CALIBRATION OF CONTINUOUS FLOW DISSOLUTION TESTING APPARATUS

P.S. Daniels, P.J. Rue, J.M. Padfield, Glaxo Group Research Ltd., Ware, Herts.

Calibration of dissolution equipment is recognised as an essential part of dissolution testing and the USP Apparatus Suitability Test uses a disintegrating tablet (prednisone) and a non-disintegrating tablet (salicylic acid) for this purpose. This test does not include continuous flow methodology, but obvious time and labour saving advantages justify its use provided that it does not affect dissolution rates. To circulate the dissolution medium in a continuous flow test requires a pump and filtering system. As a number of sources have suggested that the calibrator tablets are insufficiently sensitive to modifications to the test procedure, we have studied the effects of disturbances produced by reintroduction of the medium to the beaker and by the presence of a sampling probe on the dissolution of the calibrators, using Apparatus 2 of the USP XX.

Initially two series of calibrations were performed in which the sample tube and filter, consisting of a plug of cotton wool held between two micropipette tips, were in position throughout the test. In one series the dissolution medium was circulated throughout the test. In the second series the pump was operated only for the last five minutes to allow proper mixing of the medium in the beaker with that in the pipes. The results showed that reintroduction of the medium had no effect on the dissolution rate of the calibrator tablets.

The effect of sampling probe size on the dissolution of a tablet has previously been studied by Wells (1981), who concluded that the displacement volumes of sampling probes should be as small as possible. Our studies using calibrator tablets, confirm that the presence of a sampling probe may affect the dissolution rate of some tablets. When the sampling probe was in position throughout the test, the percent dissolved at 30 minutes for the prednisone tablet was about 5% greater at 50rpm and about 8% greater at 100rpm, than when the probe was introduced only at the time of sampling. The dissolution rate of the salicylic acid tablets is unaffected by the presence of the probe.

The sampling probe was modified by the replacement of the cotton wool filter by a Technicon Reagent Filter - (made of sintered polyethylene) and a further series of calibrations carried out. There was no significant difference between the percent dissolved at 30 minutes with the probe in position and that without, for either tablet.

It is probable that the relatively large and irregularly-shaped micropipette tip filters disturb the hydrodynamics of the dissolution medium thereby increasing the turbulence in the upper region of the beaker. As the prednisone tablet disintegrates, small particles of drug are dispersed throughout the beaker by the action of the paddle. With the sample probe present, these particles which move into the upper region of the beaker are subjected to increased turbulence which causes more rapid dissolution. The dissolution of the salicylic acid tablet is not affected by the sampling probe, due to the fact that the increased turbulence is confined to the region above the paddle. Thus the region below the paddle, in which the non-disintegrating tablet remains throughout the test, experiences similar hydrodynamics whether the probe is present or not. It is probable that, because of its smaller volume and its more regular shape, the Technicon filter does not disturb the hydrodynamics of the medium.

We conclude that the prednisone calibrator tablet has a small intertablet variability and that it is sensitive to, at least the reported perturbation. Continuous flow methodology should be calibrated using USP calibrator tablets and results compared with those from the same apparatus using manual sampling techniques. We recommend that small volume, regularly shaped filters be used for continuous flow testing. This is particularly important for those products which disintegrate to give buoyant or dispersed particles.

Wells, C.E. (1981) J. Pharm. Sci. 70 (2) 232-233

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