between disintegration rates of tablets with increase of propyphenazone content. The increase of DSS content from 0.5 to 1% w/w with the same concentrations of propyphenazone gave a statistical significance in disintegration rate differences of tablets with propyphenazone equal or greater than 30% w/w.

On the other hand, the statistical data processing, using the t-test, referring to tablet hardness and friability, did not show significant differences between them with the increase of either propyphenazone or DSS contents in tablets.

Investigating the release of propyphenazone from tablets I and II by dissolution test, it has been found that dissolution rate depends on the amount of drug present in the tablet (Figs. 1 and 2).

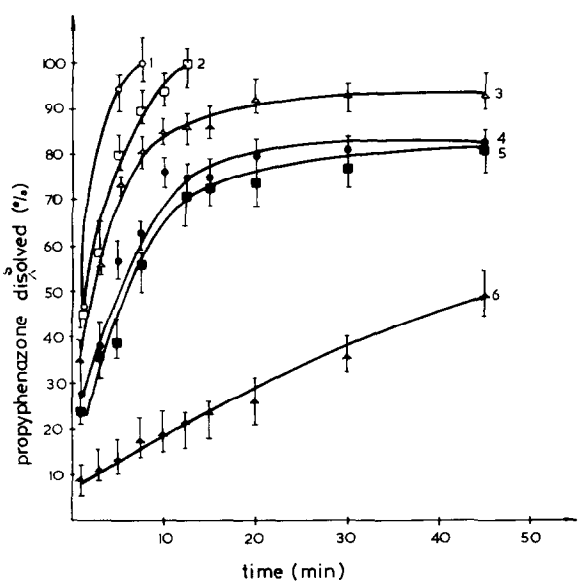

Fig. 1. The release of propyphenazone from tablets I containing: (1) 10%, (2) 20%, (3) 30%, (4) 50%, (5) 70% and (6) 85% of drug. Each point represents the mean value of 5 determinations and vertical lines show the ranges.

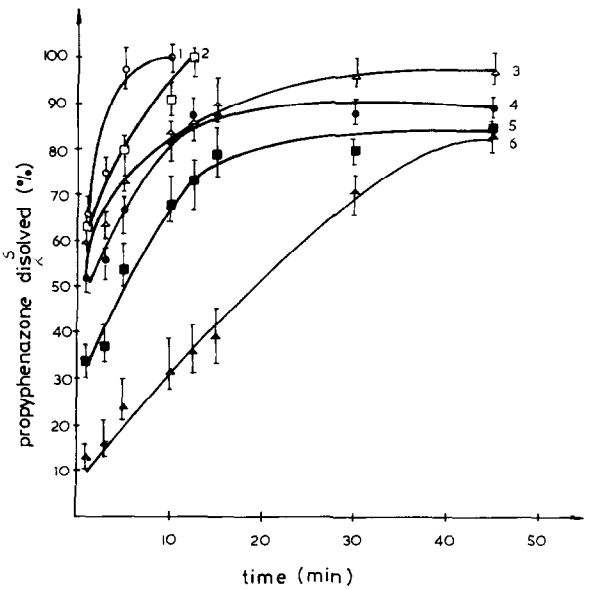

Fig. 2. The release of propyphenazone from tablets II containing: (1) 10%, (2) 20%, (3) 30%, (4) 50%, (5) 70% and (6) 85% of drug. Each point represents the mean value of 5 determinations and vertical lines show the ranges.

It is obvious that the increase of the concentration of poorly soluble drug (wherein the ratio of total tablet mass/drug changes from 10 to 1.2) results in increased aggregation levels of propyphenazone particles which in turn causes sustained release. As the system becomes more hydrophobic, the role of DSS in the process of propyphenazone release becomes more important.

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