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COMPARATIVE IN-VITRO STUDY AND EVALUATION OF DIFFERENT BRANDS OF NAPROXEN TABLETS MARKETED IN BANGLADESH

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Abstract

Naproxen is an NSAID that works by blocking down the hormones responsible for inflammation as well as pain and usually prescribed for the treatment of pain and inflammation, specified for the conditions such as arthritis, tendinitis spondylitis, and ankylosing. The quality of pharmaceutical finished products is one of the foremost disquiets to pharmaceutical industries. This study was designed to compare and evaluate several in-Vitro quality parameters of four commercially available brands of naproxen 250 mg tablet in Bangladesh including weight variation test; thickness; hardness; disintegration time; potency; and dissolution test according to established USP specifications. All four samples from four different pharmaceuticals were compliant with USP specifications for weight variation test; hardness test; thickness test; and disintegration time. In case of potency test only sample 2 (87.80%) failed to meet the USP specifications. All the samples had dissolved more than 80% of their labelled claim within 45 minutes of the test where the dissolution profile of sample 2 was very close to the lower limit of USP specification. The findings reported in this study can assist the Drug Control Authority to get an idea about the quality status of the marketed Naproxen tablets in Bangladesh

Keywords: *In-Vitro, United States Pharmacopeia (USP); disintegration time; potency; dissolution test.*

Introduction

One of the major challenges to pharmaceutical product quality, as recognized by the Food and Drug Administration (FDA), is the limited information on current quality of marketed pharmaceutical products due to a lack of formal means for post market surveillance [1]. Oral tablets are the most widely used dosage form due to compactness, ease in manufacturing and convenience in terms of self-administration and almost all drug molecules can be formulated in a tablet [2, 3]. Post market monitoring of generic drugs can serve two purposes, for one it is a confidential tool in evaluating quality, therapeutic efficacy and overall safety of commercially available brands and the other more practical purpose is ascertaining the chemical and biopharmaceutical equivalency of multiple generic brands in the market [4, 5]. Acute musculoskeletal disorders and traumatic sports injuries, although self-limiting, often benefit from pain management therapy and it has been shown that pain, or fear of pain, is the biggest single factor in delaying full rehabilitation [6]. Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties that relieves pain, fever, swelling, and stiffness [7]. The efficacy and tolerability of prescription doses of naproxen in approved rheumatologic indications, including osteoarthritis, has been established since its approval in 1976. The sodium salt has been available in the United States for prescription use since 1980 and was approved by the US Food and Drug Administration [8]. Naproxen is the most widely used NSAIDS for pain and inflammation caused by trauma, infection, auto immune disorders, neoplasms, joint degeneration and other causes [9]. NSAID provide their analgesic and anti-inflammatory clinical benefits via inhibition of the cyclooxygenase-2 (COX-2) isoenzyme, a rate-limiting enzyme in the prostaglandin biosynthetic pathway [10]. It is a non-selective NSAID, which means it inhibits both COX-1 and COX-2 enzymes with nearly comparable IC50 values and in the process exhibits significant side effects in the gastrointestinal tract [11]. Everyday NSAIDs are taken by more than 30 million people worldwide of these, 40% of consumers are older than 60 years [12]. In Bangladesh, more than 50 generic brands of naproxen tablets are available. Being an OTC drug, this large choice of available brands means that there is a higher chance of substandard products running amok in the market and thus quality and safety parameters should be monitored continuously [13].

Therefore this present study aimed to evaluate and compare in vitro quality parameters of four different locally available brands of naproxen 500 mg tablets.

Methods

Materials:

For these research work four brands of marketed Naproxen were collected from local medicine shop and those were sampled as Sample-1(Popular Pharmaceuticals Ltd.); Sample-2 (Eskayef Pharmaceuticals Ltd.); Sample-3 (Drug International Limited); and Sample-4 (The ACME Laboratories Ltd.). The samples were properly checked for their physical appearance, the name of the manufacturer, batch number, and date of manufacturing, date of expiration, manufacturing license number and D.A.R number at the time of purchase. All the research grade chemical reagents and logistical supports were provided by Pharmaceutical Technology Lab of the Department of Pharmacy, Daffodil International University, Dhaka, Bangladesh.

Weight Variation Test:

Weight of a tablet is one of the major indicators of content uniformity. The weight variation test is used prior to a batch release on the other hand, rarely for the drug stability testing [14]. Weight variation is measured by using an electronic balance (OHAUS). The % of weight variation is calculated by the following formula:

% of weight variation= {(Individual weight – Average weight)/Average weight} × 100

Hardness Test:

Tablet hardness or the tablet crushing strength is generally expressed as the load necessary to crushing a tablet placed on its edge [15]. Ten tablets were selected randomly from each brand and the minimal pressure required for crushing each tablet was recorded [16]. The hardness of the tablet was found by utilizing Monsanto type tablet hardness

analyzer. Criteria: Tablet hardness should lie between 5 to 10 kg / cm2 [17].

Thickness Test:

Thickness of tablets was important for uniformity of tablet size [18]. Variation in tablet thickness should not be immediately appearing under normal conditions, for obvious reasons of product acceptance by the consumer. In general, tablet thickness is controlled within 5% of standard value [19]. Tablets were individually placed horizontally between two jaws of the Vernier Calipers (Shimadzu, Japan). The caliper scale was run to hold the tablet which gave a visual reading of tablet thickness. According to the USP (2007), tablets should have thickness about ± 5mm.

Thickness was calculated by using the following formula:

Thickness = Main scale reading + (Vernier scale reading ×Vernier constant)

Disintegration Test:

About 900ml water was taken in 1000ml beaker and the beaker was placed into the disintegration tester (Magumps). One Carbamazepine tablet was placed in each tube of basket rack and plastic disk is placed over each tablet and the basket rack is accurately positioned into the beaker. The temperature was maintained as 37±5. A motor driven device helps to move the basket up down through a distance of 5- 6cm at a rate of 28-32 cycles per minutes. The disintegration time was recorded as time required for completely passing the tablet through the sieve in such a way that not a single particle remained on the basket of the machine. In this way disintegration time was determined for four different brands of naproxen tablets and the observed result for each sample was recorded.

Determination of Potency:

A simple and selective UV spectrophotometric method was used for determining the potency of the tablets. Potency is the strength of a dosage form. Potency determination is the chemical characteristics of a dosage form. The potency of official tablet is usually given in terms of milligrams of drug per tablet and is determined by means of an official analytical method which involves grinding several tablets in a mortar and analyzing a portion of the resulting powder [20]. To prepare a standard solution, 100mg of Naproxen was measured by the electronic balance (Elder) and placed in 100ml volumetric flask. Then the concentration of solution was attained 100µg/ml by adding Phosphate Buffer. Then a series of standard solution of Naproxen standard e.g., 1µg/ml, 3µg/ml, 5µg/ml, 7µg/ml, 9µg/ml, 11µg/ml, 13µg/ml, and 15µg/ml, were prepared by proper dilution by using Phosphate Buffer. The absorbance of both the standard and assay solutions was measured in a suitable spectrophotometer having 1-cm quartz cell at 332 nm using phosphate buffer as blank.

Content of Naproxen can be measured by using the following equation:

Content of Naproxen = As / Astd × Wstd / Ws × Wa× DF× Potency×Av. wt

Here,

As = Absorbance of the Sample

Astd = Absorbance of the standard

Wstd = Weight of standard

Ws = Weight of the sample

Wa = Amount of per tablet

Dissolution Test:

The rate of drug absorption is determined by the rate of drug dissolution from the dosage form. Therefore it will usually be important to obtain rapid drug dissolution from the dosage form [20]. In dissolution apparatus (VEEGD) the water tank was filled and temperature was set at 37±0.5°C. .Standard stock solution of Naproxen was prepared by dissolving 10 mg of API in 100 ml of phosphate buffer to produce a concentration of 0.1 mg/ml. 900 ml of the phosphate buffer was poured into one of the vessels and instruments were run till the set temperature was attained. The remaining 100 ml of the medium was used as a blank. One of the sample tablets was placed into the vessel and starts the run. Rotate the paddle at 50 revolutions per minute. At the end of the time specified (15, 30, 45, 60), 10 ml of the sample was collected and filtered. 10 ml of the filtered sample was diluted with the buffer medium. Using the same procedure, as for the blank

sample, use the phosphate buffer. Finally the absorbance was measured at 332 nm.

Statistical Analysis:

The data was expressed as mean ± S.E.M. (Standard error of the mean). Understudy's t-test was utilized for the assessment of information and $p<0.05$ acknowledged as huge

Results

Weight Variation Test:

To determine the content uniformity weight variation test is required. The weight variations of four brands of Naproxen 250mg tablet were determined and the observed results are shown in the following Table No. 1.

Hardness Test:

The hardness of selected four brands of Naproxen 250mg tablet were determined and the observed results were showed in the following Table No. 2

Thickness Test:

Tablets of each brand of Naproxen were randomly selected to conduct the thickness test. Test results were given in the table Table No. 3.

Disintegration Time:

This is the measurement time of a tablet to disintegrate tablets into particles in contact with gastrointestinal fluid. The disintegration time of all brands of Naproxen tablet has met the specification of disintegration time for tablet according to USP.

Determination of Potency:

The potency of four samples Naproxen tablet were determined. The obtained results were shown in the Figure No. 1.

Dissolution Test:

The dissolution rate of four brands of Naproxen tablets was determined. According to USP specification for Naproxen tablets, each brand must be dissolved more than 80% of its labelled claim within 45 minutes of the test [21].

Discussion

Weight Variation Test:

Weight variation test revealed that the tablets were within the range of Pharmacopoeia specifications [22]. According to USP, for the average weights of tablets (mg) are 130 or less, 130-324 and more than 324 the maximum percentage difference should be ±10, ±7.5, ±5 respectively [23]. From the experiment results (Table No, 1), it was obvious that weight variation limit values of all branded tablets were within maximum limit differences and no abnormality has occurred.

Hardness Test:

Hardness is one of the most important physical features for evaluating tablet as it affects tablet friability, disintegration time as well as bioavailability [24]. From the results shown in Table No. 2, it was confirmed that all brands of Naproxen tablets complied with the pharmacopoeia specification of hardness.

Thickness Test:

Thickness is obviously an important issue when tablets are considered. If the tablet is thicker than the specified limit, then it cannot be swallowed properly by an average person, if the tablet is less thick than the specified limit, then it can breakdown easily. Regular monitoring of the thickness of marketed tablets can help to detect potential problems related to their content uniformity at an early stage of production [25]. It was observed that all the sample are within the limit of USP specifications of thickness and thus passed the test.

Disintegration Time:

Tablet disintegration is considered as the first stage of the bioavailability cascade because a faster disintegration time can result in quicker absorption of the API and a faster onset of action of the desired therapeutic effect [26]. If the disintegration time is perfect and matches with the standard we can easily confirm that the effectiveness of the drug is good [23]. USP recommends that all uncoated and film coated tablets should disintegrate within 30 minutes [21]. According to the USP specification of disintegration time, it is observed from the results(Table No. 4) that none of the sample exceeded the specification for disintegration time.

Determination of Potency:

For the tablets of Naproxen USP specifies that content of active ingredient should be within the limit of 90-110% [21]. The data presented in Figure No. 1, it is clear that all samples except sample 2 (87.80%) complied with this specification limit.

Dissolution Test:

Dissolution test was performed to determine the rate of release of the drug. Dissolution of a tablet depends on its disintegrating into smaller particle and eventual absorption and the rate of this dissolution is an important criterion for quality control of any tablet [27]. We analyzed both intra-sample and inter- sample variation in dissolution profiles and found that apart all other samples(Figure No. 3) had dissolved more than 80% of their labelled claim within just 45 minutes of the test where the dissolution profile of sample 2 was very close to the lower limit of USP specification for dissolution.

Conclusion

This study demonstrated a successful comparative study and evaluation of four brands of Naproxen tablet that are available in the market of Bangladesh. The quality parameter, considerable cost, consumption of time and scientific expertise of any pharmaceutical formulation are vital because therapeutic response and safety solely depends on its quality maintenance. , quality control studies must be needed for the prevention of any contamination or errors. The quality maintenance in a pharmaceutical industry depends on the number of atmospheres including personnel qualifications, active pharmaceutical ingredients quality, validation of the manufacturing process and the area etc. The results showed that all four samples from four different pharmaceuticals were compliant with USP specifications for weight variation test; hardness test; thickness test; and disintegration time. All the sample passed the potency test except sample 2 according to USP specification. All the samples had dissolved more than 80% of their labelled claim within 45 minutes of the test where the dissolution profile of sample 2 was very close to the lower limit of USP specification for dissolution. This study confirms the necessity for continuing close observation on marketed Naproxen tablets within the country to confirm the quality and this quality maintain also directly transmits to public health. To make any conclusion regarding the quality of these samples from four different brands considering the batch to batch variation more widespread studies should be accompanied including bioavailability or bioequivalence study.

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Table No. 1: Weight Variation of selected four brands of Naproxen 250 mg tablet

Tablets No	% Weight Variation			
	Sample-1	Sample -2	Sample -3	Sample -4
1	4.3	4.4	2.9	1.7
2	1.3	1.6	0.1	1.3
3	2.3	0.4	1.6	3.3
4	1.3	0.6	4.4	3.7
5	3.7	0.4	0.1	2.3
6	0.7	4.6	0.9	4.7
7	2.3	2.4	3.4	4.3
8	1.7	2.6	3.1	4.3
9	3.3	4.6	1.1	2.3
10	0.3	4.4	3.6	4.3
Average Weight(mg)	329.7	330.6	328.9	327.7
RSD%	0.503	0.700	1.39	0.973

Table No. 2: Hardness of selected four brands of Naproxen 250mg tablet

Serial No.	Marketed sample	Average Hardness(kg/cm2)
1	Sample-1	7.11
2	Sample-2	7.35
3	Sample-3	7.22
4	Sample-4	8.69

Table No. 3: Thickness of selected four brands of Naproxen 250mg tablet

Sample	Average Thickness of the tablet (mm)
Sample-1	4.10
Sample-2	4.20
Sample-3	4.15
Sample-4	4.65

Table No. 4: Disintegration time of selected four brands of Naproxen 250mg tablet

Serial No.	Marketed sample	Avg. Time(min)
1	Sample-1	8.90
2	Sample-2	10.85
3	Sample-3	9.43
4	Sample-4	13.70

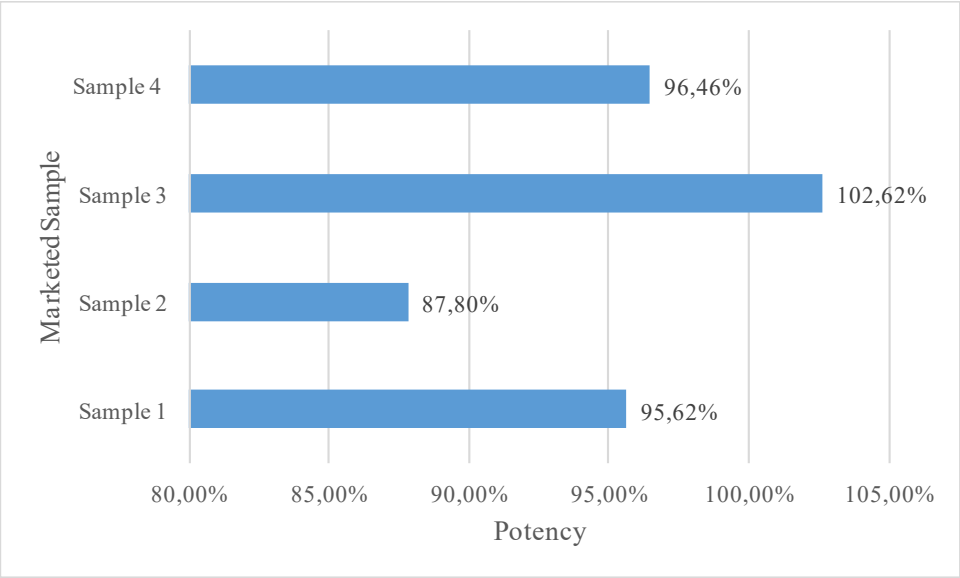

Figure No. 1: Potency of selected four brands of Naproxen 250mg tablet

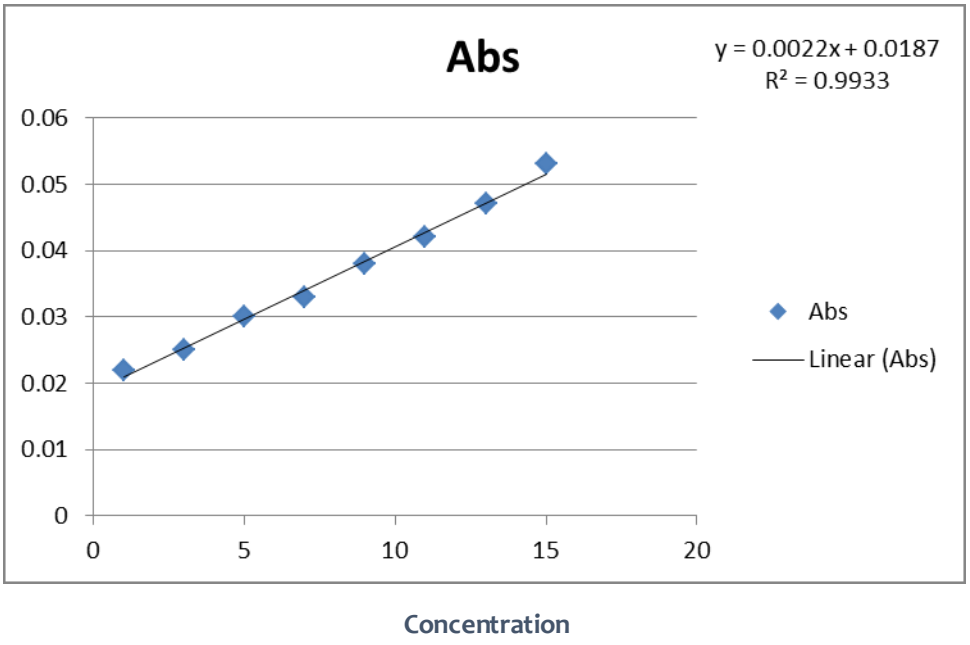

Figure No 2: UV absorption standard curve of Naproxen

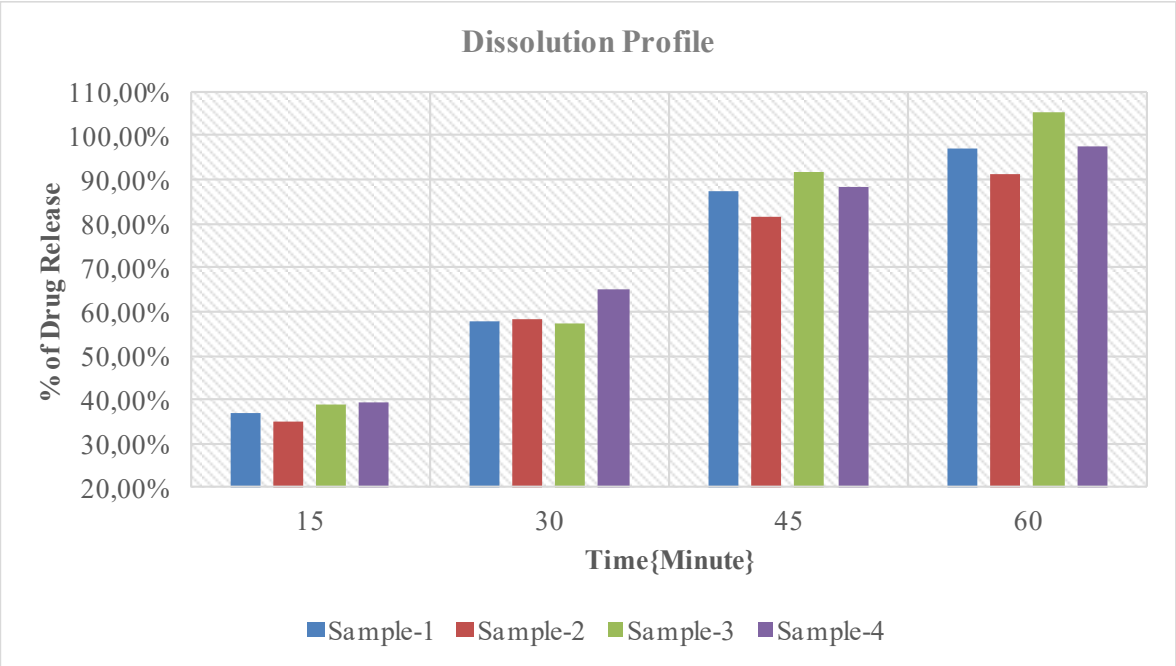

Figure No. 3: Dissolution profile of selected four brands of Naproxen 250mg tablet