A Comparative In Vitro Evaluation of Different Brands of Nimesulide tablets

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Abstract

Five Indian Brands (coded as A,B,C,D,E) of 100 mg Nimesulide tablets were evaluated for various In vitro parameters, i.e. size and shape, uniformity of weight, hardness, friability, content, disintegration time and dissolution profile. All the products met the requirements of British Pharmacopoeia for tablet formulation. The hardness of all the brands was found to be in the range of 4.2-4.4 kg, while friability was less than 1 %. The disintegration time of all brands was found to be in the range of 2min 22 sec to 5min 29 sec. All brands comply the B.P weight variation test while brands A, B, C and D comply the B.P dissolution test except brand E. Formulation additives in the tablet, physical form of the drug used in the tablet and manufacturing process vary from manufacturer to manufacturer which is responsible for the variation in the observed dissolution profiles.

Keywords: Nimesulide in tablets, hardness, disintegration time, dissolution rate, quality evaluation.

Materials and method

Collection of samples

nimesulide in tablets (100 mg) of 03 different brands (20 tablets from each brand) of were purchased from different local medicine shops located in Washim, India. The samples were properly checked for their visual appearance, manufacturing company, manufacturing date, expiry date, manufacturing license number, batch number and DAR number at the time of purchase.

Identification of sample

The brands were randomly coded as N1, N2, N3… so that the identity of the manufacturers can be blinded. All brands were labeled with a shelf life of two years and claimed to contain 100 mg of Nimesulide per tablet. All the tablets were found packaged in strip or in blister with a good condition[1]. The shape, size and colour of different branded tablets were subjected to visual inspection at the very beginning of the research work. The label information of 03 different brands of Nimesulide (100 mg) is represented in Table 1

Weight variation test

Individual weights of selected 20 tablets of each brand were measured in milligram using electronic analytical balance and from these data mean weight with standard deviation (SD) were calculated.

Hardness test

Crushing strength (N) of 03 tablets from each brand was determined with an Monsanto hardness tester. Mean hardness with standard deviation (SD) were calculated.

Friability test

20 tablets from each brand were weighed and subjected to rotation by employing a Roche friabilator (VEEGO, India) which was operated at 25 RPM for 4 minutes and then all tablets were re-weighted after removing from friabilator[3].

Disintegration test

Three tablets from each brand were employed for the disintegration test in distilled water at 37 °C using a tablet disintegration tester (VDT-2, Veego, India) as per condition described by United State Pharmacopeia,

2013. The disintegration time (DT) was noted down and it's the time taken for the entire tablet to disintegrate completely.

Standard curve preparation

The powder equivalent to 10 mg of standard nimesulide was taken and dissolved in 0.1 N HCl. Then it was diluted to produce a final concentration of 15µg/ml for working solution. Absorbance values were then measured at the maximum wavelength (λmax) of nimesulide of the serially diluted concentrations (0, 1.5, 3, 4.5, µg/ml) using a UV-VIS spectrophotometer. Maximum wavelength was obtained by scanning sample of diluted standard nimesulide from 200 to 400 nm wavelengths and it was found to be 392nm.

Measurement of potency

Sample was prepared by weighing and crushing 04 tablets, transferring amount of drug powder equivalent to 10 mg in 0.1 N HCl solution and placing it in sonicator (Hwashin Technology, Seoul, Korea). The portion of solution was filtered and the filtrate was suitably diluted. Absorbance was taken at 392 nm by using UV-visible spectrophotometer. Finally the potency of different brands was calculated using the following equation

Potency= Drug present in a single tablet / Strenght (mg) x 100

Dissolution test

The dissolution test was undertaken for 03 randomly selected tablets using USP dissolution apparatus I (Electrolab). The dissolution medium was 900 ml of 0.1 N HCl which was maintained at 37±0.5 °C. Rotations were 100 RPM. Each time 10 ml sample was withdrawn after 5 min, 15 min, 30 min, 45 min & 60 min, and was then filtered[1]. The filtrates were then suitably diluted with 0.1 N HCl. Absorbance was measured at 392 nm. Using the y =mx + c equation derived from the standard curve of API, concentrations of sample at different above mentioned times were calculated. From these data Cumulative amount release and then % Drug release were calculated using the following equation:

%Drug release = Cumulative amount release(mg) / Stength (mg) x 100

Results and discussion

Price fluctuation

There is minor price variation among the brands. Brand A1and A2 had the maximum price of tablet and brand A3 had the minimum price of tablet while there was no major variation in the quality of the tested drugs.(Table 1).

Table 2: A summary of quality control tests undertaken on different brands of Nimesulide tablet

Brand Code	Weight (mg)	%Deviation from average weight		Hardness	Friability %	DT* (min)	Potency %
		Max	Mini				
N1	5952 ± 297.6	327.36	267.84	0.75 kg/cm^2	0.28%	1.58	99.42%
N2	6840 ± 342	376.2	307.8	1.55 kg/cm^2	0.58%	1.65	98.49%
N3	7730 ± 386.5	425.15	347.85	1.05 kg/cm^2	0.45%	2.08	98.79%

Test of uniformity of weight

The objective of the weight variation test is to ensure – good manufacturing practices (GMP), appropriate size of the tablets and the content uniformity of the formulation The United States Pharmacopoeia (USP) provides criteria for tablet weight variation test of intact dosage forms which states that the percent weight variation should be within ±5% for tablets having average weight more than 324mg[5]. The tablets met the USP test if there are not more than 2 tablets outside the percentage limit and if no tablets deviate twice of the percentage limit. All the brands complied with the compendia specification for uniformity of weight as the percent deviations from average weight of all the tablets were within the acceptable range of ±5%. Minimum percent deviation from average weight was found in brand A3 (Table 2).

Hardness test

Tablet hardness testing is a laboratory technique used by the pharmaceutical industry to test the breaking point and structural integrity of a table tunder conditions of storage, transportation,and handling before usage . The hardness of the tablet depends on the materials used, amount of binder, space between the upper and lower punches at the time of compression and pressure applied during the process of compression [5] . Hardness influences many tablet properties including disintegration, dissolution and friability. High hardness values may result in increased disintegration times and decreased dissolution times. As opposed to this situation, high friability values may be observed in case of low hardness values [18, 11] .Brand N2 had the highest average hardness (1.55 kg/cm^2) whereas brand N1 had the lowest average hardness (0.75 kg/cm^2) (Table 2). A force of about 40 N is the minimum requirement for a satisfactory tablet [1]. Hence the tablets of all the brands comply with this requirement[15,16].

Friability test

Friability (the condition of being friable) testing is a method, which is also employed to determine physical strength of compressed and uncoated tablets upon exposure to mechanical shock and attrition. In simple words, friability test tells how much mechanical stress tablets are able to withstand during their manufacturing, distribution and handling by the customer[6]. Throughout pharmaceutical industry, friability testing has become an accepted technology [12] It is a compendial test and met the USP specification if friability is not more than 1% [10, 11] The friability was found to be between the ranges of (0.4-0.9) %, thus all the brands met the friability specification (Table 2)[13].

Disintegration test

Disintegration test is performed to find out that within how much time the tablet disintegrates. Disintegration test is very important for all coated & uncoated tablet because the dissolution rate of drug depends on the disintegration time, which ultimately affect the rate of absorption and subsequent bioavailability of drug [13] According to BP/USP specification, Uncoated tablets should disintegrate within 5 -30 min . Here uncoated dispersible Nimesulide tablets of all the brands met the requirement as the disintegration time (DT) was found to be between the ranges of (1-5) minutes (Table 2).

Potency test

Potency is a measure of drug activity expressed in terms of the amount of API (in percentage) required to produce an effect of given in this test is done for determining the toxic and therapeutic effect of the drug. The potency of the tablet should comply with the specification because very highly potent drug may give toxic effect & very less potent drug may give sub-therapeutic effect. All the brands showed potency within the range of (95-105)% of labeled amount of drug and complied according to USP.

Table 3: Dissolution profile of Three brands of Nimesulide tablets

Time (Min)	Brand N1	Brand N2	Brand N3
0	0	0	0
5	0.54	0.58	0.52
10	1.23	0.75	0.76
15	1.295	0.93	0.96

Dissolution test

For this test USP dissolution apparatus was used. To test for dissolution, one tablet was placed in each vessel (6 vessels) for each brand, containing 900 ml of 0.1 M hydrochloric acid (HCl) as a dissolution medium maintained at 37 ± 0.5 °C. The rotational speed of the apparatus was held constant at 50 rpm. When the temperature was set each tablet desired time, 20 ml solution was collected and filtered. The filtrate was then analyzed by UV spectrophotometer at the wavelength of 392 nm, using 0.1 M HCl as blank. The percentage of drug release at each interval was calculated by using standard Nimesulide. As per USP-NF tablets meet with this test if not less than 75% dissolves in 45 min. According to BP tablet comply with this test if not less than 80% dissolves in 45 min [10, 11, 13].was placed in each basket for 30 min.

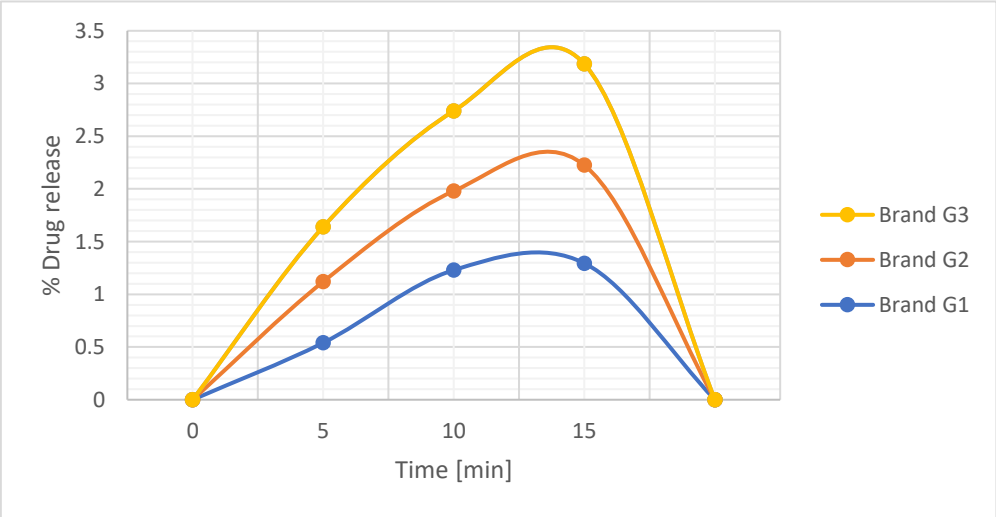

Fig 1: Comparative average % drug release of Nimesulide tablet of Three brands

Conclusion

Nimesulide tablets have been analysed to find their correct quality status. For this purpose, the marketed sample of three brands of Nimesulide tablets was analysed by using established methods and apparatus. The result of weight variation, hardness, disintegration time, dissolution and assay potency tests of all marketed products comply with pharmacopoeial limit. All of the brands have proved that they have the quality which meets the BP and the USP specification. The present study, although performed on a limited scale yet on the basis of professional judgment the data reported in this study can help the Drug Control Authority to get an idea about the quality status of the marketed Nimesulide preparations in India.

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