A COMPARISON OF THE EFFECTIVENESS OF SEVERAL DISINTEGRANTS IN CAPSULES OF 4-ETHOXYCARBONYLPHENOXY-2'-PYRIDYL METHANE (BRL 10614)

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The use of disintegrants to improve the bioavailability of drugs formulated into hard gelatin capsules has been reported in the literature (Newton & Razzo, 1974; Newton & Rowley, 1975). One may expect the use of disintegrants to be particularly important where a high dose drug is to be filled by a process involving compression.

This communication reports a comparison of the effects of four disintegrants in capsules containing 500mg of BRL 10614, a cohesive, crystalline, chemically stable, basic drug. The capsules were filled by Zanasi LZ 64, which dosed a soft cylindrical plug of filling mix into each shell. The purpose of the study was to formulate capsules which could be filled with acceptable weight uniformity on available machinery, which would have a rapid in-vitro dissolution rate, and which would be chemically and physically stable for at least eighteen months.

Initially small batches of capsules were made for measurement of dissolution rates in 0.06 N HCl by a stirred flask method (see Table). The dissolution rate was enhanced by 1.5 and 3% Primojel or 3% Nymcel. Increasing the concentration of these disintegrants to 5% produced no further improvement. Maize starch and Polyclar AT were ineffective.

Disintegrant Description	Moisture content after drying*	% Dissolved after 30 min % Disintegrant 0	1.5	3.0	5.0
Maize Starch	3.9%	59.1	-	-	54.1
Primojel (sodium starch glycollate)	0.3%	59.1	76.8	90.6	91.9
Nymcel ZSB 16 (low substituted SCMC)	0.5%	59.1	-	76.3	73.7
Polyclar AT (cross linked PVP)	4.9%	59.1	-	44.5	59.4

* all disintegrants were dried overnight at 60°C before use.

In the second series of experiments, 1200 capsule batches were made containing (a) no disintegrant, (b) 1.5% Primojel, (c) 3% Primojel, (d) 3% Nymcel, and long term stability tests set up. The conclusions may be summarised as follows:

(i) Uniformity of fill weight was satisfactory for all batches. (coefficient of variation 0.7-2.0%).

(ii) No degradation was detected in any of the capsules by GLC or TLC after sixteen months at 37°C.

(iii) Dissolution rates were more reproducible from capsule to capsule when a disintegrant was present (standard deviation 3.2-5.8%) than when it was not (standard deviation 6.7-11.1%).

(iv) The dissolution rates of the stored capsules generally showed only small differences from the initials so that the rank order of disintegrant effectiveness (Primojel >Nymcel >no disintegrant) remained unchanged. However, the dissolution rate of the capsules with 1.5% Primojel increased significantly with time of storage at 37°C, so that after sixteen months they were similar in performance to capsules with 3% Primojel.

Newton, J.M. & Razzo, F.N. (1974). J. Pharm. Pharmac., 26, Suppl., 30P-36P.
Newton, J.M. & Rowley, G. (1975). U.S. Patent No. 3,859,431.

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