Research Article

Indian Journal of Science and Research

Dey B & Sahu S., Ind. J. Sci. Res. 2022, 2(3), 67-71

ISSN 2583 – 2913

# COMPARATIVE EVALUATION OF DIFFERENT BRANDS OF LEVOFLOXACIN TABLETS FROM THE LOCAL MARKET

**Bivha Dey* and Satish Sahu**

**Abstract***:* Levofloxacin a fluoroquinolone antibiotic is widely used for the treatment of various bacterial infections. The different brands of Levofloxacin are available in the market with same dose. Although the dose is same, the activity of the drug sometimes varies from brand to brand. This may lead to the severe health implications to the patients. Considering the health risk factors and the safety of the patients, the current study has been conducted to examine the various brands of Levofloxacin tablets obtained from the Bilaspur region of the Chhattisgarh state.

**Methods:** Various brands (six brands) of Levofloxacin tablets were collected from the local market of Bilaspur of Chhattisgarh state. The various physicochemical parameters (uniformity of weight, hardness, diameter, thickness, disintegration test) and *in vitro* drug release study were performed.

**Results:** The various brands of Levofloxacin tablets were collected and evaluated. The weight variation results showed that all the tablets were as per pharmacopoeial standards. The friability study showed that the weight loss was not more than 1% and ranges from 0.4 % to 0.56 %. The hardness of all the brands of Levofloxacin tablets were from 6.56 kg/cm$^2$ to 8.63 kg/cm$^2$. Disintegration times of all the brands were nearly 6 min to 14 min and complied with the pharmacopoeial standards. The *in vitro* drug release of six brands of Levofloxacin tablets showed that about 90% drugs was released within 30 min in both the pH 1.2 and pH 4.5.

**Conclusion:** The various brands of Levofloxacin tablets were evaluated for its physicochemical properties and i*n vitro* drug release study. The results showed no noticeable changes in the physicochemical properties but remarkable changes were observed in the Levofloxacin release from the various brands of tablets. The results further suggest for the evaluation of antibacterial activity of the different brands of Levofloxacin on a large number of strains.

**Keywords:** Levofloxacin, Physicochemical property, *In vitro* drug release.

**Introduction***:* The quality control of drugs, which is in an international framework were regulated their problem related to the quality, safety and effectiveness of generics and proprietary drugs in the market. Health professionals are confronted with a wide choice of multi-source generics and trade name, imported and locally produced with unproven effectiveness, safety, quality and bioequivalence. Pharmacopeial testing confirms these properties according to fixed standards. *In vitro* dissolution testing can also be used in some cases not only to determine the quality of the pharmaceutical products but also to demonstrate bioequivalence to the brand name product. Due to the importance of Levofloxacin tablet as an antibiotic for widely resistant bacteria and the importance of price on a community basis, six running brands of Levofloxacin products that are available in local market of Bilaspur were analysed Levofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class have a light yellowish-white to yellow-white crystal or crystalline powder.[1,2] Levofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria.[2] It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase iv which is an

*Corresponding author

**School of Pharmacy, Chouksey Engineering College, LalKhadan, Masturi Road, Bilaspur (CG)**

E-mail: bivhadey1707@gmail.com

Published on Web 30/09/2022. www.iisronline.org

enzyme necessary to separate replicated DNA, thereby inhibiting cell division. The fluoroquinolones interfere with DNA replication by inhibiting an enzyme complex called DNA gyrase. Antibiotics are among the most frequently prescribed medications for cure disease by killing or inhibiting bacteria. It is increasing a number of available antibiotics, prescribing these drugs has become a challenge. Levofloxacin is the optical S- (- ) isomer of ofloxacin which has been developed by the Daiichi Seiyaku Pharmaceutical Co. Ltd, in Japan. Ofloxacin is a racemic mixture, but the S- isomer has antibacterial activity 32- to 128- fold more potent than the R- isomer – hence most of the antibacterial activity of ofloxacin is due to the S- isomer. [3]

The prime objective of the present study was to evaluate and compare the physicochemical equivalence of different brands (Brand A, B, C, D, E & F) that are available in local market of Bilaspur in Chhattisgarh state. It has been done in Bilaspur market because CG was come in rural area, maximum peoples are taken medicine in Raipur or Bilaspur and it is nearer to my research centre therefore all brands are taken from this market. In the present day where more than 85% of drugs can be obtained from more than one sources; for example Levofloxacin tablets that manufactured by more than 15 companies might be chance of presence of some spurious along with sub- standard drugs that makes the patients conscious about the selection of safest, effective as well as economical medicine. The proposed study has been performed to provide the guideline to the physicians and pharmacists on the bases of which they can select the drugs for their patients. The physical parameters i.e. weight variation; thickness, hardness, friability, disintegration, dissolution as well as chemical assay were considered during the present study. [4 , 6]

**Materials and Methods:** Six brands of Levofloxacin (500 mg) tablets were obtained from local market of Bilaspur. Reference Levofloxacin was kind gift from Aventis Pharmaceutical Pvt. Limited. Hydrochloric acid is purchased from Merck, Potassium dihydrogen Posphate and Sodium Hydroxide was procured from Sigma Aldrich. Distilled water was prepared freshly.

**Methods:** The hardness, diameter, thickness, uniformity of weight and disintegration test is performed for all the brands of tablet. The dissolution study of Levofloxacin tablets is carried out in USP Type II (paddle) dissolution test apparatus (Labindia Disso-2000). The drug release is measured by Spectrophotometer (Electrolab TDT O8L). Electronic balance (Mettler Toledo, England), Hardness Tester (Dr. Schleuniger), pH meter (Jenway model no 7530), Friability Test Apparatus (Pharma test Germany), disintegration apparatus (Electrolab, ED-2 SAPO) are used for physicochemical analysis.

***Weight variation:*** Weight variation test were performed on twenty units of each brands and % deviation was calculated. According to USP for tablets weighing less than 130 mg, between 130-325 mg and above than 325 mg deviation limits should be ±10%, ±7.5% and ±5 % respectively. [2, 3]

***Hardness:*** Crushing strength is an important parameter to evaluate the compression forces. If a tablet requires more force to be broken, dissolution profile will be affected. Ten units of each brand were used. Minimum and maximum force needed to break the tablet was determined as per the British Pharmacopoea-2007. [4]

***Friability test for tablets:*** Six tablets were weighed and placed in the apparatus where they were exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets were weighed and the weight compared with the initial weight. The loss due to abrasion was a measure of the tablet friability. Maximum weight losses of not more than 1% of the weight of the tablets are tested as per BP-2002. [5]

***Disintegration Test:*** 6 tablets from each generic and innovator brand products were employed for the disintegration test in water at 37 ± 0.5 °C using a disintegration apparatus. The disintegration time was taken to be the time, when no particle remained on the basket. All the tablets of different brands under study were found to be within limit i.e. to disintegrate within 15 minutes.

***Preparation of dissolution medium pH 1.2:*** 8.5 ml of Hydrochloric acid is dissolved in 1000 ml of distilled water to make it 0.1 (N).

***Preparation of dissolution medium pH 4.5:*** 6.8 g of Potassium dihydrogen phosphate is dissolved in 1000 ml of distilled water.

***Dissolution Study:*** The dissolution profile of Levofloxacin tablets was evaluated using Type II dissolution testing apparatus as per the method described in USP-23. The tablets are dissolved in 900 ml of dissolution medium of pH 1.2. The speed of the paddle is set into 50 rpm and temperature is maintained at 37°C ± 0.5. Samples are collected at predetermined time intervals 5, 10, 15, 20, 25 and 30 minutes and filtered (Millipore) to remove any insoluble excipients and analysed by UV-spectrophotometer at 293 nm. Equal

volume of fresh medium is replaced into dissolution medium after each sampling in order to maintain sink condition. The same process has been carried out with the dissolution medium pH 4.5 and samples are analysed spectrophotometrically. [2, 5, 13]

***Preparation of standard curve:***

Accurately 56.26 mg of Levofloxacin hemihydrates is weighed and dissolved in 100 of pH 1.2 dissolution medium. From this solution serial standard dilution are prepared and absorbance are measured by spectrophotometer. The standard graph is plotted between concentration and absorbance. The same has been repeated for the dissolution medium pH 4.5 and standard curve is obtained.

**Physicochemical parameters:** The various physicochemical parameters were studied and the results were depicted in Table 1. The uniformity of tablet weight varied brand to brand. The more weight was observed in the Brand B whereas the less weight was observed in Brand C (Fig. 1). This variation may be due to the different ratios of excipients used by the formulation. There were no noticeable differences in the friability results. The different values of hardness (Table.1) (Fig. 2) may be the problem with drying of granules while manufacturing of the tablets. The noticeable differences in disintegration time between the brands were due to the different solubility of excipients in dissolution medium.

**Results and Discussion**

**Table 1: Physicochemical characteristics of six brands of Levofloxacin (500mg) tablets**

| Brands | Uniformity of weight (mg) | Friability (%) | Hardness (kg/cm2) | Disintegration (min) |
|---|---|---|---|---|
| **Brand A** | 521.89 ± 8.83 | 0.09 ± 0.16 | 7.53 ± 0.78 | 6 ± 1.02 |
| **Brand B** | 522.35 ± 8.72 | 0.04 ± 0.24 | 8.63 ± 0.89 | 7 ± 0.98 |
| **Brand C** | 485.22 ± 2.02 | 0.49 ± 1.06 | 7.63 ± 0.89 | 9 ± 0.71 |
| **Brand D** | 490.45 ± 2.42 | 0.51 ± 0.8 | 8.14 ± 0.02 | 14.12 ± 0.55 |
| **Brand E** | 509.03 ± 4.02 | 0.56 ± 0.21 | 6.56 ± 1.19 | 12.14 ± 0.67 |
| **Brand F** | 512.01 ± 0.62 | 0.08 ± 1.07 | 8.59 ± 0.21 | 13.5 ± 0.99 |

Note: The values are expressed as mean ± SD for n=10

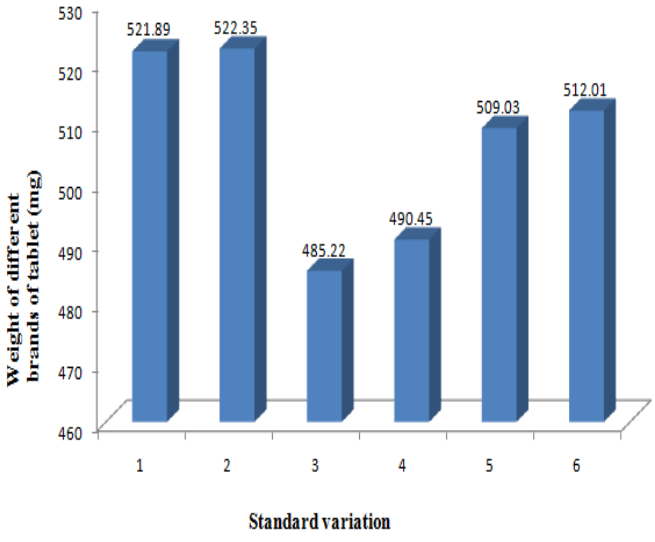


**Fig. 1 Comparison of weight variation different the brands**

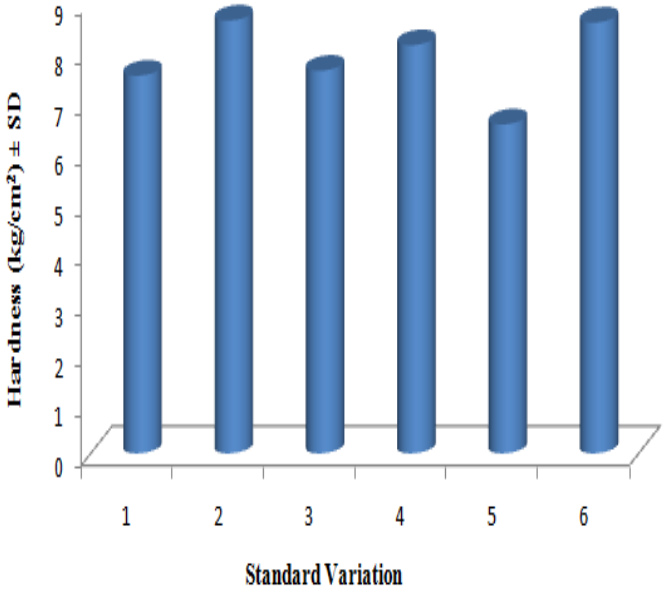


**Fig. 2 Hardness variations of the different brands of Levofloxacin tablets**

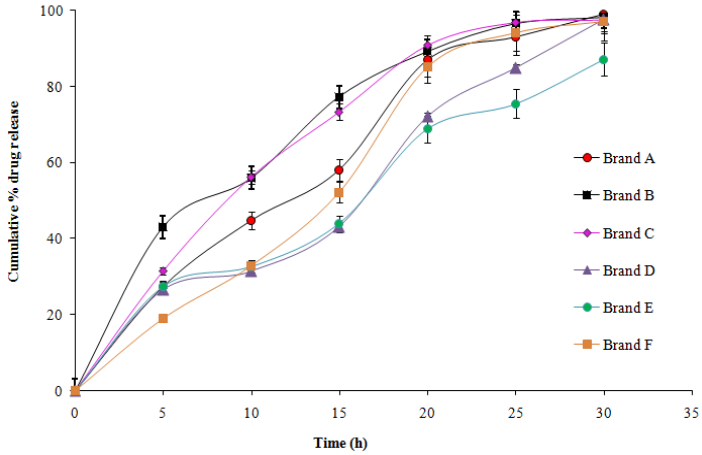


**Fig 3: *In vitro* levofloxacin from six different marketed formulations in pH 1.2**

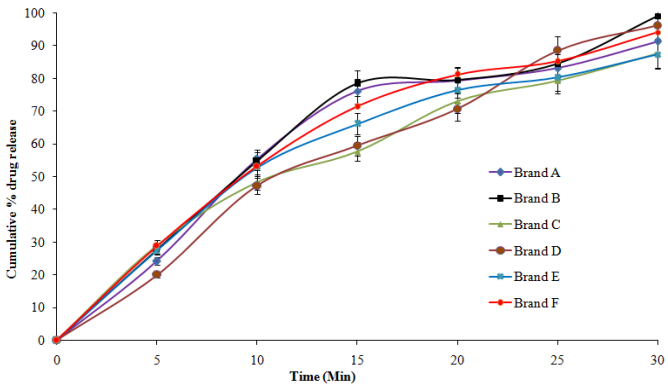


**Fig.4: *In vitro* levofloxacin release from six different marketed formulations in pH 4.5**

**Result:** Study the quality of different brands of Levofloxacin(500mg) tablets was evaluated through weight variation, diameter, thickness, hardness, friability disintegration time, dissolution and chemical assay. It helps to recognize the comparative difference of quality control test and release of drug in different formulation. Any changes in these characteristics may significantly affect the safety and efficacy of the product. Therefore it is very important to keep a check on each and every step during the formulation and manufacturing of a drug product. Comparative study of different brands indicated that the pharmaceutical equivalency of different brand is as important as the biological and clinical equivalency.

**Discussion:** More than 10-15 local and multinational pharmaceutical companies in all over Chhattisgarh are manufacturing Levofloxacin tablets, making it difficult for a physician and pharmacist to evaluate which one is better for his patient. This fluctuation in the price of same drug makes it difficult for the health care authorities. In vitro dissolution testing is an important tool used for development and approval of generic dosage forms. According to FDA (2000) [19], a drug product is considered to be very rapidly released if ≥85% of the drug is dissolved in 15minutes, which corresponds to gastric emptying half-life ($T_{50}$%) in fasting conditions.

The objective of the present study was to compare the quality of locally produced and imported products which are available in the Bilaspur market and to examine the possibility of vivo bioequivalence study.

The FDA recommended dissolution medium for Levofloxacin Tablet is 0.1N HCl (pH 1.2) but Fig.3 shows that 4 brands (Brand A, B, C & E) released more than 85%. Only 2 brands (Brands D & F) failed to release more than 85% drug in this medium.

The mean $T_{50}$% gastric residence (emptying) time is 15-20 minutes under fasting conditions. The conclusion is that a drug product undergoing 85% dissolution in 15 minutes under dissolution test conditions in 0.1N HCl behaves like a solution and generally should not have any bioavailability problems. But some significant variations in the ***in vitro*** dissolution profiles were observed when the dissolution media was changed. The dissolution medium has changed in phosphate buffer (pH 4.5) (Table 3) and in phosphate buffer (pH 6.8) (Table 3) complies with current US FDA (1997) criteria for rapidly dissolving drug products (no less than 85% dissolved in 20-30 minutes).

These results suggest that the formulation design and the manufacturing process are affect the dissolution and thus the bioavailability of the drug product so that when properly formulated, to reached its site of absorption in a solution form.

**Conclusion:** Levofloxacin is one of the most promising newer quinolones that has been shown to be active against both gram positive and gram negative organisms. The result of this parameter indicated that this test should be performed on a large number of strains for confirming the superior antibacterial activity of different brands of Levofloxacin when compared with each other.

**Acknowledgement:** The authors would like to thanks, Department of Pharmaceutics, Faculty of Pharmacy, school of pharmacy for the use of Laboratory Facilities.

**References**

1. Snyder RL. "Practical HPLC Method Development" A wiley-interscience Publication, second edition, 12-74.
2. Dey B. Formulation & Analysis of Levofloxacin Hemihydrate By RP-HPLC In Bulk & Tablet Dosage Form , Journal of harmonized research in pharmacy 3(2), 2014, 64-77
3. Peter Y. The design of dosage forms, in Pharmaceutics. The Science of Dosage Form Design. 2nd Edition Marcel Dekker, Inc. New York. 2002, 1.
4. British Pharmacopoea (2002) Appendix: XII, PP. H A2- 53.
5. Remington AR. The Science and Practice of Pharmacy. 20th edition. Easton Pennsylvania: Mack Publishing Company. 2000 ; 882-885.
6. The United States Pharmacopeia 27. The United States Pharmacopeial Convention, Rockville, MD, USA, 2004; 2011-2012.
7. WHO Prequalification of Medicines Programme .General noteson Biopharmaceutics Classification System (BCS)-based biowaiver applications, 2011.
8. British Pharmacopoeia Volume I &II. British Pharmacopoeia commission. The stationery office limited, London; 2007; 249 –267.
9. United States Pharmacopeia and National Formulary USP 32–NF 27. The United States Pharmacopoeial Convention, Inc.: Rockville, MD., 2007.
10. Ashour S, Al- Khalil R. Simple extractive colorimetric determination of levofloxacin by acid-dye complexation methods in pharmaceutical preparations. Farmaco.2005;60(9): 771- 5.
11. Alvarez- Lerma Fet.ol. Levofloxacin an UCI. Observational study investigating the use of levofloxacin in ICU patients. EnfermInfeccMicrobiolClin. 2004; 22(4): 220- 6.
12. Liechtenstein SJ, Rinehart M. Levofloxacin Bacterial Conjunctivitis Study Group. Efficacy and safety of 0.5% levofloxacin ophthalmic solution for the treatment of bacterial conjunctivitis in pediatric patients. J AAPOS. 2003; 7(5): 317- 24.
13. Bundrick W. Levofloxacin versus ciprofloxacin in the treatment of chronic bacterial prostatitis: a randomized double- blind multicentre study. Urology. 2003; 62(3): 537- 41.
14. Scheen AJ. Pharma- clinics. The drug of the month. Levofloxacin (Tavanic). Rev Med Liege. 2000; 55: 1015- 7, Vol 3, Issue1, 152222
15. Jennifer M. Andrews. Determination of minimum inhibitory concentrations. Journal of Antimicrobial Chemotherapy 2001; 48(SI): 5- 6.