DISSOLUTION OF PROPANTHELINE BROMIDE TABLETS B.P.

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Arising from a complaint by a clinician that some propantheline tablets administered to patients failed to produce the expected response, an investigation was conducted to measure the dissolution rates and disintegration times of seven commercially available brands of propantheline bromide 15mg tablets B.P. Propantheline bromide is very soluble in water having a very bitter taste and is thus presented as sugar coated tablets. No dissolution rate problems would be expected to exist with these tablets, but initial studies indicated that wide dissolution rate differences occurred both on an intra- and inter-batch basis. For each brand therefore a number of batches were investigated and individual measurements were made from at least three tablets from each batch. Since there is no official dissolution rate requirement for propantheline bromide tablets and manufacturers are therefore not required to measure dissolution rates, the identity of the various brands is not disclosed.

Dissolution rate measurements were performed in the B.P. apparatus using 500ml of 0.1 NHCl as dissolution medium and the basket rotating at 100 r.p.m. The amount of propantheline bromide in solution was measured at 243nm. For each tablet the time for 7.5mg propantheline to dissolve was interpolated from the plotted dissolution profiles ($t_{50\%}$). Disintegration times were measured in the E.P. apparatus. Some of the results obtained are shown in table 1.

Table 1. Dissolution and disintegration data

Brand	Batch	Mean $t_{50\%}$ mins.	Disintegration time mins.	Brand	Batch	Mean $t_{50\%}$ mins.	Disintegration time mins.
A	1	>120	>60	D	1	>120	>60
	2	72.3	>60	E	1	10.5	21.8
	3	>120	>60		2	17.3	21.2
B	1	>120	>60		3	20.6	22.0
	2	12.8	23.2	F	1	3.6	5.4
	3	12.7	28.4		2	5.4	5.2
C	1	82.3	>60		3	5.7	6.0
	2	30.9	49.0	G	1	8.3	8.6
	3	29.5	24.6				

All the tablets from brand A exhibited very poor dissolution rates with no improvement when the sugar coating and sub-coating was separately removed. Very hard non-disintegrating tablet cores and what appeared to be a thin transparent film around the cores as observed by Barrett & Fell (1975), may have prevented dissolution from taking place. Dissolution rates from brand B tablets showed wide intra-batch variability due to the random splitting of the sub-coating during dissolution (Barrett & Fell 1974). Inter-batch variability was found with brand C tablets, which by further investigation was probably due to the thickness of the sub-coating, since removal of this coating produced cores with fast dissolution rates. Brand D like brand A had very poor dissolution rates, with no improvement when the sugar and sub-coating was removed. The sugar coating was unusually resistant to being washed off and had therefore to be carefully scraped away with a scalpel. Batches E,F & G generally had satisfactory dissolution rates with the exception of brand E, where a large intra-batch variability existed due to the unusually long dissolution time of one of the tablets from batch 3. For all the tablets disintegration times were found to generally correlate with $T_{50\%}$ values. The results indicate that sugar coated tablets of very soluble drugs may present problems as regards dissolution and that large inter- and intra-batch dissolution variability may exist.

Barrett, D. & Fell, J.T. (1974) J. Hosp. Pharm. 32, 192-196
Barrett, D. & Fell, J.T. (1975) J. Pharm.Sci. 64, 335-336