Life Science Informatics Publications

Research Journal of Life Sciences, Bioinformatics, Pharmaceutical and Chemical Sciences

Journal Home page http://www.rjlbpcs.com/

RJLBPCS

ISSN 2454-6348

Original Research Article **DOI: 10.26479/2018.0404.32**

COMPARATIVE STUDY ON QUALITY ANALYSIS ON MARKETED DICLOFENAC SODIUM TABLETS OF DIFFERENT BRANDS AVAILABLE IN BANGLADESH

Abdullah Al Ragib[1]*, Tariqul Islam[2], Sazaul M. Sazib[2], Faruk Hosain[1]

1.Department of Applied Chemistry and Chemical Engineering,

Noakhali Science and Technology University, Noakhali-3814, Bangladesh.

2.Department of Pharmacy, Noakhali Science and Technology University, Noakhali-3814, Bangladesh.

ABSTRACT: Diclofenac Sodium is a type of non-steroidal anti-inflammatory drug which is established to treat different symptoms by lessens the substances in the body that cause the pain and swelling to occur. The study was assessed to find out the physicochemical parameters of different brands of diclofenac sodium tablets in Bangladesh to comply them mostly with the standard parameters of BP/USP specifications. The tablets present in the market of different popular brands were chosen for the study of different quality control test like physical appearance, hardness, friability, disintegration time, weight variation, dissolution rate & potency were evaluated. The observed hardness results were shown not more than 4-10 kg-ft. and the friability results were also shown not more than 1 % that matched the BP/USP specification. According to in vitro dissolution of pharmacopeia, Megafen (73.82%) and A-fenac (68.61%) dissolution profile didn't match with the standard limit. Potency tests were also done by following standard protocol in which all brands met with the standard. This study is expected to be a point of appreciation in constructing consciousness between population and prescriber communities to have the greater surplus of medicines by choosing the appropriate products among different commercial brands.

KEYWORDS: Diclofenac sodium, anti-inflammatory drug, pharmacopeia, dissolution rate, potency.

Corresponding Author: Abdullah Al Ragib*

Department of Applied Chemistry and Chemical Engineering,

Noakhali Science and Technology University, Noakhali-3814, Bangladesh.

Email Address: ragibnstu@gmail.com.

1. INTRODUCTION

The oral route of delivery is the most preferred administration route as it offers one of the safest and most convenient methods of drug administration. So, it is necessary to evaluate the perfect quality maintain of each drug for human health. Tablet dosage form is one of a most preferred dosage form all over the world. Almost all drug molecules can be formulated in a tablet and process of manufacturing of tablets is very simple, and is very flexible [1]. Diclofenac sodium is a popular tablet in which sodium salt of [o-(2, 6-dichloro aniline) phenyl] acetate are present with active ingredients in pharmaceuticals are used as non-steroidal anti-inflammatory drug (NSAID) in the management of mild to moderate pain particularly when inflammation is also present as in cases of rheumatoid arthritis and also post-operative condition [2,3]. Besides, the excipients such as glidants, diluents, binders or granulating agents, lubricants can involve to ensure efficient tableting and disintegrates to promote tablet break-up in the digestive tract; sweeteners or flavors to enhance taste; and pigments to make the tablets visually attractive [4]. The pharmacological results are believed because of blocking the conversion of arachidonic acid to prostaglandins by inhibiting cyclo-oxygenase enzymes. After oral administration, it is completely absorbed [2]. However, due to its first pass metabolism, only about 50% of the absorbed dose is systematically available. The half-life of diclofenac sodium in plasma varies from 1-3 h, with mean peak plasma levels of approximately 0.5 μg/ml and 1.0 μg/ml occurring after about 2 h after a single dose of 25 mg and 50 mg of enteric-coated tablets respectively. About 99% of the drug is bound to human plasma proteins, mainly albumin [5]. It is available in the various formulations such as injections, tablets, gel, suppositories and powdered form [6]. Pre-requirement of drug products that should be chemically and pharmaceutically equivalent must be identical in strength, quality, purity, active ingredient release profile and also in the same dosage form, for the same route of administration [7]. Because of the widespread use of this drug, quality control testing should be done for diclofenac marketed products to ensure safety; efficacy; accepted quality; rationality of use to protect public health [8]. The objective of this work was therefore to evaluate the pharmaceutical quality of ten different brands diclofenac sodium tablets dispensed in Bangladesh and to choose the best brand name by comparing the quality results**.**

2. MATERIALS AND METHODS

The quality analysis of diclofenac sodium tablets were studied through the evaluation of weight variation, hardness, friability, disintegration time, dissolution rate, potency study. The study was performed by doing these various test procedures which are the key factor in exploring the quality of the different brands of these tablets.

Collection of Sample

There are about more than thirty products of diclofenac sodium tablets in Bangladesh. Ten variably popular brands were collected from the local retail markets (Maijdee, Noakhali). About thirty tablets

of each brand were collected for the analysis. All brands of diclofenac sodium contain 50 mg per tablet but Orafen SR brand contains 100 mg diclofenac sodium per tablet. 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. Here the physical appearances of different brands were also shown in table 1 and the level information about the sample of the different pharmaceutical company of Bangladesh in table 2.

Reagents, instruments and equipment's used

Distilled water, phosphate buffer (pH 7.4), Tablet Hardness tester USP-1217 (Electrolab: EH-01P), test tubes, basket rack, standard motor drive device (speed motor), Electrolab EF-2 friabilator, USP dissolution apparatus; Whatman filter paper (10 mesh); Pipette; Volumetric flask; UV-visible spectrophotometer (SHIMADZU UV Spectrophotometer: UV-1800- 240V), constant temperature bath (37 ± 0.5^0C), volumetric flask, analytical precision balance (AGN 220C, AXIS, Poland), dissolution beaker etc.

Determination of weight variation of tablets

Ten tablets of each brand of diclofenac sodium were taken and weighed individually with the mentioned an analytical balance. The average weight and the percent deviation of the tablets for each brand were calculated [9]. Then % of weight variation is calculated by using the following formula is given below:

Percentage weight variation= (average weight – individual weight)/ individual weight x 100 %

Determination of hardness of the tablets

Tablet hardness or the tablet crushing strength is generally expressed as the load necessary to crushing a tablet placed on its edge [7]. Hardness denotes the capability of a tablet to withstand mechanical shocks during handling in manufacturing and prevent the destruction of tablets from packaging and transportation. The tablets were placed between the two jaws of the hardness tester and the hardness was measured as the strength needed to crush the tablets. Then the average crushing strength was calculated along with the standard deviation. This was triplicated. The acceptable range of hardness or crushing strength of tablet is 4 to 7 kg-f (kilogram of force). During the study, the hardness of all tablets was determined using Tablet Hardness Tester [10]. Ten tablets of each brand were taken and the hardness of the tablets was determined [11].

Table 1: Physical appearance of difference brands of pharmaceutical company

Brand Name	Color	Shape characteristics and other
Clofenac	White	Round, enteric coated
Ultrafen	White	Round, enteric coated
Orafen SR	White	Round, enteric coated

Megafen	White	Round, enteric coated
Diclofenac	White	Round, enteric coated
Volcan	White	Round, enteric coated
Anodyne	White	Round, enteric coated
Erdon super	White	Round, enteric coated
Mobifen	White	Round, enteric coated
A-fenac	White	Round, enteric coated

Determination of friability of the tablets

Most of the cases friction and shock forces cause tablets to chip cap or break [12]. The friability test has also close relation with tablet hardness and is necessary to evaluate the capability of the tablet to withstand abrasion in packaging, handling, and shipping [13]. In this study, it was examined using Electrolab EF-2 Friabilator. The measure of the tablet friability is easily done from the loss due to abrasion. The value of friability was expressed in percentage (%). A number of 10 tablets for each brand are weighed and placed in the friabilator in which rolling and repeated shocks of tablets are done as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable. Then the percentage loss of weight of the tablets was calculated by using the following formula [14].

Percentage friability= {(Initial weight- Final weight)/ Initial weight} x100

Determination of disintegration time on tablets

After oral administration, the solid form of compressed tablet must be in solution for the action of active ingredients in the human body. So, the disintegration test is another important quality assurance technique to evaluate the quality, bioavailability, and effectiveness of tablets. Generally, disintegration is the mechanical break-up process of tablets into smaller granular particles and the length of time which is required to measure for causing disintegration is known as disintegration time [7]. The standard disintegration time for USP-NF coated tablet must be not more than 30 minutes. Tablet Disintegration was determined in the tablet disintegration tester (USP, Electrolab: ED-2L) [10]. The temperature was maintained in distilled water at 37°C throughout the experiment for each tablet of all the brands. Ten tablets of each brand were selected and placed in each of the cylindrical tubes of the basket and the disc was used. The time taken to break each tablet into small particles and pass out through the 10-mesh screen was recorded. The disintegration time was taken to be the time no particle remained on the basket of the system [10, 11].

Dissolution rate test of tablets

Generally, dissolution is the process of a solid drug to undergo solution, which affects the rate of drug absorption under standardized conditions of liquid or solid interface, temperature, and solvent

composition [15]. This quality assurance type drug release pattern during a certain period of time is important for the perfect activity of a medicine in an internal organ of a human body in a definite time. Dissolution test for each brand of diclofenac sodium tablet was carried out by USP dissolution type apparatus [10, 16]. In this apparatus, 900 ml phosphate buffer (pH: 7.40) was used as dissolution medium. The process was maintained at 37 ± 0.5°C by a constant temperature bath with a selected speed of 50 rpm by a variable speed motor [10]. In general, a single tablet is placed of each brand in a basket tied to the bottom of the shaft connected to a motor. Samples were withdrawn at 25 ml from the medium in which replacing of equal volume of the amount of fresh dissolution medium (phosphate buffer) must be immediately done. Diluted filtered samples were suitably analyzed by using UV Spectrophotometer (Shimadzu UV Spectrophotometer: UV-1800-240V) at 257nm. By measuring the absorbance, the percentage (%) of drug release after 30 minutes of various brands was calculated [10]. The obtained data was denoted (Table 5) and (figure 2).

Table 2: Level information about the sample of the different pharmaceutical company

Manufacturer	Brand Name	Batch No.	Mfg. Date	Exp. Date	Mfg. Lic. No.	DAR No.
Square Pharmaceuticals Ltd.	Clofenac	207002	August, 13	October, 14	235 &460	321-15-65
Beximco Pharma	Ultrafen	05218	July,13	July,15	379 &119	186-131-66
Rangs Pharmaceuticals Ltd.	Orafen SR	12k015	November,12	November,15	166 &49	82-27-65
Jayson Pharmaceuticals Ltd.	Megafen	03421	July,13	June,14	127 &389	210-255-39
Opsonin Pharma Ltd.	Diclofenac	02311	August,13	October,15	12 & 80	025-149-65
Biopharma Ltd.	Volcan	2885	April,13	May,15	427 &188	276-71-67
IbnSina Pharmaceuticals Industry Ltd.	Anodyne	2210	August,13	August,15	150 &405	239-67-06
Aristopharma Ltd.	Erdon Super	113J38	October,13	October,16	308 &171	143-95-65

ACI Ltd.	Mobifen	42E0714	July,13	July,15	132&363	170-51-65
ACME Laboratories Ltd.	A-fenac	TA3027	June,13	June,16	250 &115	036-144-65

Potency determination of tablets

100 mg of standard diclofenac sodium was weighed accurately in an analytical balance and was taken in a 100 ml volumetric flask and hence the concentration is 1mg/ml. 50 – 60 ml of Phosphate buffer was added and was shaken mechanically for 30 min. The volume was made up to 100 ml mark with the same solvent. 10 ml of the above solution was diluted to 100 ml with Phosphate buffer solution. Thus the concentration is 0.1mg/ml. Our target concentration is 0.01mg/ml so the solution was re-diluted. Again, 10 ml was taken from the 0.1mg/ml solution and then diluted to 100ml and hence the concentration is 0.01mg/ml. Besides, 1 tablet of 100 mg diclofenac sodium was placed in 900ml dissolution beaker. 10ml of the solution is withdrawn from the dissolution beaker after 30 minutes. 10 ml of the sample solution has been taken into a 100mL volumetric flask and diluted up to 100ml with phosphate buffer. And the final conc. will be 0.01mg/ml. The absorbance of both standard and sample were measured in a suitable UV-VIS spectrophotometer at 275 nm using phosphate buffer solutions as blank. Each sample was run in duplicate and average of the results was taken into consideration.

3. RESULTS AND DISCUSSION

Weight variation

The weight of ten different brands of diclofenac sodium tablets was determined with the help of an electronic balance and the observed results have been included in the table below (Mean values ± SD, n=3).

Table 3: Average weight of different brands of diclofenac sodium tablets

Brand Name	Average weight (g)	Weight variation limit
Clofenac	0.256± 0.003	−1.951 to +1.561%
Ultrafen	0.363± 0.002	−1.101 to +0.551%
Orafen SR	0.170± 0.004	−2.941 to +3.530%
Megafen	0.180± 0.010	−2.220 to +1.670%
Diclofenac	0.212± 0.011	−1.415 to +2.830%
Volcan	0.226± 0.005	−2.212 to +1.780%
Anodyne	0.284± 0.005	−1.411 to +1.760%
Erdon super	0.171± 0.009	−1.754 to +3.510%
Mobifen	0.255± 0.012	−1.960 to +2.351%
A-fenac	0.161± 0.009	−1.251 to +1.241%

According to the BP, for the average weight of tablets (mg) are 80 or less the maximum percentage differences allowed ±10 and for the limit 80-250 mg, the percentage difference should be ±7.5 and more than 250mg this should be ±5. Besides, 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 [7]. From the experiment results (table 3), it was obvious that weight variation limit values of all branded tablets were within maximum limit differences and no abnormality has occurred.

Hardness and friability of tablets

Hardness is one of the most important physical features for evaluating tablet [10]. It may affect tablet friability, disintegration time and bioavailability. Too hard tablets may result in a decrease in the release of the drug. A digital hardness tester was used to measure the hardness of 10 different brands (Mean values ± SD, n=3).

Table 4: Hardness and friability of different brands of diclofenac sodium tablets

Brand Name	Average Hardness (kg-f)	Friability (%)
Clofenac	4.979± 0.38	0.141± 0.005
Ultrafen	6.468± 0.45	0.225± 0.003
Orafen SR	4.721± 0.35	0.700± 0.004
Megafen	6.221± 0.42	0.286± 0.004
Diclofenac	6.224± 0.41	0.354± 0.007
Volcan	4.191± 0.35	0.322± 0.003
Anodyne	9.156± 0.75	0.141± 0.004
Erdon super	4.389± 0.37	0.593± 0.006
Mobifen	7.435± 0.65	0.140± 0.006
A-fenac	7.176± 0.61	0.783± 0.007

The observed results are shown that all different brands of tablets hardness limit 4-9 kg-f (Table 4). In the study, it was found that most of the brands of diclofenac sodium group passed the test of hardness and had acceptable crushing strength of between 4.191 kg-f to 6.468 kg-f except Anodyne brand which was the hardest of all the diclofenac sodium tablet brands with a hardness of 9.156 kg-f, indicated that it was above the limit range of between 4 to 7 kg-f stated [17]. On the other hand, Mobifen and A-fenac brands had a crushing strength was 7.435 and 7.176 kg-f respectively which also denoted that those brands above the standard limit. It may either due to using different granulation techniques or using different excipients. Besides, the friability of the tablets which is determined using friabilator was found between 0.141–0.783% (Table 4) this indicates an impressive and accepted result.

Calculation of disintegration time on tablets

The rate of drug absorption and therapeutic efficacy of the drug is dependent upon the disintegration time. If the disintegration time is perfect and matches with the standard we can easily confirm that the effectiveness of the drug is good [7]. The disintegration time was measured according to the above denoted procedure and the observed results are shown in Table 5 (Mean values ± SD, n=3). According to the BP/ USP specification of disintegration time, it is observed from the results that none of the samples exceeded the specification for disintegration time.

Table 5: Disintegration time of different brands of diclofenac sodium tablets

Brand Name	Average DT (min)
Clofenac	5.34± 0.003
Ultrafen	6.387± 0.005
Orafen SR	8.16± 0.007
Megafen	4.40± 0.002
Diclofenac	5.29± 0.005
Volcan	5.67± 0.006
Anodyne	4.77± 0.003
Erdon super	7.08± 0.010
Mobifen	4.61± 0.003
A-fenac	12.20± 0.011

Calculation of dissolution test on tablets

The process by which drug dissolves out of a dosage form and is made available for absorption from the gastrointestinal tract. The outcomes of the in vitro release of branded tablets were shown in table 6 and figure 3. By the finish (30 minutes) of the in-vitro release test, the percentage drug release for most of the brands were showed more than 90% except Megafan and A-fenac brands were found to 73.82 % and 68.61% respectively. The results obtained from the study revealed that most of the brands passed the BP/USP general specifications.

Table 6: Count of the percent of drug release after 30 minutes of various brands of diclofenac sodium tablet preparation

Brand Name	Drug release (%)
Clofenac	98.34
Ultrafen	99.75
Orafen SR	98.05
Megafen	73.82
Diclofenac	97.35
Volcan	91.34
Anodyne	102.05

Erdon super	98.34
Mobifen	99.15
A-fenac	68.61

The graphical representation of this test is below figure 1.

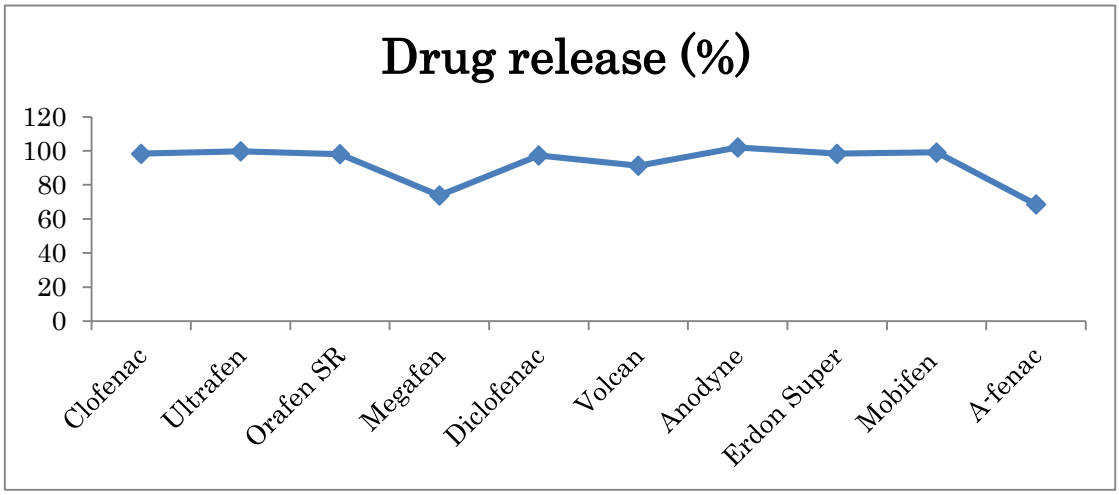

Figure 1: Comparative Drug release profile of diclofenac sodium tablets

Calibration curve of pure diclofenac sodium

The values of Abs. (absorbance) were plotted against respective concentrations (Figure 2). The conc. (concentration) showed linearity when the curve was plotted indicating it obeyed beers law. The linear equation was y= 25.69x + 0.002 and regression coefficient R^2 was also 0.998

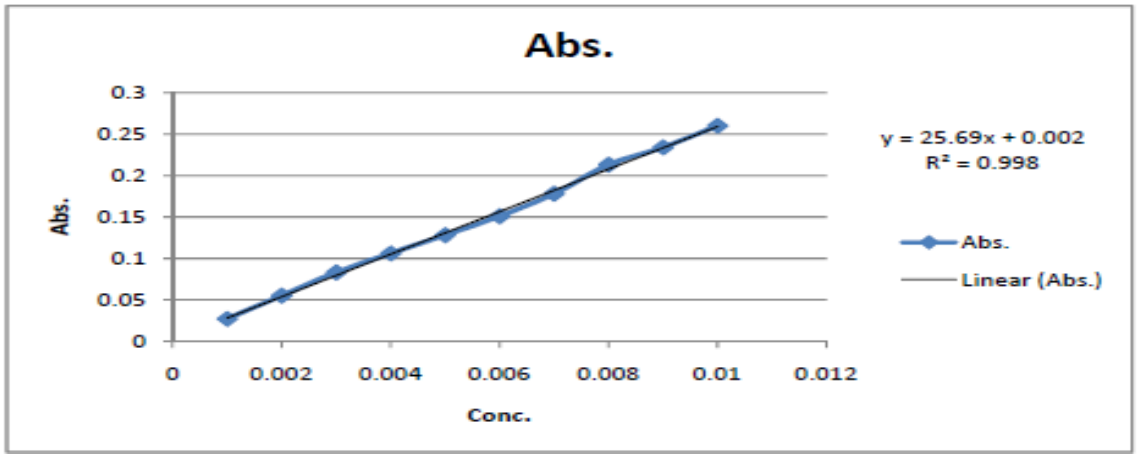

Figure 2: UV absorption calibration curve of pure diclofenac sodium at 275 nm

Potency determination of diclofenac sodium tablets

Determination of the tablet potency was performed according to the USP method. The potency value was found to be between 90.01% -102.5% (Table 7) which is within the USP limit. It denotes the presence of diclofenac sodium in all the brands perfectly.

Table 7: Potency count of various brands of diclofenac sodium tablets

Brand Name	Potency (%)
Clofenac	98.9
Ultrafen	98.11
Orafen SR	97.05
Megafen	102.5
Diclofenac	101.45
Volcan	95.04
Anodyne	91.2
Erdon super	96.06
Mobifen	100.3
A-fenac	90.01

These potency values are also expressed in graphical presentation in figure 3.

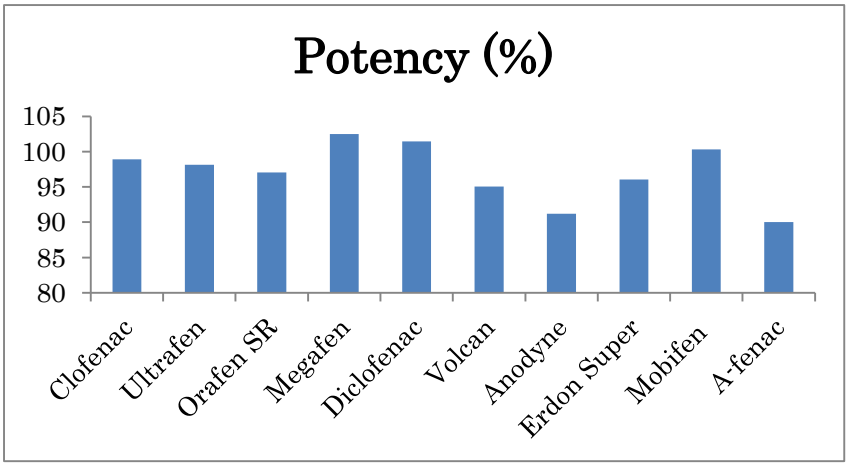

Figure 3: Comparative potency profile of diclofenac sodium tablets of different brands

4. CONCLUSION

The current pharma market of Bangladesh is flooded with various non-steroidal anti-inflammatory drug preparations like diclofenac sodium tablets [18]. So it is necessary to justify the perfect quality of this tablet of various brands. The quality parameter, considerable cost, time consumption and scientific expertise of any formulation are important because therapeutic response and safety depends on its quality maintenance [19]. 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. [20, 21]. Weight variation, hardness, friability, disintegration time, dissolution test, potency profiles of all branded tablets used in the study were within BP/USP specified limits. Most of the brands showed acceptable disintegration time, potency, hardness, friability and dissolution profile. However, A-fenac and Megafen showed low dissolution profile compared to the other brands. This study can be a good recommendation in case of finding compatibilities of the sample formulations with the

specifications stated in official Pharmacopeia. This study confirms the need for continuing close observation on marketed diclofenac sodium tablets within the country to ensure the quality and this quality maintain also directly relates to public health. In addition, public health issue is important for the development of Bangladesh.

ACKNOWLEDGEMENT

The authors are grateful to the Department of Pharmacy, Noakhali Science and Technology University for providing the research facility for this investigation.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Kamble ND, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV. Innovations in tablet coating technology. International Journal of Applied Biology and Pharmaceutical Technology. 2011; 2(1):214-218.
2. Sultana T, Sohel MD, Kawsar MH, Banoo R. In Vitro Dissolution Study and Assay of Diclofenac Sodium from Marketed Solid Dosage form in Bangladesh. J Bioanal Biomed. 2017; 9:118-122.
3. Raja SN, Meyer RA, Campbell JN. Peripheral mechanism of somatic pain. Anesthesiology. 1988; 68:571-590.
4. Joseph NM, Degu M, Palani S. Alzheimer's disease: Comparative quality evaluation of six brands of enteric coated diclofenac sodium tablets marketed in Addis Ababa. Int J Pharm Sci Res. 2017; 8(12):5386-5391.
5. Giri TK, Parveen N, Thakur D, Tripathi DK. In vitro Evaluation of Commercially Available Enteric Coated Tablet Containing Diclofenac Sodium. IJRPBS. 2012; 3:875-881.
6. Shamsipur M, Jalali F, Ershad S. Preparation of a diclofenac potentiometric sensor and its application to pharmaceutical analysis and to drug recovery from biological fluids. J. Pharm. Biomed. 2005; 37(5):943-947.
7. Jakaria M, Mousa, AY, Parvez M, Zaman R, Arifujjaman, Sayeed MA, Ali MH. In vitro Comparative Study of Different Brands of Dexamethasone Tablet Available in Bangladesh. IJPQA. 2016; 7(2):24-28.
8. Lavand'homme PM, Roelants F, Waterloos H, De Kock MF. Postoperative analgesic effects of continuous wound infiltration with diclofenac after elective cesarean delivery. Anesthesiology. 2007; 106:1220 –1225.
9. Rahman ZU, Khan I, Baig A, Quraishi AR, Zahir F. Post-Market In-Vitro Comparative Evaluation of Quality Control Parameters of Paracetamol Compressed Tablets Manufactured in Local Industrial Zones of Kpk Pakistan. The Pharma Innovation. 2013; 2(3):11-15.

10. Karmakar P, Kibria MG. In-vitro comparative evaluation of quality control parameters between paracetamol and paracetamol/caffeine tablets available in Bangladesh. International Current Pharmaceutical Journal. 2012; 1(5):103-109.
11. Chandrasekaran AR, Han CY, Yang Chung AC, Cheang LW, Ping LS. Post–market In vitro Equivalency Evaluation of Paracetamol Tablets in Kedah. Malaysia International Journal of Pharmaceutical Sciences and Nanotechnology. 2011; 4(2):1403-1407.
12. Deshpande RD, Gowda DV, Mahammed N, Maramwar, DN. BI-layer tablets- an emerging trend: a review. IJPSR. 2011; 2(10):2534-2544.
13. Saleem M, Shahin M, Srinivas B, Begum A. Evaluation of tablets by friability apparatus. IJRPC. 2014; 4(4):837-840.
14. Kalakuntla R, Veerlapati U, Chepuri M, Raparla R. Effect of various super disintegrants on hardness, disintegration and dissolution of drug from dosage form. J. Adv. Sci. Res. 2010; 1(1):15-19.
15. Patel k, Prasad RK, Bajpai M. Enhancement of Dissolution Rate of Domperidone Using Melt Granulation Technique. Der Pharmacia Lettre. 2011; 3(2):25-33.
16. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy, Edn 3, Lea & Febiger, Philadelphia, 1986, pp.296-300.
17. Musa H, Sule YZ, Gwarzo MS. Assessment of physicochemical properties of metronidazole tablets marketed in Zaria, Nigeria. Int J Pharm Pharm Sci. 2011; 3(Suppl 3):27-29.
18. Tazin F. Pharmaceutical Industry of Bangladesh: Progress and Prospects. The Millennium University Journal. 2016; 1:19-20.
19. Bajaj S, Singla D, Sakhuja N. Stability testing of pharmaceutical products. Journal of Applied Pharmaceutical Science. 2012; 2(3):129-138.
20. James WT, Leslie TG. Goodman and Gilman's Pharmacological basis of therapeutics. McGraw-Hill companies inc., 2001, pp.1105-1108.
21. Gupta AK. Tablet. Introduction to pharmaceutics-I. Edn 3, CBS Publishers and Distributors, India, 1994, pp. 239-274.