WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 7, Issue 2, 1203-1211. Research Article ISSN 2277– 7105

# QUALITY CONTROL PARAMETERS OF TWO DIFFERENT BRANDS OF CIPROFLOXACIN TABLETS IP AVAILABLE COMMERCIALLY AS PER INDIAN PHARMACOPOEIA

**Barnali Gogoi, Himakshi Baishya*, Ripunjoy Bordoloi, Sanjib Kumar Sarma and Dr. Parthajyoti Gogoi**

Regional Drugs Testing Laboratory (RDTL), Sixmile- 781022, Guwahati, India.

Article Received on
30 Nov. 2017,
Revised on 20 Dec. 2017,
Accepted on 10 Jan. 2018
DOI: 10.20959/wjpr20182-10794

***Corresponding Author**
**Himakshi Baishya**
Regional Drugs Testing Laboratory (RDTL),
Sixmile- 781022, Guwahati, India.

## ABSTRACT

The aim of our present study is to evaluate the quality of two brands of Ciprofloxacin Tablets I.P which are available commercially whether they qualify the entire test mentioned in Indian Pharmacopoeia thereby suggesting their quality and efficacy for use among the general public. The study was exclusively experimental that used Indian Pharmacopoeia 2014 to check the *in vitro* quality of Ciprofloxacin Tablets I.P using different analytical techniques and procedure. All the two brands under the study were within the specification for weight variation test for tablet. The test for identification, assay and dissolution were carried out by High Performance Liquid Chromatography using U-HPLC System (Thermo- Dionex) equipped with an UV detector and stainless steel column (25cm × 4.6mm × 5µm) packed with octadecylsilane chemically bonded to porous silica. The dissolution study was carried out in Apparatus 1 of I.P. The dissolution medium used was 900ml of water, with the speed and time of apparatus set at 50rpm and 30 minutes respectively. The research work indicated that two different brands did not show much difference in their results and they were found to be within the acceptance limits. Hence the release pattern of the two brands of Ciprofloxacin tablets IP were found to be therapeutically effective.

**KEYWORDS:** Ciprofloxacin, Indian Pharmacopoeia, Quality control.

## INTRODUCTION

The quality in the pharmaceutical industry has become a very important and sensitive issue. The world has gathered together to unite its practices, guides and the launching of the Food

and Drug Administration (FDA) current good manufacturing practices (cGMP) for the 21st century - there has been a growing awareness for the significance of the quality of the pharmaceutical products. In the pharmaceutical industry, it is essential for controlling the errors during the every stage in production process since total quality of the product must be ensured according to compendia of drugs.[1] Manufacturing practices which result in good quality finished products and has adequate considerations for safety of the employees is recognized as GMP. GMP is concerned with both production and quality control (QC).[2] QC is the part of GMP by which QC personnel analyses the quality of all factors involved in production in order to eliminate errors at every stage in production. The purposes of QC are to produce a perfect finished product by preventing or eliminating errors at every stage in production. QC is a team work and we have to remember that quality must be built into a drug product during product and process design and it is influenced by the physical plant design, space, ventilation, cleanliness and sanitation during routine production.[3]

Pharmacopoeias are called drugs standard.[4] There are various types of pharmacopoeia such as Indian Pharmacopoeia (IP), British Pharmacopoeia (BP), United States Pharmacopoeia (USP), European Pharmacopoeia (PhEur), International Pharmacopoeia (PhInt) and Japanese Pharmacopoeia (JP) in different parts of the world and they have laid down the specified limits within which the value should fall in order to be compliant as per the standards. The objective of this study is to show the quality parameters for pharmaceutical tablets according to pharmacopoeias that are part of in-process and finished products quality control tests.

Ciprofloxacin hydrochloride is synthetic broad spectrum antimicrobial agents for oral administration. Ciprofloxacin hydrochloride IP, a fluoroquinolone, is the monohydrochloride monohydrate salt of 1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid. Ciprofloxacin given as an oral tablet is rapidly and well absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability is approximately 70% with no substantial loss by first pass metabolism. The binding of ciprofloxacin to serum proteins is 20 to 40% which is not likely to be high enough to cause significant protein binding interactions with other drugs. Ciprofloxacin is present in active form in the saliva, nasal and bronchial secretions, mucosa of the sinuses, sputum, skin blister fluid, lymph, peritoneal fluid, bile and prostatic secretions. Ciprofloxacin has also been detected in lung, skin, fat, muscle, cartilage and bone.

Four metabolites have been identified in human urine which together account for approximately 15% of an oral dose. The metabolites have antimicrobial activity, but are less active than unchanged ciprofloxacin. The serum elimination half-life in subjects with normal renal function is approximately 4 hours. Approximately 40 to 50% of an orally administered dose is excreted in the urine as unchanged drug.[5]

The objective of this research work is to evaluate the quality of two brands of Ciprofloxacin hydrochloride Tablets I.P available commercially, in order to verify whether the product complies with the standard or not. The basic purpose was to establish their quality prior to determining interchangeability with the innovator product. The Indian Pharmacopoeia is an official document meant for overall Quality Control and Assurance of Pharmaceutical products marketed in India published by the Indian Pharmacopoeia Commission (IPC) on behalf of the Ministry of Health & Family Welfare, Government of India.

**Table 1: List of Commercial Brands of Ciprofloxacin Tablets IP Tablets I.P 40mg.**

| Product code | Batch No. | Manufacturer | Mfd date | Exp date |
|---|---|---|---|---|
| A | CP5-125 | Ghanshyam Pharmaceuticals | 06/2015 | 05/2018 |
| B | 16015 | Cadila Pharmacueticals Ltd | 09/2016 | 08/2019 |

## MATERIALS AND METHODS

In this study the active pharmaceutical ingredient (API), Ciprofloxacin was obtained from M/S Regent Biotech. We have procured two commercial brands of Ciprofloxacin Tablets IP from retail pharmacies located in Guwahati and they are listed in table 1.

### Quality control parameters

### Weight variation test

Twenty tablets were selected at random, weighed individually and the average weight was calculated from total. Then percentage deviation from the average weight was then calculated. According to IP standards, not more than two of the individual weight deviates from the average weight by more than the percentage shown below and none deviates by more than twice that percentage.

### Identification Test

Reversed phase High Performance Liquid Chromatography (HPLC) was used for carrying out the identification test on U-HPLC System (Thermo- Dionex) autosampler integrated with UV detector. The software employed was Chromeleon chromatography data system.[6]

**Assay**

The assay was carried out by HPLC. This test was done to determine the actual amount of active ingredient present in the tablet and its compliance with the labeled amount. The chromatographic conditions maintained throughout the procedure were a stainless steel column (25cm × 4.6mm) packed with octadecylsilane chemically bonded to porous silica (5µm). The mobile phase, mixture of 87 volumes of 0.025M phosphoric acid, previously adjusted with triethylamine to a pH of 3 and 13 volume of Acetonitrile. The mobile phase was pumped into the system at a flow rate of 1.5ml per minute with Spectrophotometer wavelength set at 278nm and injection volume of 10µl. The mobile phase prior to use was degassed under vacuum by filtration through 0.2µ nylon membrane.[6]

**Preparation of Reference solution**

Ciprofloxacin hydrochloride working standard (WS) equal to 15.2 mg was accurately weighed and dissolved in 50ml of the 0.01M hydrochloric acid. The prepared solution was sonicated for 10 minutes making final concentration equivalent to 304mcg and filtered through 0.45µm filter.[6]

**Preparation of Test solution**

Of all the two batches 20 tablets of each batch were weighed separately and powdered. An accurately weighed powder containing 1.25g of Ciprofloxacin was taken. 400ml of 0.01M hydrochloric acid was added and sharked for 20 minutes, diluted to 500ml with 0.01M hydrochloric acid and filtered. Then 10ml of the filtrate was diluted to 100ml of 0.01M hydrochloric acid. The prepared solution was sonicated until complete mixing and filtered through 0.45µm filter.[6]

**Dissolution**

Dissolution test was carried out on all two different brands in Apparatus 1 of I.P. (TDT-08L, Electrolab) with six individual tablets of each brand. The dissolution medium used was 900ml of water with the speed and time of apparatus set at 50rpm and 30 minutes respectively. During the entire analysis the temperature was maintained at 37±0.5°C. A suitable volume of the dissolution medium was withdrawn at the end of analysis and filtered through Whatman filter No. 40. The quantity of Ciprofloxacin released into the dissolution medium was calculated as percentage in relation to the value declared on product label. The absorbance of both reference and test solutions were measured at the maximum at about 276nm using using a UV-Vis Spectrophotometer.

**Preparation of Reference solution**

An accurately weighed quantity of Ciprofloxacin hydrochloride RS working standard (WS) was prepared in dissolution medium to obtain a final concentration of 5.5 mcg.[6]

**Preparation of Test solution**

Test solutions were not further diluted as the concentration was equivalent to 5.5 mcg.[6]

## RESULTS AND DISCUSSION

**Weight variation**

The weight variation of the tablet shows that none out of 20 tablets deviates from 5% limit for both the brands. Hence the uniformity of the sample complies IP.

**Identification Test**

Tis test was found to be in compliance with the criteria mentioned in I.P. which states that the principal peak in the chromatogram obtained with test solution in assay corresponds with the peak in the chromatogram obtained with reference solution.

**Assay**

In this test the determination of actual amount of active ingredient present in the formulation was found to be within the acceptance limit of (90-110) % in all the two different brands of Ciprofloxacin Tablets IP under study and are listed in table 2. Figures 1, 2 and 3 show the chromatograms of standard Ciprofloxacin Tablets IP and tested Ciprofloxacin Tablets IP obtained from HPLC.

**Dissolution**

In this study the different brands were evaluated for their in-vitro drug release which indicated that although the results varied among the different formulations but they were within the acceptance limit of not less than (NLT) 80% in water. The results are listed in table 4.

**Table 2: Results of Assay of the two brands of Ciprofloxacin Tablets IP.**

| Product code | Batch No. | Identification (HPLC) | Assay (HPLC) |
|---|---|---|---|
| A | AT-000117 | Complies | 97.05(90-110) %. |
| B | AI6008019 | Complies | 95.09(90-110) %. |

**Table 3: Results of Content Uniformity of the two brands of Ciprofloxacin Tablets IP.**

| Sl. No. | AT-000117 | Sl. No. | AI6008019 |
|---|---|---|---|
| Tablet 1 | 97.15 | Tablet 1 | 94.48 |
| Tablet 2 | 97.12 | Tablet 2 | 94.26 |
| Tablet 3 | 97.24 | Tablet 3 | 94.13 |
| Tablet 4 | 97.18 | Tablet 4 | 94.34 |
| Tablet 5 | 97.29 | Tablet 5 | 94.13 |
| Tablet 6 | 97.17 | Tablet 6 | 94.23 |
| Tablet 7 | 97.32 | Tablet 7 | 94.69 |
| Tablet 8 | 97.24 | Tablet 8 | 94.26 |
| Tablet 9 | 97.35 | Tablet 9 | 94.20 |
| Tablet 10 | 97.24 | Tablet 10 | 94.49 |
| Average-97.23%<br>Limit-(82.64-111.81) % | | Average-94.32%<br>Limit-(80.172-108.469)% | |

**Table 4: Results of comparative dissolution studies of the two brands of Ciprofloxacin Tablets IP as percentage drug release in water.**

| Sl No. | CP5-125 | Sl No | 16015 |
|---|---|---|---|
| Tablet 1 | 105.78 | Tablet 1 | 109.70 |
| Tablet 2 | 105.96 | Tablet 2 | 108.95 |
| Tablet 3 | 105.22 | Tablet 3 | 108.77 |
| Tablet 4 | 105.03 | Tablet 4 | 108.58 |
| Tablet 5 | 105.40 | Tablet 5 | 108.39 |
| Tablet 6 | 105.59 | Tablet 6 | 108.21 |
| Limit(NLT) 80% | | Limit(NLT) 80% | |

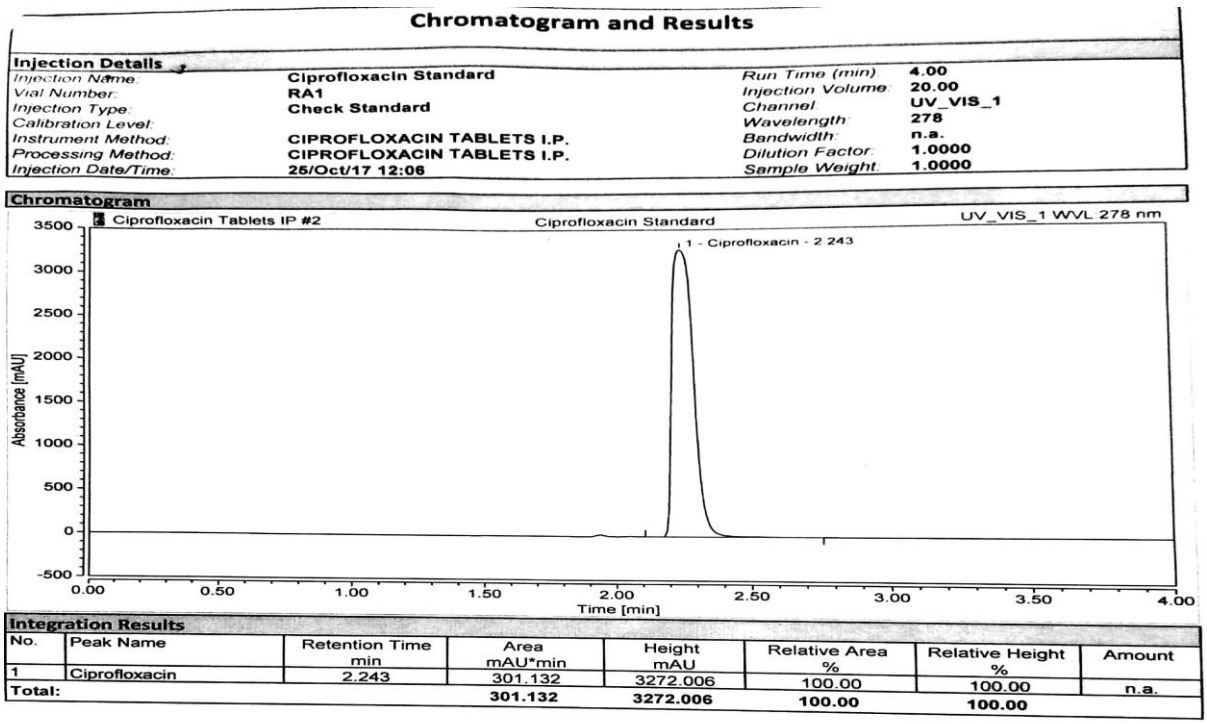


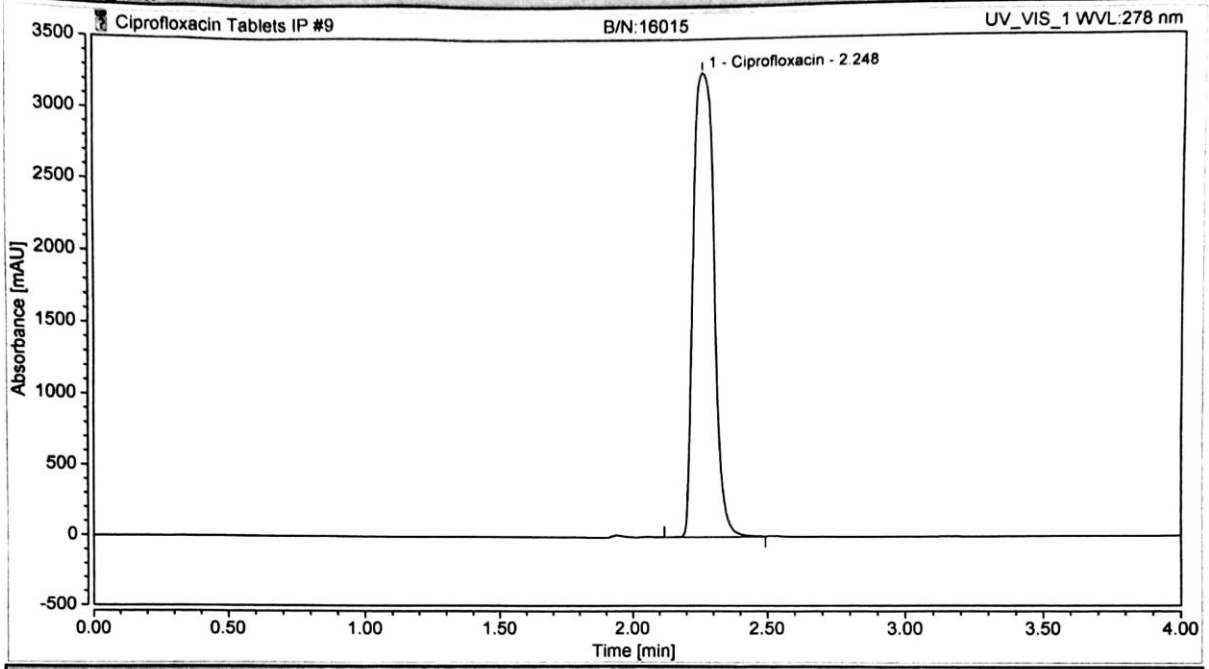

**Fig. 1**

## Chromatogram and Results

**Injection Details**

| | | | |
|---|---|---|---|
| *Injection Name:* | **B/N:16015** | *Run Time (min):* | **4.00** |
| *Vial Number:* | **RA3** | *Injection Volume:* | **20.00** |
| *Injection Type:* | **Unknown** | *Channel:* | **UV_VIS_1** |
| *Calibration Level:* | | *Wavelength:* | **278** |
| *Instrument Method:* | **CIPROFLOXACIN TABLETS I.P.** | *Bandwidth:* | **n.a.** |
| *Processing Method:* | **CIPROFLOXACIN TABLETS I.P.** | *Dilution Factor:* | **1.0000** |
| *Injection Date/Time:* | **25/Oct/17 12:43** | *Sample Weight:* | **1.0000** |

**Chromatogram**




**Integration Results**

| No. | Peak Name | Retention Time min | Area mAU*min | Height mAU | Relative Area % | Relative Height % | Amount |
|---|---|---|---|---|---|---|---|
| 1 | Ciprofloxacin | 2.248 | 289.438 | 3260.865 | 100.00 | 100.00 | n.a. |
| **Total:** | | | **289.438** | **3260.865** | **100.00** | **100.00** | |

**Fig. 2**

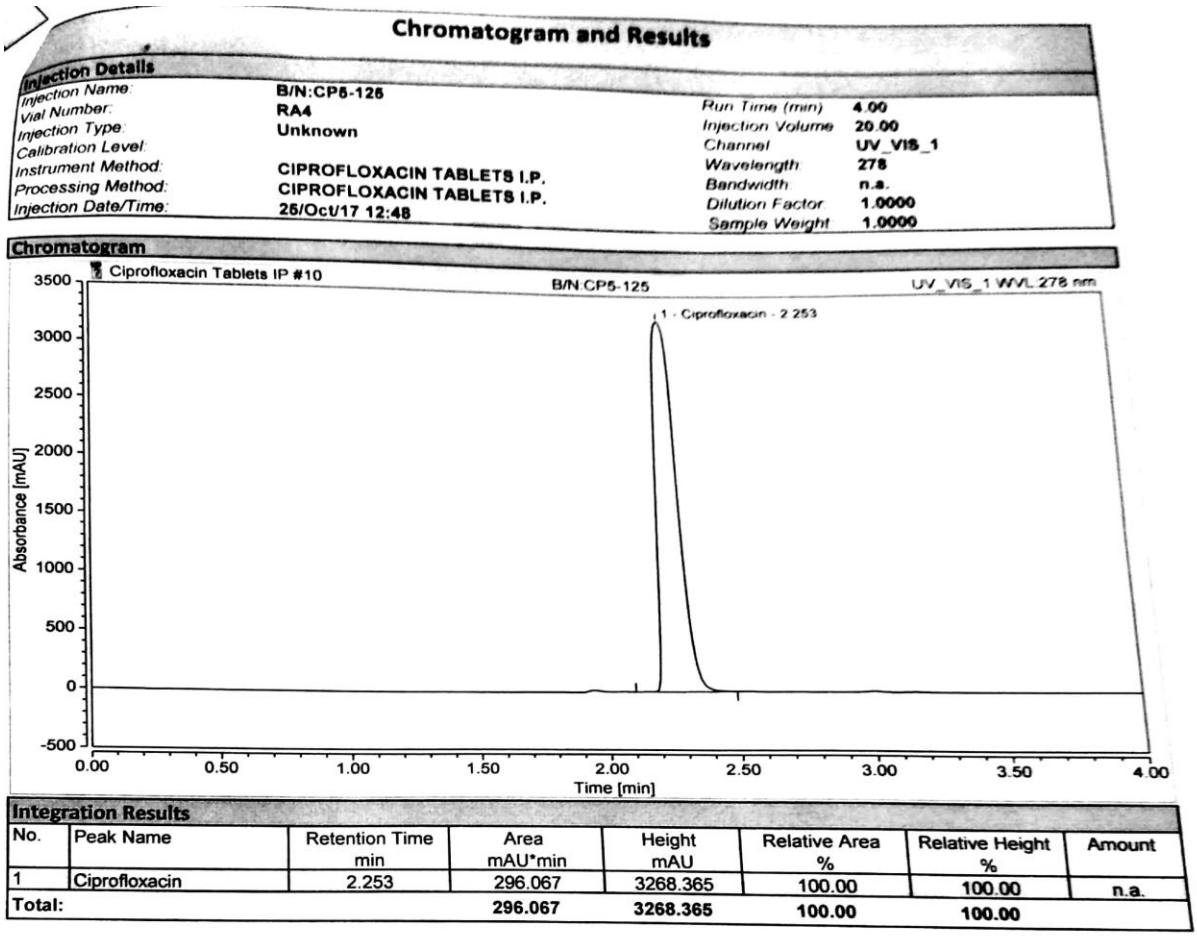



**Fig.3**

## CONCLUSION

Thus, monitoring of branded drugs in the market is vital. WHO has issued many guidelines for global standard and requirements for the assessment, authorization, registration, marketing as well as quality assurance of the pharmaceutical products. Monitoring marketed drugs can lessens a country's economical problem on health issues from diseases due to fraud and substandard drugs usage. Initial quality control evaluation of the drugs is essential and in vitro dissolution testing can be a valuable predictor of the in vivo bioavailability and bioequivalence of tablet dosage forms. Quality control methods of assessment are useful to monitor quality characteristics of various marketed brands and product consistency of batch-to-batch drug release. In addition, drugs that having three or more batches must be assessed and monitored to ensure its interchangeability with innovator brand. The qualitative analysis as given in the monograph of Ciprofloxacin Tablets IP in Indian Pharmacopoeia were

performed using different analytical methods and were found to meet the requirements in all respects All the brands have passed all the official tests prescribed by Indian Pharmacopoeia (IP). Formulation additives in the tablet, physical form of the drug used in the tablet and manufacturing processes vary from manufacturer to manufacturer which is responsible for the variation in the observed dissolution profiles. Both the brands under study were evaluated for test of identification, assay, and dissolution and their comparative results in the entire test conform with the limits as given under acceptance criteria. Hence it is concluded that the main aim behind this research work was to check that whether the two brands of Ciprofloxacin Tablets IP align with the acceptance criteria and also that two brands can be substituted for one another in terms of quality depending upon their availability.

**ACKNOWLEDGEMENT**

Sincere thanks to The Director of Regional Drugs Testing Laboratory (RDTL) Guwahati for supporting us in carrying out this research work.

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