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Ranitidine tablets: an improved dissolution method

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Ranitidine tablets contain ranitidine hydrochloride and are usually film coated. The USP monograph stipulates a dissolution method that comprises water (900 ml) as dissolution medium and apparatus 2 (paddles) at 50 rpm. Not less than 80% should be dissolved in 45 min [1].

Although ranitidine hydrochloride is very soluble in water it exhibits a tendency to stick to solid surfaces when exposed to moisture. This propensity seems to be enhanced in combination with film forming agents like hydroxypropyl methylcellulose. Consequently, tablets may stick to the bottom of the dissolution vessels resulting in an incomplete mixing and uneven dissolution. Therefore, it has been suggested to employ baskets instead of paddles in the dissolution test or, alternatively, to use sinkers with the paddle method in order to minimize the sticking effects [2]. However, it may be argued that although baskets prevent sticking of tablets to the bottom of the dissolution vessels, sticking to or occlusion of the basket screen remains as a potential source of error. Moreover, use of sinkers is hampered by the commercial unavailability of such devices in a standardized form.

Several other instances are known in the scientific literature describing alternative dissolution methods to that of the USP for ranitidine tablets, for instance baskets, rpm not stated [3], baskets, 100 rpm [4], 0.1 N hydrochloric acid, paddles, 100 rpm [5] and 0.1 N hydrochloric acid, paddles, rpm not stated [6]. In the last paper, 45 commercial ranitidine tablet samples from the German market were investigated. Conceivably, this may reflect difficulties encountered with the USP procedure.

In view of this it was determined to investigate the effects of slightly increased stirring rates (55 and 60 rpm) of the paddles on the supposedly sticky tablet material at the bottom of the dissolution vessels. The tablets employed in the study were a generic form of 150 mg ranitidine tablets which had a dissolution profile comparable with that of the originator's product: Zantac® tablets 150 mg (Glaxo Wellcome). Four different methods were employed and these along with the results are depicted in the Table.

Table: Dissolution methods and results (n = 6)

Method		Amount dissolved after 45 min
1	Water, 900 ml, paddles, 50 rpm	93.2% (86.0–97.1%) c.v. 4.7%
2	Water, 900 ml, baskets, 50 rpm	88.2% (75.1–95.9%) c.v. 8.7%
3	Water, 900 ml, paddles, 55 rpm	96.8% (95.7–98.6%) c.v. 1.0%
4	Water, 900 ml, paddles, 60 rpm	97.8% (96.9–99.0%) c.v. 0.7%

These results show that a slightly increased stirring rate (55 rpm) of the paddles eliminates the experimental artifacts due to the stagnant region in the dissolution vessels resulting in very little variability in the data. It is proposed that this method is not less discriminating than the USP procedure. Finally, it should be mentioned that the British Pharmacopoeia does not specify a dissolution method in its monograph on ranitidine tablets, possibly indicating that there is little or no direct correlation between dissolution and bioavailability for this drug delivery system [7].

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