Jahangirnagar University J. Biol. Sci. **10**(1 & 2): 9-17, 2021 (June & December)

Quality assessment of ciprofloxacin tablets - an antimicrobial drug marketed in Bangladesh

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Abstract

Ciprofloxacin is a syntheticfluroquinolone derivative. It is prescribed as a potent antibiotic to treat bacterial infections. An attempt was made to assess the quality of six brands of ciprofloxacin tablets marketed in Bangladesh. Various physicochemical tests, *viz*., weight variation, hardness, friability, disintegration, dissolution and assay for the content of the active ingredient, were performed in accordance with the methods described in the United States Pharmacopoeia 38 (USP 38). UV-Vis spectrophotometric technique was used for dissolution test while High Performance Liquid Chromatography (HPLC) was used to estimate the potency. All the samples passed the physical tests carried out except one sample (code 004), which failed the friability test.Dissolution profile of each brand was satisfactory. All the brands of examined for the content of the active ingredient complied with the limit stipulated in USP 38 for ciprofloxacin except two brands (003 and 004) which showed slightly higher potency of the drug.

Key words: Ciprofloxacin tablet, Antimicrobial drug, Potency, Dissolution, Physical test, High Performance Liquid Chromatography.

INTRODUCTION

Ciprofloxacin is classified as a fluorinated 4-quinolone or fluoroquinolone antibacterial agent, which has a broad spectrum of activity. It also shows satisfactory pharmacokinetics while used in systemic infections (Alyahawi & Alsaifi, 2018).The structure of the drug is given below (Qureshi *et al.*, 2010)

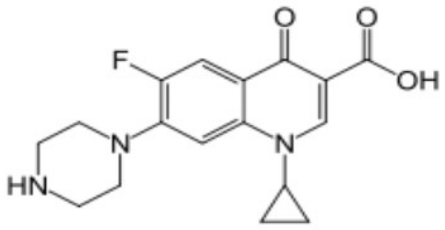

Fig. 1. Chemical structure of ciprofloxacin

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Safe and effective drug products can be produced by maintaining good manufacturing practices for each and every batch. It is necessary to confirm the required excellence of the product, and this can be done by performing different qualitative and quantitative tests throughout the manufacturing process as well as at some stages in the shelf life (Chow, 1997). Different bioavailability tests show that formulation factors greatly influence the therapeutic efficacy of medicinal products (Ofoefule *et al*., 1998). Mostly tablet dosage forms have been assessed to measure the significance of formulation factors (Rubinstein, 1990). Different dosage forms of drugs should be analyzed to receive the sign of proof of their quality for relevant therapeutic use and to meet the guidelines of Drug Administration. Many regions of the globe, especially underdeveloped and developing countries, face shortage of well-equipped drug monitoring cell for upholding quality of drugs in the market. As a result, poor quality drugs as well as forged drug products are being marketed in massive quantity (Amin & Kokwaro, 2007). To control this situation,specific guidelines have been issued to maintain a global standard by World Health Organization (WHO, 1996; WHO, 2005). Many evidence suggests that counterfeit drugs exert a serious danger to communal health, especially in developing countries (Pecoul *et al*., 1999; WHO, 2005). The existence of low quality or fake medicinal products in the market impacts nations of any size and income level (Alubo, 1994; Iglesias-Rogers, 2001). Moreover, there is a high frequency of reports that sub-standard drugs are being manufactured by different pharmaceutical companies (Ham, 1992). Incidence of the delivery of counterfeit medicines exists in developing countries as well as in Europe and USA (Shakoor *et al*., 1997). It is therefore important to assess the quality of drugs being marketed in any country at intervals.And it is evident from the literature that many researchers, like Kahsay & Egziabher, 2010, Jaman *et al.*, 2015, Igboasoiyi *et al.*, 2018, Joda *et al.*, 2018, and Ganbat *et al.,* 2020, carried out qualitative and quantitative analysis of different brands of ciprofloxacin tablets which were collected from markets or community pharmacies of different countries. A critical analysis of these studies shows that many products were not of required quality. The results also suggest the necessity of post-marketing investigation of drugs to ensure adequate healthcare of patients. At this backdrop, the present work was undertaken to check and update the quality of different brands of ciprofloxacin tablets marketed in Bangladesh. The findings of the work are reported, analyzed and discussed in this paper.

MATERIALS AND METHODS

Sample collection: Six brands of ciprofloxacin tablets were randomly purchased from different retail pharmacy outlets in Bangladesh.They were coded and then evaluated for physicochemical qualityusing various techniques as described below in this section.

Weight variation: The weight uniformity of ciprofloxacin tablets was tested following USP 38. The weights of twenty tablets were determined individually using an electronic balance (model: AR2140, Ohaus Adventurer electronic balance, USA). The mean tablet weight was calculated and recorded.

Hardness test: The hardness of 10 randomly selected tablets from each of the brands was determined by a manual hardness tester (model: MHT-20,Thermonik, India). The mean hardness was calculated and recorded.

Friability test: The weight of 20 tablets selected from each brand at random was determined collectively as initial weight (W_i). The tablets were placed in a friabilator (model: FTA-20, Thermonik, India) set to rotate at 25 rpm for 4 minutes. At the end of the run, the tablets were de-dusted and the final weight (W_f) was taken. Friability was calculated from the equation given below and recorded.

$$\text{Friability (\%)} = \frac{W_i - W_f}{W_i} \times 100$$

Disintegration Time (DT) test: Disintegration time test for the tablets was carried out according to the specification given in USP 38. A 900 mL beaker was filled with warm (37 ± 0.5 °C) water. Six tablets were placed into the basket-rack assembly and connected to the disintegration apparatus (model: TD-2, Thermonik, India). The apparatus and the timer were started simultaneously, and the time required for each tablet to disintegrate was recorded from visual observation of completion of disintegration. The average time was calculated from theobtained data.

Assay of ciprofloxacin tablets: All the six batches of ciprofloxacin tablets were assayed for the drug content according to the method outlined in USP 38. The assay was carried out using High Performance Liquid Chromatography (model: SPD-20AV, Shimadzu, Japan). A stainless-steel column (25 cm x 4.6 mm) of Phenomenex (USA) packed with ODS stationary phase of 5 µm particle size was placed and set in the HPLC unit for the analysis of ciprofloxacin in the selected brands of tablets. The UV-Vis detector was used to detect the active ingredient in the tablets at 278 nm. Phosphoric acid, the pH of which was adjusted to 3.0 ±0.1 (adding triethylamine drop by drop), was used for mobile phase preparation. Mobile phase comprised of a mixture of acetonitrile and phosphoric acid (13:87v/v). Flow rate of mobile phase was 1.5 mL/min. Injection volume was 10 µL and oven temperature was set at 40°C.

Five tablets (500mg/tablet) of a brand were weighed and finely powdered. This quantity of the powdered tablets contained ciprofloxacin equivalent to 2500 mg (5 x 500 mg) and it was taken into a 500 mL volumetric flask. A diluent was prepared by mixing phosphoric acid (pH 2.0 ± 0.1) and acetonitrile in the ratio of 87:13 (v/v). 350 mL of this diluent was added into the ciprofloxacin containing volumetric flask. The flask with its content was sonicated for 20 minutes and after sonication more diluent was added to make the volume up to 500mL mark. Then 10 mL solution was taken into a 250 mLvolumetric flask and the volume was adjusted with the same diluent. It was considered as the sample solution. Similar procedure was followed to prepare the sample solution of other five (5) brands. Fifty (50) mg of the reference standard in powdered form was dissolved in the previously prepared diluents taking separately in a 250 mL volumetric flask and the volume was adjusted. The sample and standard solutions were made ready in the vials and they were placed within the chamber of the HPLC unit and 10 µL of each

was injected (by auto injector) to the mobile phase of HPLC system to obtain their chromatograms. The assay of each sample was repeated two times and the mean result was obtained from the determinations. The content of ciprofloxacin was calculated from the peak areas of the chromatograms of the test and reference standard solutions using the following equation (1):

Content of ciprofloxacin in mg per tablet

$$= \frac{A_{sam} \times W_{std} \times 500 \times 250 \times P_{std} \times 331.34 \times Av.Wt}{A_{std} \times 250 \times W_{sam} \times 10 \times 100 \times 367.81}$$

Here,
331.34 = Molecular weight of ciprofloxacin
367.81= Molecular weight of anhydrous ciprofloxacin hydrochloride
A_{sam}= Area of sample solution
A_{std} = Area of standard solution
P_{std} = Potency of standard (99.16%)
W_{sam} = Weight of sample in mg
W_{std} = Weight of working standard in mg
Av. Wt. = Average weight of tablet in mg

Dissolution test: The dissolution test was conducted using theApparatus II(model: DT 126, ERWEKA, Germany) following the method described in USP 38. The medium (900 mL) used was 0.01N HCl. Thesample (ciprofloxacin 500 mg tablet) of a brand was introduced in each beaker of the dissolution tester. The apparatus was run for 30 minutes at 50 rpm for each brand. Solution was then taken from each of the beaker of the dissolution tester to measure separately the absorbance at 276 nm using a UV VIS spectrophotometer (model: UV-1601PC, SHIMADZU, Japan). The content was calculated using following equation (2) and the obtained results were presented in the (Table-6) of the result section.

$$\text{Release rate \%} = \frac{A_{sam} \times W_{std} \times 1 \times 900 \times 100 \times P_{std} \times 100 \times 331.34}{A_{std} \times 100 \times 100 \times 500 \times 1 \times 100 \times 367.81}$$

Where,
A_{sam}=Absorbance of sample solution
A_{std}=Absorbance of standard solution
P_{std}=Potency of working standard in percentage
W_{std}=Weight of working standard in mg

RESULTS AND DISCUSSIONS

Generic products must gratify the same standards of quality, efficacy and safety as those applicable to the innovator products. In this study, quality of six different brands of generic ciprofloxacin tablets were evaluated and thereby information pertaining to their quality aspects are made available for regulatory bodies, manufacturers and the relevant people through this paper.

Physicochemical tests (*viz.* weight variation, hardness, friability, disintegration time), dissolution and assay for the content of active ingredients of the studied brands of ciprofloxacin tablet were performed following USP 38 as described in the methodology part of this paper. Obtained results of weight variation, hardness, friability and disintegration test are presented in the Table-1 to Table-4 and those of assay and dissolution test are shown in the Table 5 to Table 6. The results are expressed in terms of relative standard deviation (RSD) in percentage in appropriate cases.

Table 1. **Weight Variation Test Results of the samples of Various Tested Brands of Ciprofloxacin Tablet (n=6)**

Brand code	Mean weight (mg)	Weight variation (± %)
Code 001	682	1.99
Code 002	726	1.15
Code 003	790	3.25
Code 004	775	0.95
Code 005	822	4.00
Code 006	706	3.38

Table 2. Hardness Test Results of the Samples of Various Tested Brands of Ciprofloxacin Tablet (n=6)

Brand code	Hardness (kg/cm^2)	RSD (± %)
Code 001	7.00	0.12
Code 002	6.50	0.20
Code 003	9.00	0.34
Code 004	5.00	0.41
Code 005	4.50	1.81
Code 006	6.50	1.10

Table 3. **Friability of the Samples of Various Tested Brands of Ciprofloxacin Tablet (n=6)**

Brand code	Friability (%)
Code 001	0.06
Code 002	0.03
Code 003	0.93
Code 004	1.50
Code 005	0.83
Code 006	0.97

Table 4. **Disintegration Time (DT) of the Samples of Various Tested Brands of Ciprofloxacin Tablet (n=6)**

Brand code	Mean time (min)	RSD (± %)
Code 001	3	0.11
Code 002	8	0.25
Code 003	17	1.13
Code 004	5	0.44
Code 005	3	0.89
Code 006	11	1.20

Consultation of specifications of USP 38 for weight variation (±5%), DT (Not More Than 30 min) and repeated hardness tests reveals that the results were in compliance with the specifications. Friability for the sample coded as 004 was found beyond the limit (more than the specified limit of 1% as mentioned in USP 38). Non-compliance of friability standards may be areflection of noncompliance to GMP guidelines, and with poor friability of a tableted product, patients may not get the right quantity of drug even though they take correct dose of the medicine as per their prescriptions. Friability is a measure of tablets' strength that governs a tablets' tendency to powder, chip or break when handled. Incorporation of granules with very small amount of moisture and use of deep concave punches in poor condition or worn at surface edges might have played roles in failing the friability test.

Potency (the content of ciprofloxacin) of each of the tested brands was calculated from the chromatogram of a representative sample of the respective brand (Fig. 2) and the chromatogram of the reference standard (Fig. 3) with due consideration of the declared content of ciprofloxacin in the reference standard. Results obtained are presented in the Table 5.

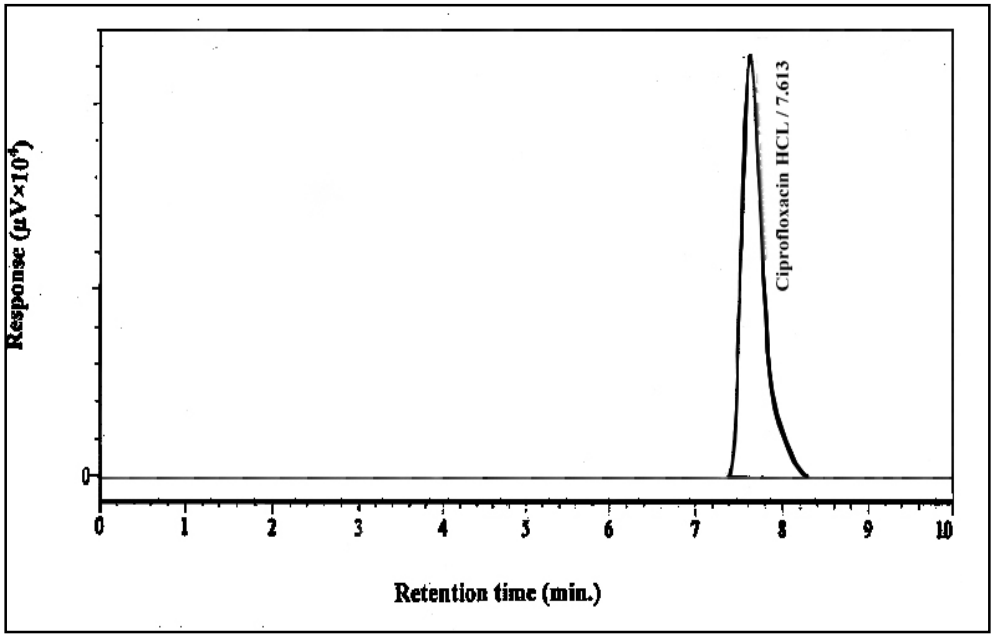

Fig. 2. Chromatogram of a Representative Sample of Ciprofloxacin Tablet (Code 001)

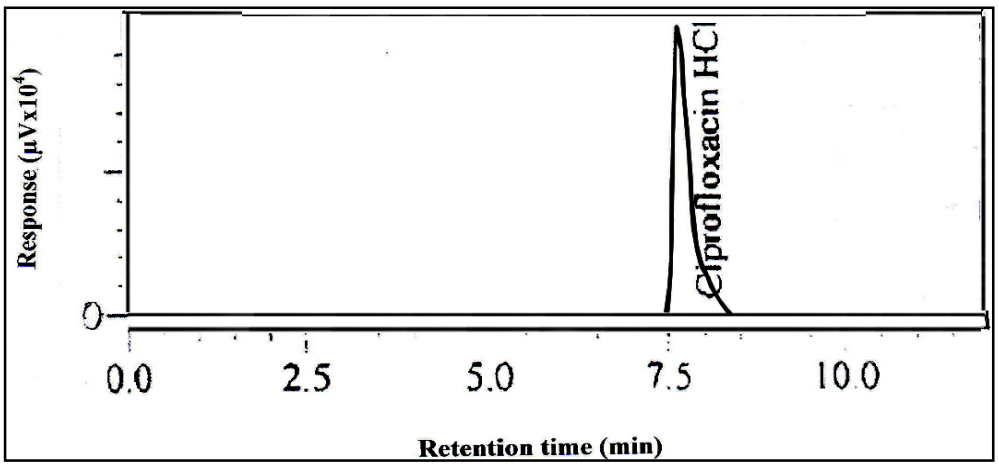

Fig. 3. Chromatogram of the Reference Standard of Ciprofloxacin Tablet

Table 5. Potency of the Samples of the Tested Brands of Ciprofloxacin Tablet (n=6)

Brand code	Potency (%)	RSD (± %)
Code 001	100.31	0.22
Code 002	105.71	1.56
Code 003	111.62	1.29
Code 004	112.42	1.43
Code 005	105.36	0.76
Code 006	110.15	1.12

It is evident from the Table 5 that the potency of the samples of 2 brands (code 003 and code 004) are non-compliant with USP 38 specification (90% - 110%). Overdose may be toxic in most cases. The tested samples (code 003 and 004) showed just slightly higher potency than the acceptance limit. Non-uniformity of drug distribution ingranules and irregularity of the hopper flow could have contributed to the noncompliance in the potency of the samples coded as 003 and 004. Some reports suggest that lack of monitoring by skillful regulatory bodies and poor-quality control practices may also allow substandard drug products to find their way to the market (Risha *et al*., 2003). Instances of using over-dose of the drug have also been found that might have occurred due to not adhering adequately to qualityassurance measures during the manufacturing process of products (Hebron *et al*., 2005).

In vitro dissolution test serves as an important indicator for forecasting the *in vivo* bioavailability and bioequivalence of oral solid dosage forms (Itiola & Pilpel, 1996). Dissolution profiles of the samples of the tested brands of ciprofloxacin tablet (Table 6) show that the results are in good agreement with USP 38 specification (Not LessThan 80%).

Table 6. **Dissolution Profiles of the Samples of the Tested Brands of Ciprofloxacin Tablet (n=6)**

Brand code	Dissolution Rate (%)	RSD (±%)
Code 001	91.29	1.13
Code 002	85.98	0.99
Code 003	82.40	2.10
Code 004	87.15	1.54
Code 005	88.75	2.25
Code 006	89.92	1.46

Assessment of various quality aspects of drug products and publishing the data obtained plays an important role in monitoring the quality of drug products. The findings of the present work might be contributory in this regard. Manufacturers should give due attention to maintain all the quality aspects of their products to ensure the efficacy and safety of their products, which in turn will bring benefit topatients through curing their diseases and saving their hard-earned money. Regulatory authorities should also be more watchful and keep their pressure on manufacturers for ensuring manufacture of quality products.

REFERENCES

Alubo, S.O. 1994. Death for Sale: A study of drug poisoning and deaths in Nigeria. *Soc. Sci. Med.,* **38**: 97-103.

Alyahawi, A. and Alsaifi, A. 2018. Quality control assessment of different brands of Ciprofloxacin 500 mg tablets in Yemen. *Universal J. Pharm. Res.,* **3**(4): 31- 35.

Amin, A.A. and Kokwaro, G.O. 2007. Antimalarial drug quality in Africa. *J. Clin. Pharm. Ther.,* **32**(5):429-440.

Chow, S. 1997. Pharmaceutical validation and process controls in drug development. *J. Drug Information.,* **31**: 1195-1201.

Ganbat, A., Dorj, G., Sunderland, B., Sanjjav, T., Tompurev, A., Luvsandorj, T., Borbaatar, B., Dorj, Ga. and Khurelbat, D. 2020. Post marketing quality assessment and comparative dissolution study of ciprofloxacin tablets marketed in Mongolia. *Drug Des.*, **9**(2): 168.

Ham, M.T. 1992. Counterfeit drugs: Implications for health. *Adverse Drug React. Toxicol. Rev. II*, **11**: 59-65.

Hebron, Y., Tettey, J.N.A., Pournamdari, M. and Watson, D.G. 2005. The chemical and pharmaceutical equivalence of sulphadoxine/ pyrimethamine tablets sold on the Tanzanian market. *J. Clin. Pharm. Ther.,* **30**: 575-581.

Igboasoiyi, A.C., Offor, A.C. and Egeolu, A.P. 2018. Quality assessment of various brands of ciprofloxacin hydrochloride tablets sold in Uyo Metropolis. *Nigerian J. Pharm. Applied Sci.Res.,***7**(2): 89-93.

Iglesias-Rogers, G. 2001. Argentina to crack down on pharmaceutical black market. *The Lancet*, **358**: 47.

Itiola, O.A. and Pilpel, N. 1996. Effects of interacting variables on the disintegration and dissolution of metronidazole tablets. *Pharmazie,* **51**: 987-989.

Jaman, M., Chowdhury, A.A., Rana A.A., Masum, S.M., Ferdous T., Rashid, M.A. and Karim, M.M. 2015. *In vitro* evaluation of Ciprofloxacin Hydrochloride. *Bangladesh J. Sci. Ind. Res.*, **50**(4): 251-256.

Joda, A.E., Tayo, F. and Aina, B.A. 2018. Quality assessment of ciprofloxacin tablets obtained from community pharmacies in Lagos,Nigeria. *Ife J. Sci.,* **20**(1): 155-168.

Kahsay, G. and G/Egziabher, A. 2010. Quality assessment of the commonly prescribed antimicrobial drug, ciprofloxacin tablets, marketed in Tigray, Ethiopia. *MEJS*, **2**(1): 93-107.

Ofoefule, S.O., Orisakwe, Ibezim, E.C. and Esimone, C.O. 1998. Mechanisms of nifedipine release from sustained release tablets formulated with some polymeric materials. *Boll.Chim.Farmac.,* **137**: 223-227.

Pecoul, B., Chirac, P., Trouiller, P. and Pinel, J. 1999. Access to essential drugs in poor countries: A lost battle? *J. Am. Med. Ass.,* **281**: 361-367.

Qureshi, M.N. and Rahman, I.U. 2012. Comparative analysis of ciprofloxacin in different pharmaceutical products by high performance liquid chromatograph. *Sci. Tech. Dev.,* **31** (1): 69-73.

Risha, P.G., Vervaet, C., Vergote, G., Bortel, L.V. and Remon, J.P. 2003. Drug formulations intended for the global market should be testedfor stability under tropical climate conditions. *Eur. J. Clin.Pharmacol.*, **59**: 135-141.

Rubinstein, M.H. 1990. Tablets. *In*: Aulton, M.R. (ed.) Pharmaceutics: **The Science of Dosage Form Design,**Istedn., Churchill Livingstone, UK, pp. 304.

Shakoor, O., Taylor, R.B. and Berhens, R.H. 1997. Assessment of the incidence of substandard drugs in developing countries.*Trop. Med. Int. Health.*, **2**: 839-845.

WHO (World Health Organization), 1996. WHO Technical Report Series (TRS) 863 - 34th Report of the WHOExpert Committee on Specifications for Pharmaceutical Preparations.World Health Organization, Geneva.

WHO (World Health Organization), 2005. Regional strategy for improving access to essential medicines in the Western Pacific Region 2005-2010. World Health Organization, Geneva.