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Research Article

IN VITRO BIOEQUIVALENCE STUDY OF FOUR BRANDS OF NIMESULIDE TABLETS MARKETED IN INDIA

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ABSTRACT

The availability of numerous brands of nimesulide in our drug market today places clinicians and pharmacists in a difficult situation of choice of a suitable brand or the possibility of alternative use. The aim of the present study was to predict the bioequivalence of four brands of nimesulide tablets marketed in India using in vitro tests. The in vitro dissolution study was carried out on the four brands of nimesulide tablets using the paddle method according to US Pharmacopoeia (USP) guidelines. Other general quality assessment tests like hardness and disintegration time were also determined and all these generic tablets passed compendial specifications. All the brands tested passed the standard for disintegration time. There were slight differences in the dissolution profiles of the four brands. All the brands except NM1, however, released >45% of nimesulide within 30 min. Based on the in vitro tests, NM2, NM3 and NM4 are considered bioequivalent and interchangeable. NM1 has very low dissolution rate, which will likely result in poor bioavailability. The results show the need for constant monitoring of new brands of nimesulide introduced into the drug market to ascertain bioequivalence and conformity with pharmacopoeia standards.

Keywords: Nimesulide tablets, Bioequivalence, Disintegration time, I*n vitro* dissolution.

INTRODUCTION:

Nimesulide, a non-steroidal anti-inflammatory drug (NSAID) with anti-inflammatory, analgesic and antipyretic effects, was first launched in Italy in 1985 [1]. A handful of drug, Nimesulide was the most controversial drug as even though it was banned in US, Britain, Canada, Sweden, Denmark, Australia, New Zealand, Japan and other 168 countries, the drug was freely available in India, being aggressively marketed by prominent drug companies. Though the drug was banned in most of the countries following information suggesting an increased risk of liver toxicity compared to other drugs in the same class, the then

drug authorities in India claimed that no adverse drug reaction report had been received on the use of Nimesulide in the country so far to necessitate a ban [2, 3].

The availability of numerous brands of nimesulide in our drug market today places clinicians and pharmacists in a difficult situation of choice of a suitable brand or the possibility of alternative use. Besides, there are growing concerns that various nimesulide formulations may have different bioavailability and that development of resistance will accelerate if sub-optimal doses are used. Despite the considerable different use in India, there are no reports on the bioavailability and bioequivalence of the various brands of nimesulide tablets marketed in India [4]. Hence the present investigation has been carried out.

In the present study, we set out to assess the in vitro dissolution of four brands of Nimesulide tablet marketed in India. The results of the study will provide a rationale for the interchangeability or otherwise of the selected brands. Other general quality assessments of the tablets are also determined.

MATERIALS AND METHODS

A total of four brands of nimesulide designated as NM1, NM2, NM3 and NM4 were compared. Pure sample of nimesulide was obtained as a gift sample from Cipla, Goa. All solvents used were of analytical grade and were purchased from S.D. Fine chemicals, ltd, Mumbai.

Different brands of nimesulide studied were selected based on frequency of prescription, use and availability in hospital and community pharmacy shelves.

The tablets were evaluated for hardness and disintegration time. The dissolution tests were carried out using the paddle method according to US Pharmacopoeia (USP) guidelines, operated at 75 rpm in a dissolution bath containing alkaline borate buffer pH 8.4, with sink condition maintained at a temperature of 37 ± 0.5ºC. One tablet chosen randomly from each of the tablets was put into the basket suspended in the dissolution medium. Samples (5ml) were withdrawn at intervals for a total of 120 min. At each withdrawal 5 ml of fresh dissolution medium was used to replace the withdrawn sample. Each sample was filtered, diluted and the absorbance reading determined at 254 nm using UV spectrophotometer against the blank, alkaline borate buffer pH 8.4. The concentration was thereafter determined from the calibration curve of pure nimesulide [5].

RESULTS

The four brands of nimesulide tablet showed slight variation in crushing strength and significant variation disintegration time (Table 1). NM1, NM2, NM3 and NM4 have crushing strength values <5 kgs and are considered suboptimal. All the brands tested disintegrated in <5 min (Table 1). The

calibration curve as shown in Fig.1.has good correlation (R^2= 0.987).

The dissolution profiles for brands NM1, NM2, NM3 and NM4 indicate that all the brands except NM1 released >45% of the active ingredient within 30 min.

Table 1: Results for Hardness and Disintegration tests

Formulation	Thickness (mm)	Hardness (kgs)	Disintegration Time (Sec.)
NM1	4	3.7	32.75
NM2	4	3.9	98
NM3	4.5	2.4	255
NM4	4	4.8	60

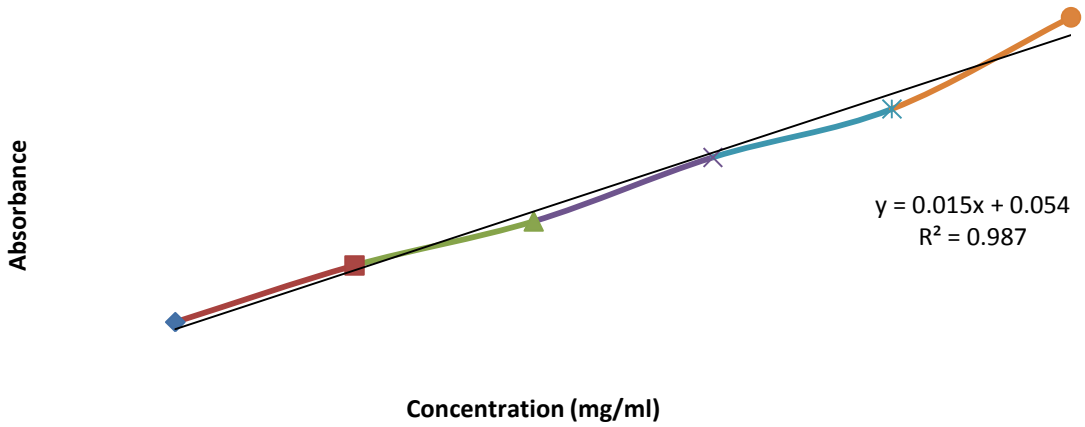

Figure 1: Calibration plot of Nimesulide in alkaline borate buffer pH 8.4

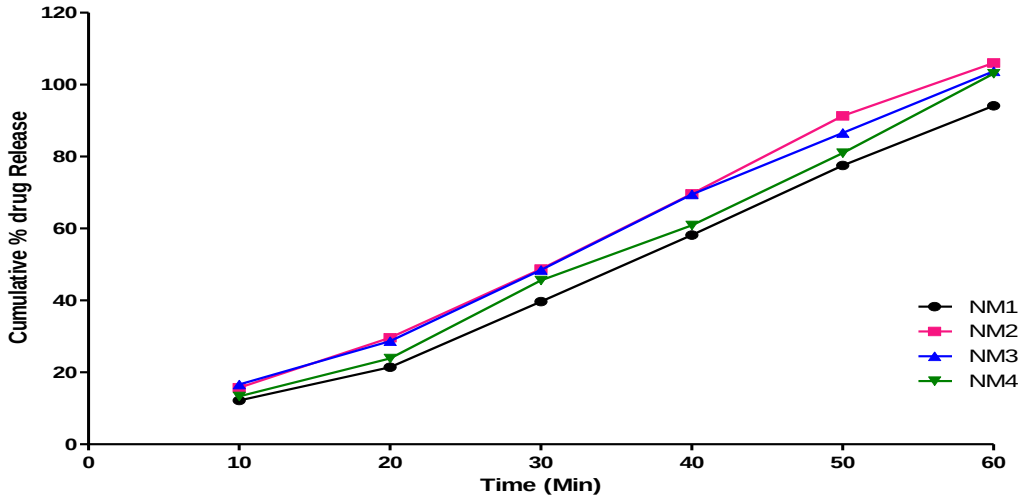

Figure 2: Percent drug release of Nimesulide with time in alkaline borate buffer pH 8.4

DISCUSSION

Our results based on the in vitro dissolution show that significant variation exists in the bioavailability of nimesulide from the nine brands of nimesulide tablets. However, all the brands except NM1 released >45% nimesulide within 30 min and as such passed the British Pharmacopoeia standard for dissolution test of uncoated tablets[6]. In conclusion, our results indicate that all the brands of nimesulide tablet included in this study apart from NM1 seem to have high dissolution rate and hence very good bioavailability. NM2, NM3 and NM4 can be considered bioequivalent and interchangeable.This study highlights among other things the need for constant monitoring of the new products introduced into our drug market with the view to ascertain bioequivalence and conformity with pharmacopoeia standards. There is need, however, to carry out in vivo studies to further substantiate the in vitro predictions.

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