

Quantitative and Qualitative Estimation of Marketed Naproxen Tablets Available in Bangladesh

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Abstract

Naproxen is a non-steroidal anti-inflammatory drug (NSAID) working as a non-selective cyclooxygenase (COX) inhibitor to treat inflammation, pain, fever, and various disease conditions. The current study was conducted to determine and compare several *in vitro* quality parameters, often commercially available 500 mg naproxen brands available in Bangladesh. According to the existing protocols, different physical parameters such as uniformity of weight, hardness, friability, disintegration time and dissolution were determined. A validated UV-visible spectrophotometric approach was used to assess the content uniformity of drug material in the collected brands. All the brands taken for this study complied with the official specifications of physical parameters. These brands contained active ingredients ranging from 91.37% up to 101.18%. On the other hand, two brands (C4 and C8) of naproxen tablets failed to meet the specification of United States Pharmacopoeia (USP), 90-110% of the labeled claim for the 500 mg naproxen tablet. These sub-standard brands possessed only 88.16% and 86.67% naproxen sodium. In conclusion, the current study indicated that eight out of the ten brands complied with quality parameters and can be used correspondingly.

Key words: Naproxen, comparative study, dissolution, friability, hardness, disintegration.

Introduction

Headache is presumably the most notorious of cerebral pains, happening in an expected 9% of men and 16% of women (Goldstein and Chen, 1982). Migraine headache is considered a familial problem described by repetitive assaults of migraine commonly variable in intensity, frequency and duration. Assaults are ordinarily one-sided in beginning, regularly connected with anorexia, queasiness and regurgitating. At times, they are gone before by or related with neurological and state of mind disturbance (Friedman *et al.*, 1962).

The etiology of headaches is unpredictable, including vascular and neuronal mechanisms (Anttila *et al.*, 2018). The researcher has established that platelet aggregation occurs more quickly in case of migraine than normal conditions, and adenosine-di-

phosphate, serotonin and prostaglandins are released, which are considered as some symptoms of migraine (Solomon *et al.*, 1990). Migraine-like symptoms are produced when administering prostaglandin E1 (PGE1) through intravenous infusion, followed by another potent prostaglandin analog named prostacyclin (PG1) (Grant and Goa, 1992). Studies showed that naproxen, as well as naproxen sodium, are effectively used for the treatment of migraine and also used for the prophylaxis of migraine (Bellavance and Meloche, 1990).

Naproxen is an NSAID (non-steroidal anti-inflammatory drug) that belongs to the aryl acetic acid class of NSAIDs (Angiolillo and Weisman, 2017) and inhibits the cyclooxygenase (COX) enzyme in a non-selective manner. The drug is typically marketed in sodium salt form, which is safe

for breastfeeding women. In general, naproxen inhibits the COX I and II enzymes, lowering the production of inflammatory mediators known as prostaglandins. As a NSAID, naproxen thus has anti-inflammatory properties (Davanzo *et al.*, 2014). Therefore, it is also used as an anti-inflammatory agent to treat a variety of inflammatory symptoms and conditions caused by the overproduction of inflammatory mediators, which produce pain and fever (Weisman and Brunton, 2020).

Both an immediate release and extended-release formulation of naproxen are offered. Because extended-release tablets take longer to work than rapid-release formulations (also known as "sustained release" or "enteric coated"), extended release formulations are less helpful when instant pain relief is needed (Altman *et al.*, 2015). For the treatment of chronic, or long-lasting disorders where long-term pain relief is preferred, extended release formulations are more helpful. According to reports, naproxen's plasma half-life in healthy persons is between 10 and 20 hours. Drug elimination and plasma half-life in children and adults seem to be similar (Maderuelo *et al.*, 2019).

Several pharmaceuticals are manufacturing these preparations in Bangladesh. The main objective of this research was to evaluate the quantitative and qualitative estimation of some widely used marketed brands of naproxen tablets available in Bangladesh.

Materials and Methods

Sample collection: Ten brands of marketed (production date not more than three months ago from the purchase) naproxen sodium immediate release tablets were obtained from various drug stores in Dhaka, Bangladesh at M.R.P. Before purchasing, the samples were thoroughly examined for their manufacturer's name, physical appearance, batch number, manufacturing date, and expiry date. The labeled active ingredient of naproxen sodium was 500 mg and packaged in the strip or blister packing. The maximum retail prices of all these brand tablets were between 7 to 10 taka per unit.

Coding of samples: This research work was not designed as a double-blind study because the sources of samples were known. However, the samples' codes were used per scientific ethics, and all the collected brands were coded as C1, C2, C3, C4, C5, C6, C7, C8, C9, and C10.

Equipment used: The comparative study was conducted by using the laboratory facilities of the Department of Pharmacy, State University of Bangladesh, Dhaka. The used equipment was UV-VIS Spectrophotometer (Shimadzu Corporation, Japan), Automated Eight Basket Tablet Dissolution Tester (Veego, India), Electronic Balance (Mettler Toledo, Japan), Hot Air Oven (Daihan, Korea), pH Meter (Hanna Instruments, Romania), Hardness Tester (Veego, India), Friability Tester (Veego, India), Disintegration Tester (Veego, India) and Sonicator (Indiamart, India).

Evaluation of physical parameters: Physical parameters including uniformity of weight, hardness, friability and disintegration time were evaluated according to the official method of USP pharmacopoeia (Bithi *et al.*, 2017).

Uniformity of weight: The weight of the tablets represents the net weight of the content present per tablet. This test is critical because each tablet's content must be consistent in order to maintain dose accuracy. During this process, ten tablets are weighed, and the average weight of each tablet is determined using the following equation:

$$\% \text{ Weight variation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

The pharmacopoeia provides a permissible variable in the variation of weights of the individual tablets expressed as a percentage of the average weight. The tablets meet pharmacopoeial specifications if not more than two tablets are outside the percentage limit (B.P., 2015).

Hardness test: The force required to break a tablet in a diametric compression test has been defined as tablet hardness. The crushing strength of ten tablets from each brand was measured using a

hardness tester, and an average value was taken. According to the official specification, hardness of immediate-release tablets should be within 0.8 to 4 kg (B.P., 2015).

Friability test: Ten tablets were weighed accurately and placed in a friabilator, which was subjected to 100 revolutions at a rate of 25 revolutions per minute. The tablets were, therefore, de-dusted and reweighed accurately. The following equation was used to calculate the percentage of weight loss–

$$\text{Percent loss of weight} = \frac{\text{Loss of weight}}{\text{Initial weight}} \times 100$$

According to the official specification, tablet friability should be controlled within 1% (B.P., 2015).

Disintegration test: This was determined at 37°C using disintegration testing apparatus until no particle remained on the basket of the system. The time taken for six tablets of each brand was recorded. According to pharmacopoeial specifications, the immediately released tablet should disintegrate within 30 mins (B.P., 2015).

Dissolution rate determination: The drug release from the obtained samples was evaluated using the USP type II (paddle type) dissolution test apparatus. 900 ml of 0.1N HCl was used as the dissolution medium (pH 1.2). The experiment was carried out at 37.0 °C with a rotation speed of 50 rpm. After 40 minutes, 10 ml samples were removed and analyzed by UV spectrophotometer at 332 nm after appropriate dilution (Costa and Lobo, 2001). According to the

pharmacopoeial specifications, 80% of drugs should be dissolved within 45 minutes (USP, 2006).

Content uniformity: 25.0 mg of standard naproxen sodium USP was weighed and dissolved in a 50 ml volumetric flask, and the desired volume was made up. 10 ml of the prepared solution was taken in another 50 ml volumetric flask, and the volume was made up to 50 ml and mixed well. Methanol was used as a diluent for both standard and sample solutions. The absorbance was measured at the wavelength of 332 nm (Alam et al., 2017). According to USP requirements, active ingredients should present within 90-110 % (USP, 2006).

Results and Discussion

Uniformity of weight determination: The weight variations of all samples were evaluated, and all samples met the official specification (Table 1).

Hardness and friability test: These two tests are crucial in determining the strength of the tablets. All collected samples were tested for hardness and friability, and all were found to be within the specified range (Table 1).

Disintegration time and dissolution studies: After administration, disintegration is critical for the release of active ingredients. To allow for rapid dissolution, the active ingredient must be released as quickly and efficiently as possible from the tablet matrix. The disintegration time and dissolution studies performed on the collected samples revealed that all the collected brands met the pharmacopoeial specifications (Table 2).

Table 1. Uniformity of weight, hardness and friability test of all the collected samples.

Sample code	Uniformity of weight (mg)	Hardness (Kg)	Friability (% loss)
C1	1015.6 ± 2.0	4.1 ± 0.78	0.0061
C2	1080.2 ± 2.0	5.4 ± 0.88	0.0235
C3	1018.8 ± 2.9	5.2 ± 1.01	0.0299
C4	1056.4 ± 2.8	6.5 ± 0.95	0.0277
C5	1078.8 ± 4.7	4.1 ± 0.44	0.0063
C6	1026.7 ± 2.6	5.1 ± 0.36	0.0245
C7	1079.3 ± 2.4	4.6 ± 0.79	0.0124
C8	1027.9 ± 2.3	4.7 ± 0.48	0.0038
C9	1047.5 ± 2.8	5.1 ± 0.86	0.0386
C10	1069.7 ± 2.1	4.7 ± 0.53	0.0159

Table 2. Disintegration time test, % released by dissolution study and content uniformity of all the collected samples.

Sample code	Disintegration time (min)	Dissolution (% release)	Content uniformity (%)
C1	2.54	85	99.11
C2	2.77	83	101.18
C3	2.98	84	91.37
C4	4.94	80	88.16
C5	2.34	88	92.37
C6	5.33	85	101.03
C7	4.68	82	100.67
C8	3.88	88	86.67
C9	3.85	87	92.33
C10	3.45	81	100.33

Out of the ten brands of naproxen immediately released tablets, two were found to be sub-potent based on content uniformity of naproxen sodium content (Figure 1). Five vital physical parameters, including uniformity of weight, hardness, friability, disintegration time and dissolution were evaluated because these parameters are important from the point of therapeutic value as well as gaining the patients' confidence in the product. In this study, all of these parameters were found within the official range.

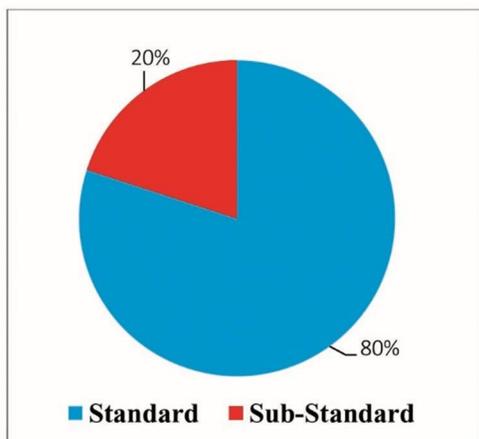


Figure 1. Over all analytical profile of collected naproxen tablet samples.

Conclusion

Currently, Bangladesh produces more than 95 % of its population's essential drugs. Although the

quality of the drugs is satisfactory, some counterfeit and substandard drugs are available in the market based on this study. Though the current study was conducted on a small scale, the data reported in this study might be helpful to the Drug Control Authority for understanding the quality status of the marketed naproxen tablets in Bangladesh based on professional judgment. However, more studies are required to endorse the current study findings.

Conflict of interest

There are no conflicts of interest declared by the authors.

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