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Disintegration Test for Hard Gelatin Capsules

Keyphrases □ Disintegration—hard gelatin capsules, modification of USP and NF tests for tablet disintegration □ Dosage forms—hard gelatin capsules, disintegration test, modification of USP and NF tests for tablet disintegration

To the Editor:

A proposed disintegration test procedure for capsules was published in the USP XX Comment Proof (Vol. 3, No. 56) dated August 14, 1978. This procedure was based on a series of collaborative studies conducted by the Disintegration Test Review Committee of the Pharmaceutical Manufacturers Association (PMA) Quality Control Section. Highlights of these studies are presented in this communication.

The USP and NF describe disintegration tests for five tablet categories. The PMA project was aimed at developing a similar test for hard gelatin capsule products using the apparatus and methodology for tablet disintegration with as few changes as necessary. Three test samples (No. 2 hard gelatin capsules containing 0.5, 1.0, and 1.5% magnesium stearate in lactose) were used in the studies to evaluate procedure variables. Comments on each variable follow.

A cross section of disintegration baskets used in industry was examined. The baskets generally fell into two categories: those with notched shafts and those having shafts equipped with hooks. The former type provides a rigid mounting to the motorized device, and the motion is primarily vertical; the latter basket type provides a nonrigid attachment where the motion is both vertical and rotational. Studies showed that the mounting mode had no influence on the test results. Disintegration times were identical, within normal variation, regardless of the type of mounting used.

The disintegration time of the three test samples could not be differentiated when the plastic disks described in the USP and NF were placed into the basket-rack assembly. The disintegration time for each sample was ~3 min. By eliminating the disks and placing a 10-mesh wire screen on top of the baskets to retain the capsules within the tubes, the disintegration times for the 0.5, 1.0, and 1.5% samples were 12, 25, and 39 min, respectively.

The compendia are not specific about the disintegration test vessel. Committee members reported that both the size of the vessel and the volume of the test vehicle affected the hydrodynamics of the system, thereby influencing the disintegration rate. A 1000-ml, low-form beaker containing ~900 ml of medium was the most convenient and compatible with the dimensions of the basket-rack assembly.

Purified water was a satisfactory test vehicle for the three samples. Reproducibility in disintegration time was improved by the addition of 0.1% benzalkonium chloride. The use of simulated gastric fluid was investigated, but it was reported that hydrogen chloride vapors emanating from the fluid slowly corrode the equipment. Because of variation in the composition of compendial capsule products, collaborators recommended that both the test medium and the disintegration time limit be specified in the individual monographs.

The Committee observed that the longer the path through which the basket travels in its vertical motion, the more rapid is the disintegration time. The USP and NF specify a stroke length of 5–6 cm. In a study involving one test specimen (1.0% magnesium stearate in lactose with an average disintegration time of 25 min), the disintegration time decreased by almost 6 min when the stroke was adjusted from the lower limit, 5 cm, to the upper limit, 6 cm. Therefore, a stroke length of 5.3–5.7 cm was recommended.

The final procedure was submitted to the USP after it was found to be workable in the laboratories of 13 PMA-member companies.

Jerry Polesuk, Chairman
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Effect of Smoking on Binding of Lidocaine to Human Serum Proteins

Keyphrases □ Lidocaine—effect of smoking on binding to human serum proteins □ Protein binding—lidocaine, effect of smoking, human serum □ Smoking—effect on binding of lidocaine to human serum proteins

To the Editor:

Cigarette smoking can have striking effects on the disposition of theophylline (1, 2), propranolol (3), and other drugs (4, 5). These changes generally have been ascribed to increased intrinsic hepatic clearance secondary to enzyme induction. However, other mechanisms may be operative. This communication describes the apparent effect

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