THE IN VIVO DISINTEGRATION OF HARD GELATIN CAPSULES

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The *in vivo* disintegration of dosage forms may be followed by radio-labelling the dose form with a short lived radionuclide, enabling the fate of the dosage form to be monitored using external scintigraphy (Casey and others 1976). The behaviour, *in vivo*, of hard gelatin capsules filled with two materials to obtain different *in vitro* disintegration times, was observed using this technique, under two physiological conditions.

Formulation A consisted of 0.1 g of Amberlite resin, Cg-400 (Cl), labelled with 30 µCi of ^{99m}Tc and filled into a No. 4 hard gelatin capsule. *In vitro* testing of this material showed that it behaved as an "ideal" pharmaceutical, having a disintegration time of 2 min. (B.P. method) and being readily dispersed in water. The mean particle size was 25 µm (Fisher Sub-sieve Sizer). Formulation B consisted of 0.1 g of the same resin milled using a fluid energy mill to 8 µm. This was labelled and packed into capsules as above. The disintegration time of these capsules was 9 min.

In vivo experiments were carried out in three human subjects. In a typical experiment, the subject ingested a capsule filled with formulation A labelled with 30 µCi of ^{99m}Tc, together with 100 ml of water, after an overnight fast. The subject was placed in a supine position on a stretcher to enable the abdomen region to be positioned beneath the collimated detector of a multicrystal scintillation camera. Data were accumulated for 60 min at 1 min intervals and stored on magnetic tape. Scintiphotos were also taken at approximately 8 min intervals throughout the period of data collection so the movement and dispersion of the capsules within the stomach could be observed and compared. The same subject then ingested another capsule of formulation A after a standard breakfast of:- 40 g cornflakes, 6 g sugar, 200 ml milk and the experiment was repeated. This experimental regimen was then repeated on the same subject with formulation B. At least one week was allowed to elapse between individual experiments on one subject.

Early results suggest that:-

1) In both formulations, the dispersion of the capsule contents is slower *in vivo* than is suggested by the *in vitro* disintegration times.

2) The gastric emptying of formulation A is faster when taken after a meal whereas the reverse is the case for formulation B.

3) Dispersion of formulation A is more rapid after a meal whereas formulation B shows little difference.

4) The scintiphotos suggest that the capsule remains stationary in the stomach, and in one case, lodged in the oesophagus and gradually emptied its contents into the stomach.

Casey, D.L., Beihn, R.M., Digenis, G.A. and Shambhu, M.B. (1976). J. Pharm. Sci., 65 1412-1413.