

COMPARATIVE ASSESSMENT OF THE QUALITY CONTROL MEASUREMENTS OF MULTISOURCE OFLOXACIN TABLETS MARKETED IN INDIA

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ABSTRACT

The main purpose of the study is to evaluate some quality control parameters to compare the quality, safety, and efficacy of five brands of ofloxacin tablets available in the Indian market. The physicochemical parameters and assay of the five brands of ofloxacin tablets were assessed through the evaluation of uniformity of tablet weight, friability, hardness, disintegration, and assay of active ingredients according to established methods. Weight variation of the tablets proved statistically that all of the tablets were in accordance to the required limits that is not more than $\pm 5\%$ deviations. Dissolution test was carried out; none had potency less than 85% within 60 minutes the required specification, not less than Q+5%. Pharmaceutical assay was carried out none had potency less than the required specification (90.00% - 100.00%). The dissolution rate and disintegration time were determined in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) without enzymes. All brands complied with the official specification for uniformity of weight, friability, and disintegration. The disintegration test revealed that the drugs had higher disintegration times in SIF (8.25) relative to those in SGF (5.0255). The UV spectrophotometric assay of ofloxacin tablets revealed that three samples contained over 95% (w/w) of labeled chemical content. The method is simple and rugged for both routine analysis and evaluation of the dissolution pattern of ofloxacin tablets as in vitro tests for batch-to-batch quality control assessment.

Keywords: Ofloxacin tablets, Dissolution, Quality control.

INTRODUCTION

The marketing of multisource drug products registered by national drug agencies in developing countries, with the view of improving health care delivery through competitive pricing, has its attendant problem of ascertaining their quality and interchangeability¹. Variable clinical responses to drugs presented as generics and batch-to-batch inconsistencies have been reported². Such unacceptable trends were exhibited in some drug products including metronidazole and metformin tablets³.

Quality control procedures, which are useful tools for batch-to-batch consistency in manufacturing, should be performed for every drug product. Drugs having more than three generic products require analysis for their biopharmaceutical and chemical equivalency. These methods ensure that any of the generic products can be used interchangeably. The observation is that most of the generics have much lower shelf prices than the innovator products, which raises the issue of the likelihood of unequal product performance.

The prediction of the in vivo bioavailability of most oral drugs depends on the in vitro dissolution studies because in vitro disintegration tests do not always give good correlation⁴.⁵. Dissolution testing of drug products plays an important role as a quality control tool to monitor batch-to-batch consistency of drug release from a dosage form and as an in vitro surrogate for in vivo performance⁶. The therapeutic efficacy of a drug product intended to be administered by the oral route depends on its rate and extent of absorption by the gastrointestinal tract. A comprehensive evaluation, however, involves the determination of uniformity of weight, chemical content, friability, hardness, and disintegration tests along with dissolution rate. Drugs that are chemically and biopharmaceutically equivalent must be identical in strength, quality, and purity. The content uniformity, disintegration, and dissolution rates must be comparable⁷.

There is an increasing need to evaluate the performance of a number of the available fluoroquinolone antibacterial agents because of the unexplainable pattern of microbial sensitivity to the members of this class of drugs. Ciprofloxacin, the most commonly employed having about 50 brands in the market, now exhibits some characteristics in microbial culture and sensitivity that indicate an unreliable switch from one product to another⁸. Ofloxacin now has about ten generic products in the market, and this number is likely to increase with time.

In this study, in vitro dissolution techniques were used to ascertain

the rate and extent of the active pharmaceutical substance of the five brands of ofloxacin tablets manufactured by five different pharmaceutical companies imported and marketed in India. The basic purpose was to establish their quality prior to determining interchangeability with the innovator product.

MATERIALS AND METHODS

Ofloxacin brands having label strength of 200 mg (Table 1) were purchased from a retail pharmacy. All tests were performed within product expiration dates. Ofloxacin powder was supplied by MICROLABS, Bangalore

The reagents used were concentrated hydrochloric acid, sodium hydroxide, and potassium phosphate, Di sodium potassium ortho phosphate. They were procured from Karnataka fine chemicals, BANGALORE. Freshly distilled water was used throughout the work.

Prepared Reagents

Simulated intestinal fluid (SIF) was prepared by dissolving 40 g of sodium hydroxide and 34 g of potassium di hydrogen phosphate phosphate monobasic in 2 L of distilled water and then diluting to volume in a 5-L volumetric flask^{9,10}.

Simulated gastric fluid (SGF) was prepared by adding 43 mL of concentrated hydrochloric acid to 2 L of distilled water in a 5-L volumetric flask; 500 mL of 2% sodium chloride solution was added, and the solution was diluted to volume^{9,10}.

Visual Inspection

The shape, size, and color of the different brands of tablets were examined visually.

Friability Test

Twenty tablets were weighed and subjected to abrasion using a Veego tablet friability tester at 25 rev/min. (Table : 5)

Hardness Test

The crushing strength of the tablets was determined using a Mosanto tablet hardness tester (Mosanto, UK). (Table : 3)

Uniformity of Weight

Tablets of each brand were weighed individually using a digital analytical balance (Adventure Ohaus, China). The percentage deviation of the individual tablets from the mean was determined. (Table 4)

Tablet Disintegration Test

Tablet disintegration was determined at 37 °C using a Veego model VTDH3 disintegration testing apparatus (Rutartek, India). (Table: 2)

Disintegration Time, Hardness, Uniformity of Weight, Friability, and Chemical Content of five Brands of Ofloxacin Tablets

Table 1: The percentage deviation of the individual tablets from the mean

S.no	Brand name	Manufacturer
A	Oflox	Cipla
B	Oflomac	Macleodos
C	Of	Jb chemicals
D	Terflox	Vision medlink
E	Floxar	Forgo

Table 2: Disintegration time

S.no	Disintegration time in SGF	Disintegration time in SIF
A	4±0.7	7±0.9
B	7±0.8	8±0.5
C	6±0.5	10±0.5
D	5±0.4	9±1.5
E	6±0.9	8±1.4

Table 3: Hardness (crushing strength) (kg/cm²)

S.no	Hardness
A	6.5±0.6
B	6.89±0.5
C	6.7±0.3
D	4.9±0.4
E	5.8±0.6

Table 4: Uniformity of Weight (g)

S.no	Uniformity of weight
A	225.75±0.01
B	243.70±0.02
C	235.42±0.03
D	247.80±0.04
E	238.25±0.02

Table 5: Friability (%)

S.no	Friability
A	0.075
B	0.065
C	0.055
D	0.054
E	0.035

Table 6: Chemical Content (%w/w)

S.no	Chemical content in sgf	Chemical content in sif
A	98	90
B	97	92
C	95	90
D	98	92
E	98	96

Dissolution Rate Determination

Dissolution rates in the simulated body fluids (i.e., SGF and SIF) were determined using a Veego dissolution rate testing apparatus using 900 mL of medium at 37 ± 0.5 °C. The basket was rotated at 100 rpm. 1 ml sample was withdrawn at time intervals of 5 mins and 1ml

of fresh dissolution medium replaced after each with-drawal. The UV absorbance was measured at 294 nm using a UV/vis spectrophotometer (Unico-2120, USA). The amount of ofloxacin in the samples was determined based on the calibration curve generated at a wavelength of 294nm. The regression value for the calibration curve in 0.1N HCL is $r^2 = 0.9989$ (FIG 1) and in 6.8 pH phosphate buffer is $r^2=0.992$ (FIG 3).

The dissolution profiles of the different brands of ofloxacin tablets were generated from the graph of the amount of ofloxacin released versus time and is represented by

(FIG 2) in Simulated gastric fluid and (FIG 4) in Simulated intestinal fluid

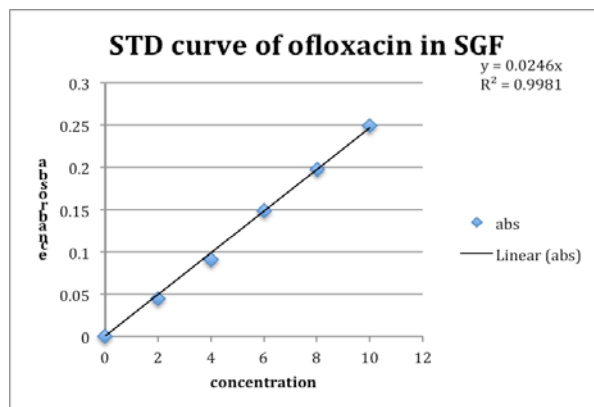


Fig. 1: It shows standard curve of ofloxacin in simulated gastricfluid

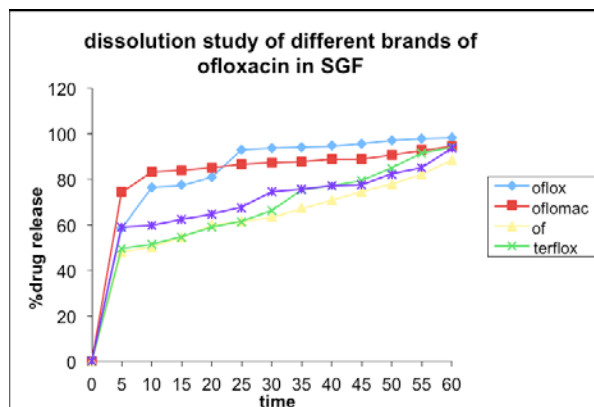


Fig. 2: It shows dissolution study of different brands of ofloxacin in simulated gastric fluid

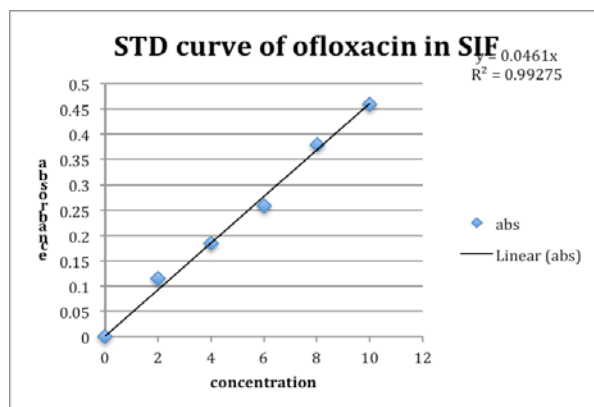


Fig. 3: It shows standard curve of ofloxacin in simulated intestinalfluid

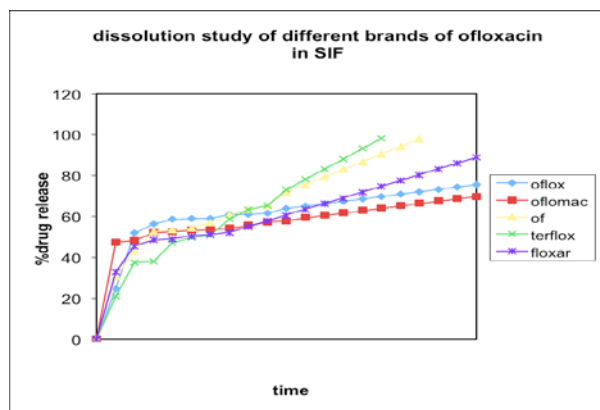


Fig. 4: It shows dissolution study of different brands of ofloxacin in simulated intestinal fluid

Chemical Content Determination

50 mg equivalent powder of different brands of ofloxacin was weighed. Each was dissolved separately in 100 mL of 1 M sodium hydroxide and shaken for 3 min, then further diluted to 200 mL with 1 M sodium hydroxide and allowed to stand for 15 min. A 2-mL aliquot of the final volume for each weight was taken and further diluted to 25 mL with water. The absorbances of the resulting solutions were determined at 294nm. The procedure was applied to the five brands of ofloxacin employed in the investigation. (Table: 6)

Statistical Analysis

Statistically significant differences among the brands were analyzed using the F-test with $P < 0.2$ considered significant.

RESULTS AND DISCUSSION

Dissolution of drug from oral solid dosage forms is a necessary criterion for drug bioavailability (i.e., the drug must be solubilized in the aqueous environment of the gastrointestinal tract to be absorbed). For this reason, dissolution testing of solid oral drug products has emerged as one of the most important control tests for assuring product uniformity and batch-to-batch equivalence^{11, 12}. The uniformity-of-weight determination for the five brands of ofloxacin tablets gave values that comply with the USP specification for uncoated tablets with a deviation less than 5% from the mean value (i.e., maximum deviation value 0.045). The strict adherence to good manufacturing practice (GMP) during the granulation and compression stages ensures tablet uniformity of weight. This is the point at which large intra batch variations in tablet weight occur. A variation beyond the pharmacopoeial limits indicates unacceptable products. All the brands also passed the friability test; none had a weight loss of up to 1% (w/w), with the maximum value being 0.075. Drug products chip at the edges during transportation as a result of abrasion; this is evidence of poor production. All the brands, however, had good compression characteristics. Dissolution Profiles for five Brands of Ofloxacin Tablets in SGF and SIF in this regard. OF has shown 88% and oflox has shown 98% of total drug release in SGF within 60 min. Whereas oflomac has shown 69% and terflo has shown 98% of total drug release in SIF within 75 min. Therefore oflox has shown good result when compared to other brands in SGF.

Summary

The presented quality control method¹³ is useful in monitoring the production consistency of batch-to-batch product release of each brand of ofloxacin and in comparing the quality characteristics of different brands marketed. The therapeutic equivalence of the drugs must also be investigated by challenging susceptible microorganisms.

CONCLUSION

It is concluded that oflox manufactured by cipla has got more bio availability with 98% of total drug release in gastric fluid within 60 min when compared to oflomac , terflo , floxar , OF and also comply with the USP specification .

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