Research Paper

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Studies on *in vitro* evaluation of some Griseofulvin tablets

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Six commercially available brands of Griseofulvin tablets (A to F) available in the Indian market were evaluated for four *In vitro* parameters such as uniformity of weight, disintegration, dissolution and assay with special emphasis on inter-pharmacopoeial difference in dissolution rate profiles. The results of the investigation revealed that although all the brands confirmed to the I.P. specifications of uniformity of weight and distintegration, four brands failed to meet the requirements of the assay. All the brands except one complied with the U.S.P. and I.P. dissolution specifications. However, three brands failed to comply with the dissolution specifications of B.P.

GRISEOFULVIN is an active antifungal agent. This drug was the first orally administered antifungal agent used for dermatophytic infections[1]. Several brands of griseofulvin tablets are available in the Indian Market of which six brands of well known pharmaceutical companies were included in the study. Griseofulvin tablets are official in I.P.[2], B.P.[3], and U.S.P.[4] Its solubility has been defined as practically insoluble in water in I.P.[5] and B.P.[6] and very slightly soluble in water according to the U.S.P.[7]. Because of its poor solubility, griseofulvin can be considered as a drug candidate which may give rise to dissolution related bioavilability problems. Dissolution testing of griseofulvin tablets was not official in the earlier edition of I.P.[8], but it has been included as one of the *in vitro* testing parameters in I.P. 1996[2]. Hence it was thought necessary to carry out the *in vitro* testing of commercially available brands with special emphasis to dissolution, using tablets of 250 mg strength.

EXPERIMENTAL

Materials

Six commercially available brands of griseofulvin tablets of 250 mg strength were purchased from the market. They were of recent manufacture at the time of study. The products were coded as A,B,C,D,E and F. All products were from different manufactures. The labelled shelf life of all products was 36 months.

The products were evaluated for uniformity of weight, disintegration, assay as per I.P. and dissolution as per I.P., B.P., and U.S.P.

Methods

(a) Assay: Twenty tablets were powdered. A quantity equivalent to 80 mg of griseofulvin was taken, treated and analysed spectrophotometrically at 291 nm as specified in I.P.[8]

(b) Dissolution: Dissolution studies were performed using a Validated USP XXII Dissolution Rate Apparatus II, Nine Hundred ml of 4% w/v solution of sodium lauryl sulphate in water was maintained at 37 ± 0.5° The apparatus was operated at 100 rpm for 60 minutes as per I.P.[2]. While as per B.P.[3], 1000 ml of 1.5% w/v solution of sodium dodecyl sulphate in water was maintained at 37±0.5°. The apparatus was operated at 100 rpm for 45 minutes. As per U.S.P.[4], 1000 ml of water containing 40 mg sodium lauryl sulphate

Table 1: *In vitro* evaluation of commercially available griseofulvin tablets

Products	Uniformity of weight		Disinte-gration time	Drug Assay (percent of labelled amount of Griseof-ulvin	Cumulative Percent drug dissolved in		
	Average weight (mg)	Maximum percent-age deviat-ion			45 min* B.P. (±SD)	60 + min I.P. (±SD)	60+ min USP (±SD)
A	358.0	+2.24 -1.12	5 min	94.01	56.54 (2.8)	61.28@ (3.1)	65.43@ (2.6)
B	355.5	+1.27 -1.55	10Sec.	96.48	86.29 (1.0)	91.76 (0.5)	92.28 (0.7)
C	346.8	+1.21 -2.54	25Sec.	91.73	86.01 (1.2)	92.23 (0.7)	92.45 (0.8)
D	372.8	+3.27 -2.90	2 min 15 Sec.	91.57	65.25 (2.8)	80.66 (1.3)	80.95 (3.0)
E	380.7	+0.34 -0.18	9 min	103.37	87.34 (1.4)	93.43 (0.4)	103.81 (1.2)
F	376.3	+1.78 -4.39	10 min	90.37	61.02 (2.6)	85.04 (3.1)	86.10 (2.8)

*, n=5; +, n=6 except for brand A; @, n=24

per ml at 37±0.5° was used and the apparatus was operated at 100 rpm for 60 minutes.

The sampling time in each case was modified i.e. instead of taking a single sample at the end of the specified time interval as given in I.P., B.P. and U.S.P., samples were withdrawn after 5, 10, 15, 30, 45 minutes for testing as per B.P. and 5,10,15,30, 45 and 60 minutes as per U.S.P. and I.P.

Analytical Procedure: The aliquots of samples were filtered. The filtrate was suitably diluted and absorbance was read spectrophotometrically at 291 nm.

Percentage drug dissolved at the end of 45 minutes as per B.P. and at the end of 60 minutes as per I.P. and U.S.P. was found out. Also values of cumulative percentage drug dissolved were found out and plotted against time.

RESULTS AND DISCUSSION

Tablets of all the brands met the general requirements of uniformity of weight and disintegration requirements as specified in I.P. (Table I).

Of the six brands tested for griseofulvin content, four brands failed to comply with the I.P. requirements which is 95 to 105 percent of the stated amount.

Results of dissolution testing revealed interbrand differences in the dissolution profiles (fig, 1,2,3). This difference could be attributed to the formulation process parameters and to drug particle size which may vary from manufacturer to manufacturer.

One point dissolution data of all brands is shown in Table 1. Brands A,D and F failed to meet the dissolution test requirements as per B.P., i.e. not

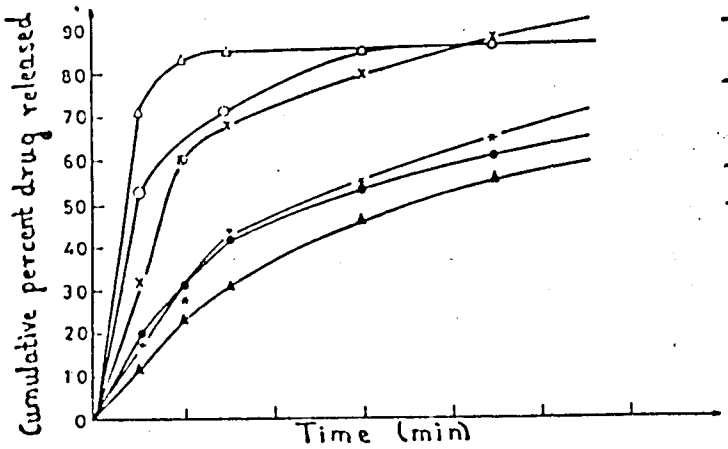

Fig. 1: Dissolution profiles of Griseofulvin Marketed tablets according to B.P. Sample A, ▲;B, O; C,Δ D, *; E, X; F, O

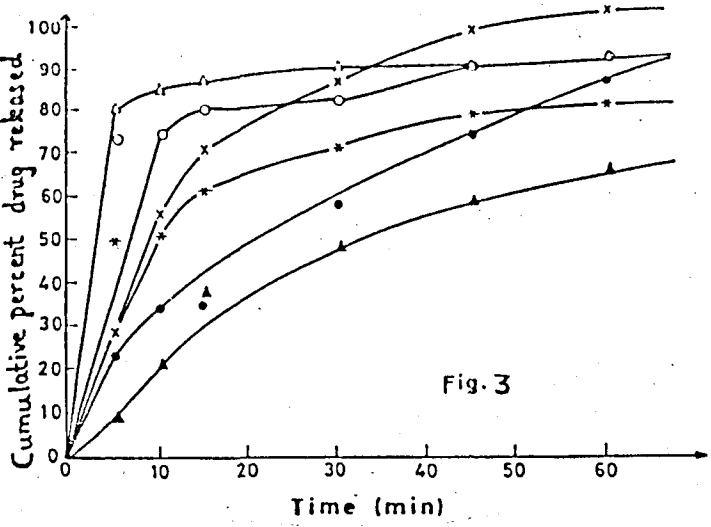

Fig. 3: Dissolution profiles of Griseofulvin Marketed tablets according to U.S.P. Sample A, ▲;B, O; C, Δ D, *; E, X; F, O

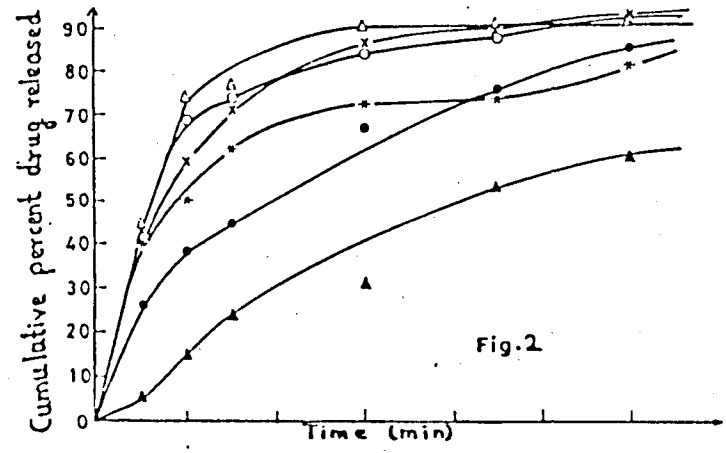

Fig. 2: Dissolution profiles of Griseofulvin Marketed tablets according to I.P. Sample A, ▲;B, O; C, ΔD, *; E, X; F, O

less than 70% of the drug should be dissolved at the end of 45 minutes. But the same brands D and F in addition to brands B,C and E complied with the I.P. and U.S.P. specifications for dissolution (Table 1). However, brand A failed to comply at all stages of the three stage I.P. and U.S.P. dissolution test whereby the sample size is increased to 12 at stage 2 and 24 at stage 3. This difference in meeting the dissolution test requirements by the same brand when tested as per I.P., and U.S.P. may be attributed to the difference in the dissolution medium recommended by the three pharmacopoeias. Though all the three pharmacopoeias have suggested the use of sodium lauryl sulphate in the dissolution medium, the concentration in which it is used varies which seems to have a significant effect on the drug solubility and hence meeting test requirements.

Thus it can be concluded that marketed griseofulvin tablet brands are not only showing inter-brand differences in their dissolution profiles but there exists inter-pharmacopoeial variation also for the same brand tested. Also four brands of marketed griseofulvin tablets failed to comply with drug assay requirements as per I.P.

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