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Quality Specification and Evaluation of Various Brands of Ciprofloxacin Hydrocholoride Tablets

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Abstract: *Ciprofloxacin HCl, is a highly popular antibacterial agent in the third world countries including India. Many companies are engaged in manufacturing and marketing the brands, purchasing the basic drug from the core suppliers. Often these brands vary in cost and companies usually claim superiority of their product to justify the higher price. There is a possibility that products containing same amount of basic drug are therapeutically equivalent. So, if it can be proved that the different brands are therapeutically equivalent, they can be substituted for each in prescription and patient can be take advantage of an economic dosage regimen. This could be achieved by assessing physicochemical equivalence of different brands of the drug. Assessment may include the evaluation of uniformity of weight, friability, hardness, disintegration and dissolution tests as well as chemical assay of tablets.*
The official method for estimation of Ciprofloxacin HCl is by HPLC .Though thismethod is affordable for big industries, the small scale industries of India often do not have these sophisticated instruments for routine procedure. The present work is aimed at investigating whether UV spectrophotometer, a very versatile method could be used for estimating Ciprofloxacin HCI in various marked brands and also to generate the baseline physicochemical and dissolution data to predict bio-equivalence through pharmaceutical equivalence five brands of tablets were taken and evaluated for all characteristics. Only three brands out of five brands of ciprofloxacin HCI tablet analyzed passed all quality specification and were physical and chemically equivalent. These three brands can be substituted in their prescription and use. This study highlight the need for constant market monitoring of product to ascertain their equivalence to pharmacopoeia standards.
Key words: *Pharmacopoeia, Ciprofloxacin HCI , Disintegration and Dissolution*

I. INTRODUCTION

Ciprofloxacin HCI, is a highly popular antibacterial agent (Stefan et al 2016 , Rodriguez 2015, Fadlallah 2016) in the third world countries including India. Tablet as solid dosage form possesses several advantages. When correctly formulated and manufactures they provide an accurate, stable dose of drug with necessary physical and chemical properties for the required duration and intensity of therapeutic action. Hence, precision of dosage, durability of physical characteristics for extended period of storage, stability of chemical and physiological activity of drug and convenience of administrationcan be achieved in form of tablets (Rawlins 2004) Stable tables may be defined as one that retain its original size, shape, weight, content, color etc. Under normal handling and storage conditions throughout their shelf life, while maintaining, the in vitro availability of active ingredients within reasonable limits with time (Ansel 1999). This is important, because the parameters which measures quality of tablets, are most important at the moment of administration to the patients. The various in-vitro test that should be conducted for the evaluation of the tablets are listed in table A These included – Weight variation, hardness, friability, Disintegration, Content uniformity and Drug Dissolution. Ciprofloxacin HCI a fluoroquinolone antibacterial and is highly popular in the third world countries including India. Many companies are engaged in manufacturing and marketing the brands, purchasing the basic drug from the core suppliers. Often these brands vary in cost and companies usually claim superiority of their product to justify the higher price. There is a possibility that products containing same amount of basic drug are therapeutically equivalent. So, if it can be proved that the different brands are therapeutically equivalent, they can be substituted for each in prescription and patient canbe take advantage of an economic dosage regimen.

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In the present study five brands of Ciprofloxacin HCI were selected and the aim was to obtain base line data towards the establishment of bioequivalence of tablets.. Various in vitro assessment test were performed – Hardness, Friability, Weight variation, Uniformity of Active ingredients, Disintegration time and Dissolution Rate.

U.V spectroscopic method for estimating the content of ciprofloxacin HCI in these 5 brand was also

established as it is relatively less expensive and versatile method as compared t the official HPLC method.

II. Material and Methods

Pure ciprofloxacin HCI powder was procured from Chhabra Distributors Pvt. Ltd. Pharmaceutical Distributors. All other chemical used were of Rankem brand Instruments used were UV-Visible double beam Spectrophotometer, Systronic – 2101,Weighing balance – Electronic balance, Dhona 200D,Distintegration apparatus – Tablets Disintegration Test Machine (IP, BP),USP standard Popular India Traders, Dissolution apparatus – Digital Dissolution Rate Test Apparatus, (IP, BP, USP Standard) Popular India Traders, Hardness tester – Monsanto Hardness Terter, Friability Tester – Tablet Friability Test Apparatus, Remi equipment. Melting point tester – Digital melting point apparatus

The five commercial Ciprofloxacin Hydrochloride tablets of I.P. grade were selected and labeled as test products A, B, C, D and E. They were priced at Rs. 45, Rs. 30.40, Rs. 25.50, Rs 52.50 and Rs 30.40 respectively. Each tablet contain Ciprofloxacin HCI I.P. equivalent to Ciprofloxacin 250 mg. Each 116 of Ciprofloxacin HCI is equivalent to 100 mg of Ciprofloxacin.

In Vitro Evaluation Of Selected Five Brands Of Ciprofloxacin HCl Tablets

Uniformity of weight: 20 tablets were selected at random and average weight was determined. Percentage deviation was found out from the average. According to I.P no tablet should deviate from the average weight by more than ±5%. The weight variation was determined and standard deviation from mean was calculated for all the test groups.

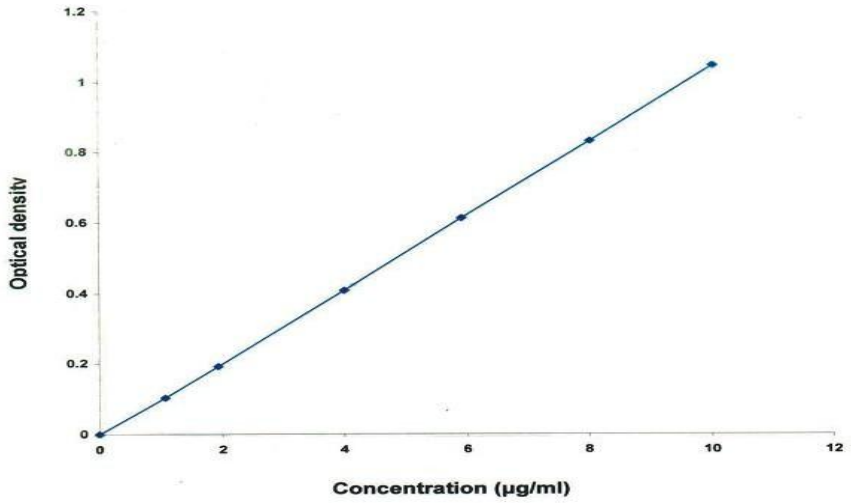
Content of active ingredient

Assay of Ciprofloxacin

20 tablets were weighed and powdered and quantity of powder equivalent to 0.1gm of Ciprofloxacin HCI was taken carefully and transferred to 100 ml volumetric flask. The volume was made up to 100ml with 0.1% glacial acetic acid (Sethi 2001) and contents were thoroughly shaken and filtered in order to get a clear solution. 5ml of this clear solution was taken and further diluted to 50ml with 0.1% glacial acetic acid and optical density was measured at 276 nm.

Standard Curve

Standard curve for Ciprofloxacin HCl was prepared by UV spectrophotometric analysis. 50 mg of pure Ciprofloxacin HCI was accuately weighed and dissolved in 0.1% glacial acetic acid to make the volume upto 100ml.Then from this solution, 1ml was withdrawn and volume was made up to 50ml with 0.1% glacial acetic acid . Again 1ml, 2ml, 4ml, 6ml, 8ml, 10ml were withdrawn in 6 different 10 ml volumetric flask and volume was made up to 10ml with 0.1% glacial acetic acid. The optical density for each sample was recorded. Standard graph was obtained as shown in figure 1 by plotting concentration Vs optical density and was used as reference for calculating % purity as well as dissolution rate.



Disintegration – The disintegration time of the tablet was determined according to IP procedure for Tablets Disintegrating Test Machine. One Tablet was placed in each of six tubes of the basket disc was added to each tube and apparatus was operated using wateras medium maintained at 37 ±2ºC. The time was noted for all the six tablets to disintegrate (Indian Pharmocopoeia 1999)

Dissolution - Dissolution test or dissolution rate studies were carried out in Dissolution testapparatus of (IP / BP / USP standards).
900 ml of water was placed in the vessel and temperature was maintained at 37ºC. One tablet is placed in the dry basket and speed was adjusted to 50rpm, 10ml dissolution was withdrawn at interval of 5,10,15,20,25 and 30 minutes in a 100ml volumetric flask. The volume was made upto 100 ml with 0.1% glacial acetic acid and were analyzed by the spectrophotometer at wavelength of 276nm.
The amount released was calculated from the formula

$$\text{Amount release} = \frac{\text{Conc. x 900 x dilution factor}}{1000}$$

Hardness test: Five tablets were taken individually and tested for hardness in Monsanto hardness tester. Amount of pressure applied to break the tablet in Kg/cm^2 was recorded, and mean of five samples were taken.
Friability Test – 20 tablets were weighed before the test and were placed in the pan of the Roches friabilator. These were allowed to undergo 100 revolutions. Then again the average weight of 20 tablets was taken and difference in the weight before and after the test was recorded.

III. Results and Discussion

***In-vitro* evaluation of selected marked five brands of ciprofloxacin HCI tablets**
Results of various invitro evaluation parameters are summarized in table 01 and are discussed at appropriate places.
Hardness- Hardness test is an essential criterion in determination of ability of tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling before storage. The results showed that the brands examined had mean hardness within the range of 8.03 to 17.2 Kg / cm^2. Generally a hardness of 4 Kg / cm^2 is normally considered to be minimum for a satisfactory tablets (British Pharmacopoeia 1998; Basak et al., 2004). Thus the tablet Brands (A-E) are found to qualify hardness test.
Friability: Friability is an unofficial test, yet it is important test as it is designed to evaluate the ability of tablets to withstand abrasion and shock without crumbling. Tablets having percentage loss less than 1% is usually considered acceptable.
The results showed that brands A, B, D, confirmed to the required standard for friability while brands C & E fail to comply. This failure could have resulted from use of inadequate or insufficient amount of binding agents during formulation inadequate moisture content during compression or insufficient comparison pressure during tableting.
Uniformity of Weight: The results of weight variation test performed on test products A to E in accordance with I.P. 1996 are summarized in table 1. The average weight is above 300 mg for which the limit is ± 5%. Test product. Thus all the test products pass the test of uniformity of weight. The maximum average deviation for weight variation for the test product are in order A> E> D> B> C.
Uniformity of Active Ingredients: The result of assay of chemical content to determine the amount of ciprofloxacin HCI in each formulation. The I.P. monograph for ciprofloxacin HCI tablet states that the tablet should not contain less than 90% and not more than 110% of the stated amount, when 20 tablets are taken for analysis. The results of this test are given in Table 1.
In was found that all the tablets pass the test for uniformity of active ingredient. However within limits, test product C showed highest content of active ingredient 103.1% whereas the test product B showed the lowest 90.4%. The content of active ingredients present in test product is in the order C>E>A>D>B.
Disintegration Test :- Disintegration test measures the time required for the tablet todisintegrate into particles. This is a necessary condition for dissolution and could be the rate determining step in the process of drug absorption. Disintegration is used as the guide in the preparation of optimum tablet formula. The results are presented in Table 1. The results showed that all brands passed the disintegration test. The disintegration time of various brands are in order A>B>D>E>C.
Dissolution Test:- Dissolution test is the measure of the amount of drug released into the medium with time. The I.P. stipulates that at 30 minutes all tablets should have released into dissolution medium an amount not less than 80% of labeled amount of drug. The dissolution profile of ciprofloxacin HCl brands are presented in Table 1.
All brands did not pass the dissolution test. However, brands D & B were highest although the amount released at 30 min and was greater for brand D 89.10%. The brandA showed profile with intermediate rate. Brand C and E showed the least dissolution rate and they did not pass the test, with amount released at 30 min being 69.40%.
The difference in dissolution rates may be due to the nature of excipient used or the formulation process. It has

been shown by Abdou (1998) that dissolution rate of a pure drug can be altered significantly when mixed with various adjuncts during the manufacturing process of solid dosage forms.

On analyzing the physicochemical properties of the 5 brands of ciprofloxacin HCI tablets it can be observed that relationship exist between disintegration time and hardness. Test product A & B with higher degree of hardness took longer time to disintegrate ascompared to products C, D, and E with lesser hardness. This substantiate the factor that hardness is associated with density and porosity which in turn influences disintegration time.

Disintegration time is a function of hardness of tablets can be proved by finding out correlation between the two. It was found to be 0.68. Furthermore, fast disintegration characteristic of test products C and E are not reflected in dissolution profile, rather thean inverse relationship exist for the two product C & E. These released less amount of % drug dissolved 70.40%.

As compared to test product A, B, & D had longer disintegration time. This could be due to the fact that disintegrating particle, though small enough to pass through screen of dissolution basket, may have retained the active drug within their hard cores, and hence did not release the drug into the dissociation medium. This implies that the product may not release a significant amount of drug on absorption into systemic circulation; Thus leading to therapeutic failure. It was further observed that though lower price ranged products C & E exhibited excellent result for % content of active ingredient but fail to meet the specific dissolution test as per I.P. This may be due to poor preparation technique during formulation and subsequent manufacturing.

On the whole, based on various physicochemical parameter, it can be inferred that products C&F though are most economical, yet they failed to comply the dissolution test and % friability test. Brands A, B and D cam be considered to be physiochemicalequivalent as they exhibited good dissolution results. Product D can be selected as the best brand followed by B and A. However product B is most cost effective brand.

Table-1: Results of In-vitro Evaluation of Ciproflox HCl Tablets

S.No	**Test Products**	**Hardness* Kg /cm^2 (mean ±SD)**	**Friabil ity % loss**	**Uniformity** of weight (mg) (mean± SD)**	**Content of active ingredient%**	**Disintegration*** time (min) (mean ± SD)**	**Dissolution*** at 30min.% (mean ± SD)**
1	A	13.1±0.32	0.52	320.2±0.40	99.1	8.30± 0.02	85 ± 0.41
2	B	17.2±0.52	0.63	354.1±0.21	90.4	8.18 ± 0.05	87.26±0.36
3	C	12.9±0.81	1.20	365.1±0.16	103.1	5.48± 0.13	79.30±0.45
4	D	12.9±0.93	0.93	343.9±0.19	97.4	6.40± 0.02	89.10±0.51
5	E	8.1±0.52	1.09	315.9±0.27	100.2	5.45± 0.04	69.40±0.26

IV. Conclusion

Only three brands out of five brands of ciprofloxacin HCI tablet analyzed passed all quality specification and were physical and chemically equivalent. These three brands can be substituted in their prescription and use. This study highlights the need for constant market monitoring of product to ascertain their equivalence to pharmacopoeia standards.

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