

# BIOEQUIVALENCE STUDY OF CETIRIZINE HYDROCHLORIDE AND PSEUDOEPHEDRINE HYDROCHLORIDE EXTENDED RELEASE TABLET IN NORMAL, HEALTHY, ADULT, HUMAN SUBJECTS UNDER FASTING CONDITION

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## ABSTRACT

**Aim:** This study was conducted in order to compare the bioavailability of two extended-release tablets containing 5 mg of cetirizine dihydrochloride and 120 mg of pseudoephedrine hydrochloride.

**Methods:** Fourty subjects were enrolled in a single-center, randomized, single-dose, open-label, two-way crossover study with a one-week washout period. Plasma samples were collected up 32 hours following drug administration and both analytes were determined by liquid chromatography-tandem mass spectrometry (LCMS/MS) method with turboionspray mode. Pharmacokinetic parameters used for bioequivalence assessment were AUC<sub>0-t</sub>, AUC<sub>0-∞</sub> and C<sub>max</sub>.

**Results:** The 90% confidence intervals obtained by analysis of variance for AUC<sub>0-t</sub>, AUC<sub>0-∞</sub> and C<sub>max</sub> were 93.79-106.89%, 93.26-106.37%, 94.14-112.44% for cetirizine and 87.19-108.31%, 87.91-109.51%, 96.34-112.64% for pseudoephedrine, respectively. Both formulations were tolerated and no serious adverse events were reported. These results were all within the range of 80.00-125.00%.

**Conclusion:** Bioequivalence between formulations was concluded both in terms of rate and extent of absorption.

**KEYWORDS:** Bioequivalence; cetirizine; pharmacokinetic; pseudoephedrine.

## INTRODCTION

### 1 BIOAVAILABILITY

Bioavailability is defined as: The rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action<sup>[1]</sup>

In pharmacology Bioavailability (BA) is a subcategory of absorption and is the fraction of an administered dose of unchanged drug that reaches the systemic circulation which is one of the principal pharmacokinetic properties of drugs. By definition when a medication is administered intravenously its bioavailability is 100%. However when a medication is administered via other routes (such as oral) its bioavailability generally decreases (due to incomplete absorption and first-pass metabolism) or may vary from patient to patient. Bioavailability is one of

the essential tools in pharmacokinetics as bioavailability must be considered when calculating dosages for non-intravenous routes of administration<sup>[2]</sup>

- It is the fraction of unchanged drug reaching the systemic circulation following administration by any route.
- To exert an optimal therapeutic action, an active moiety should be delivered to its site of action in an effective concentration for the desired period.
- This defines how much drug needs to be administered to achieve therapeutic effect.
- The influence of route of administration on drug's bioavailability is that enters the systemic circulation.  
Parenteral > oral > rectal > topical
- Intravenous injection of a drug results in 100% bioavailability as the absorption process is bypassed. In such cases the dose available to the patient called as the bioavailable dose is often less than the administered dose.
- Estimation of bioavailability is a means of predicting the clinical efficacy of a drug.
- Bioavailability testing measuring the rate and extent of drug absorption to obtain evidence of the therapeutic utility of a drug product.

Fraction of administered dose.

$$F = \frac{\text{Bioavailable dose}}{\text{Administered dose}}$$

Where F= Bioavailability

It ranges from 0 to 1 Bioavailability normally expressed as %.<sup>[3]</sup>

### 1.1.1 Type of bioavailability

- Absolute bioavailability (F) :-
- When systemic availability of drug administered orally is determined in comparison to its intravenous administration is called absolute bioavailability.
- Its determination is used to characterize a drug's inherent absorption properties from the extra vascular site.

$$\text{Absolute Bioavailability} = \frac{[\text{AUC}]_{\text{ev}} / (\text{Dose})_{\text{ev}}}{[\text{AUC}]_{\text{iv}} / (\text{Dose})_{\text{iv}}}$$

(ev-extravascular & iv- intravenous)

- Relative Bioavailability (Fr) :-
- When systemic availability of drug after oral administration is compared with that of an oral standard of same drug (such as an aqueous or non- aqueous solution or suspension) it is referred as relative bioavailability.
- It is used to characterize absorption of drug from its formulation. --

$$\text{Relative Bioavailability} = \frac{[\text{AUC}]_{\text{test}} / (\text{Dose})_{\text{test}}}{[\text{AUC}]_{\text{std}} / (\text{Dose})_{\text{std}}}$$

- Before the therapeutic effect of an orally administered drug can be realized the drug must be absorbed.

### C) Supra bioavailability: -

- Supra bioavailability is a term used when a test product displays large bioavailability than the reference product. Such formulations are usually not to be accepted as therapeutically equivalent to the existing reference product.

### 1.1.2 General Objectives of Bioavailability Studies

- Bioavailability studies are important in the determination of influence of excipients patient related factors and possible interaction with other drugs on the efficiency of absorption.
- Development of new formulations of the existing drugs e.g. innovator Vs generic Drug.
- Bioequivalence study looking for similarity of F and  $k_a$  values between products.
- One type of dosage form with another e.g. tablet versus intravenous dosage form or regular tablet with sustained release tablet.
- Bioavailability study where  $k_a$  and F are to be determined. Changes in  $k_a$  may be intentional (slow release) whereas F values should be similar.<sup>[4]</sup>

#### • Pharmacokinetic Parameters

- $C_{max}$  – Maximum measured plasma concentration after the administration of single dose of the drug expressed in terms of  $\mu\text{g/ml}$  or  $\text{ng/ml}$ .
- $AUC_{0-t}$  – The area under the plasma concentration versus time curve from time zero to the last time point with measurable concentration calculated by the linear trapezoidal method.
- $AUC_{0-\infty}$  – The area under the plasma concentration versus time curve from time zero to time infinity.  $AUC_{0-\infty}$  is calculated as the sum of the  $AUC_{0-t}$  plus the ratio of the last measurable.
- $T_{max}$ : Time of maximum measured plasma concentration. If the maximum value occurs at more than one-point  $T_{max}$  is defined as the first point with this value in each period. Gives indication of the rate of absorption expressed in terms of hours or minutes.
- $K_{el}$ : Apparent first order elimination or terminal rate constant calculated from a semi-log plot of the plasma concentration versus time curve.
- $T_{1/2}$ : Apparent first-order terminal elimination half-life will be calculated as  $0.693/K_{el}$ .<sup>[5]</sup>

The various pharmacodynamics Parameters which influence the above mentioned pharmacokinetic.

#### A) Minimum Effective Concentration (MEC):

It is defined as the minimum concentration of drug in plasma required to produce the therapeutic effect. It reflects the minimum concentration of the drug at the receptor site to elicit the desired pharmacologic response. The concentration of drug below MEC is said to be in the sub therapeutic level.

#### B) Maximum Safe Concentration (MSC):-

Also called as minimum toxic concentration (MTC) it is the concentration of the drug in plasma above which adverse or unwanted effects are precipitated. Concentration of drug above MSC is said to be in the toxic level.

### C) Onset of Action

The beginning of pharmacologic response is called as onset of action.

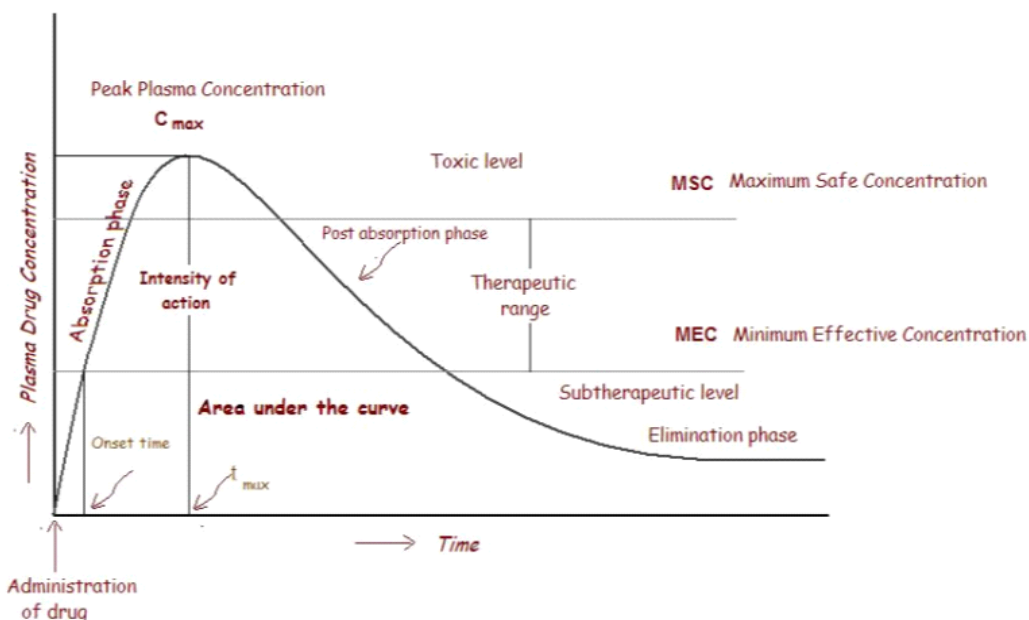
### D) Onset Time

It is the time required for the drug to start producing pharmacologic response. It corresponds to the time of plasma concentration to reach MEC after administration of drug.

### E) Duration of Action

The time period for which the plasma concentration of drug remains above the MEC level is called as duration of drug action.

F) Therapeutic Range The drug concentration between MEC and MSC represents the Therapeutic range



**Fig 1 Pharmacokinetic Parameters<sup>[5]</sup>**

## 1.2 BIOEQUIVALENCE

It is define “as the property wherein two drugs with identical active ingredients or two different doses forms of the same drug possess similar bioavailability and procedure the same effect at the site of physiological activity”.

[6]

Bioequivalence study (BE) is a comparative study of bioavailability among drug products that contain the same active agents. Bioavailability and bioequivalence of drug products and drug product selection have emerged as critical issues in pharmacy and medicine during the last three decades. Concern about lowering health costs is resulted in tremendous written increase in the use of generic drug products currently about one half of all prescriptions written are for drugs that can be substituted with a generic drug.

"Bioequivalence" means that the active ingredient of 2 drug products has the same rate and extent of absorption. When it acts on its target for example, a receptor in the brain the brand name and the generic drug should deliver the same amount of active ingredient to the target site.

### 1.2.1 Type of Bioequivalence Studies

#### I) In Vivo Studies:-

The following points are used in assessing the need for in vivo studies:

- Pharmacokinetics complicated by absorption lesser than 70% or non linear Oral immediate release products with systemic action. Indicated for serious conditions requiring assured response.
- Narrow therapeutic margin.
- kinetics, pre-systemic elimination greater than 70%.
- Unfavourable physiochemical properties like low solubility, metastable
- Conditions, instability, etc.
- Non- oral immediate release products.
- Modified release products with systemic action.

#### II) In Vitro Studies:-

If none of the above criteria is applicable comparative in vitro dissolution studies will suffice. In vitro studies are conducted in cases where

- The product is intended for topical administration (Cream, ointment gel) for local effect.
- The product is for oral administration but not intended to be absorbed (antacid or opaque medium).The product is administered by inhalation as a gas or vapor.

### 1.2.2 Type of Bioequivalence

- Chemical equivalence:-

It indicates that two or more drug products that contain the same labelled chemical substance as an active ingredient in the same amount.

- Pharmaceutical equivalence:-

It is a relative term which denotes that the drug substance in two or more forms are identical in strength, quality, purity, content uniformity, disintegration and dissolution characteristics. They may however differ in containing different excipients.

- C) Therapeutic equivalence:-

It indicates that two or more drug products that contain the same therapeutically active ingredient elicit identical pharmacological effects and can control the disease to the same extent.

### 1.2.3 Need of bioequivalence study

To obtain the marketing approval for a generic product, it is necessary that it is bioequivalent to the already established brand (i.e. reference product)<sup>[7]</sup>

## RESULTS

### 2.1 Clinical Observation

Both of cetirizine-pseudoephedrine formulations were well-tolerated at the administered dose and no significant adverse clinical events were observed. All adverse events were of mild intensity. There were no serious adverse events. However, all events resolved completely. The causality was assessed by the study physician for all adverse events.

### 2.2 Pharmacokinetic Evaluation

#### 2.2.1 Cetirizine

Fourty subjects were available for pharmacokinetic evaluation. The pharmacokinetic parameters used to assess the bioequivalence of the test formulation versus the reference were AUC<sub>0-t</sub>, AUC<sub>0-∞</sub> for the extent of the absorption and C<sub>max</sub> and t<sub>max</sub> for the rate of absorption. Descriptive statistics of the pharmacokinetic parameter for cetirizine test and reference are summarized in Table 4 where the mean values for the AUC<sub>0-t</sub>, AUC<sub>0-∞</sub>, C<sub>max</sub> and t<sub>1/2</sub> values obtained for each formulation are shown. The pharmacokinetic characteristic t<sub>max</sub> was presented as median values. For cetirizine, the mean obtained values for test and reference products were 276.98 and 257.53 ng/mL for C<sub>max</sub>; 2286.26 and 2195.42 ng.h/mL for AUC<sub>0-t</sub>; 2373.34 and 2272.65 ng.h/mL for AUC<sub>0-∞</sub>. The median t<sub>max</sub> for both formulations was 0.60 h.

**Table No 2.1 Pharmacokinetic Data for the Test Product (A) and Reference Product (B) – Cetirizine**

Subj ect	Seq	C <sub>max</sub>		AUC <sub>0-t</sub>		AUC <sub>0-∞</sub>		T <sub>max</sub>		K <sub>el</sub>		T <sub>half</sub>		AUC Extrapolated	
		Test A	Ref B	Test A	Ref B	Test A	Ref B	Tes t A	Ref B	Tes t A	Ref B	Tes t A	Ref B	Tes t A	Ref B
N		40	40	40	40	40	40	40	40	40	40	40	40	40	40
Mean	AB/ BA	276. 98	257. 53	2286. 26	2195. 42	2373. 34	2272. 65	0.7 0	0.8 0	0.0 8	0.0 8	9.2 1	9.0 1	3.4 5	3.2 9
SD		81.7 3	82.1 1	530.2 1	558.3 5	580.1 0	588.2 6	0.2 1	0.2 7	0.0 2	0.0 2	2.0 9	1.8 0	1.7 6	1.4 8
Min		152. 02	173. 31	1299. 82	1250. 92	1341. 73	1281. 31	0.3 3	0.5 0	0.0 4	0.0 5	5.7 7	5.7 8	1.5 5	1.2 6
Median		263. 11	231. 34	2183. 50	2099. 97	2248. 30	2154. 05	0.6 7	0.8 3	0.0 8	0.0 8	8.8 9	9.2 0	2.9 8	3.0 5
Max		550. 59	514. 55	3763. 61	4296. 46	4234. 68	4359. 87	1.2 5	1.5 0	0.1 2	0.1 2	15. 57	13. 47	11. 12	8.0 8
CV%		29.5 1	31.8 8	23.19	25.43	24.44	25.88	29. 92	33. 62	21. 16	20. 32	22. 74	20. 00	51. 10	45. 20

### 2.2.2 PK Ratio

Only 40 subject data are calculated because of subject No 09 withdraw from the study in period-II due to personal reason.

Pre-dose concentration (>5%) was observed in Subject number 25 in both period-I and period-II.

Hence as per study protocol subjects No 09 & 25, excluded from pharmacokinetic and statistical analysis.

**Table No 2.2: PK Ratio (A With B) of Cetirizine hydrochloride for Parameters  $C_{max}$ ,  $AUC_{0-t}$  and  $AUC_{0-inf}$**

PK Ratio (A With B) of Cetirizine hydrochloride for Parameters $C_{max}$ , $AUC_{0-t}$ and $AUC_{0-inf}$			
Subject	$C_{max}$	$AUC_{0-t}$	$AUC_{0-inf}$
N	40	40	40
Mean	112.44	105.91	106.04
SD	32.93	18.48	18.20
Min	55.74	64.79	65.66
Median	104.31	106.76	106.92
Max	205.19	142.63	142.77
CV%	29.29	17.45	17.17

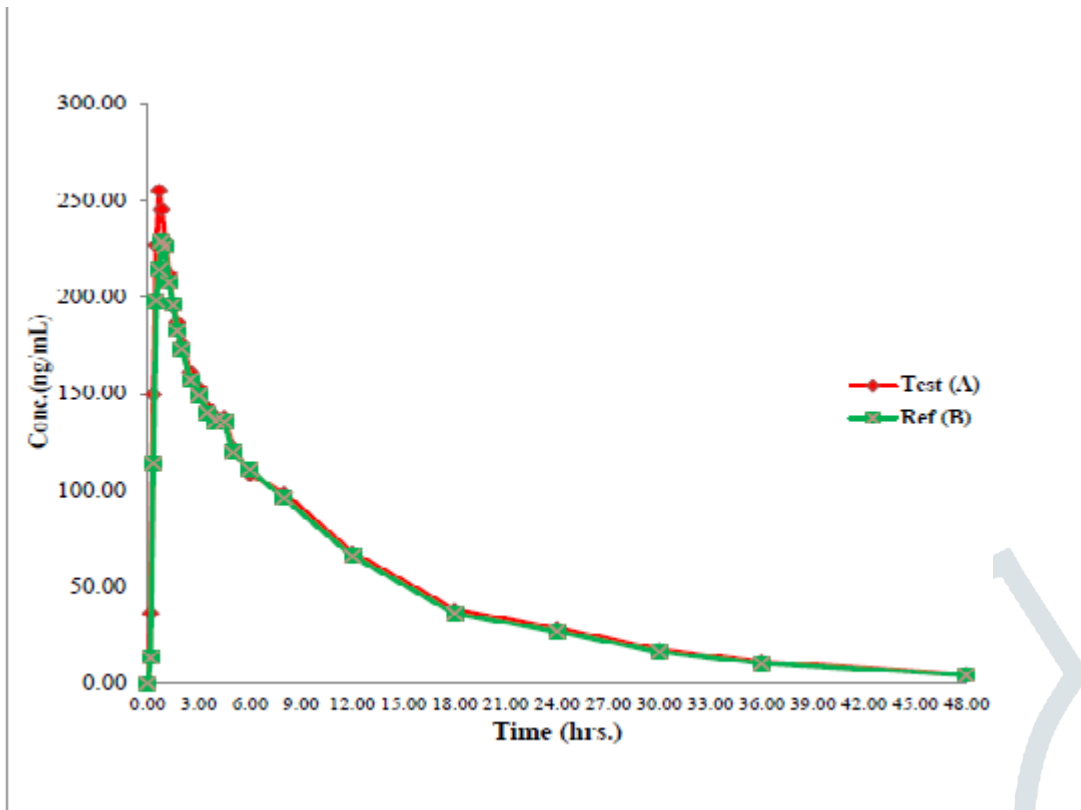
### 2.2.3 Statistical Analysis

The result obtained from the statistical analysis to establish bio-equivalence in the 42 subjects and Cetirizine hydrochloride and Pseudoephedrine Hydrochloride in both test and reference products that were performed for the estimation of least square mean difference in the test and reference formulation. log-transformed pharmacokinetic parameters  $C_{max}$ ,  $AUC_{0-t}$  and  $AUC_{0-\infty}$  of Cetirizine hydrochloride and Pseudoephedrine Hydrochloride and the 90% confidence intervals also are given in following table.

**Table No 2.3 Average Bioequivalence for the log transformed data : Cetirizine**

A = Test Product, B= Reference Product

Dependent	Form Var	Form Ref	RefGeo LSM	Form Test	TestGeo LSM	Ratio (%)	CI_90		Powe r (%)	SC V %	Bio equivalence
							Lower	Upper			
Ln ( $C_{max}$ )	Treat	B	247.20	A	267.32	108.14	100.94	115.84	99.93	18.41	Yes
Ln ( $AUC_{0-t}$ )	Treat	B	2135.44	A	2227.40	104.31	100.47	108.29	100.00	9.97	Yes
Ln ( $AUC_{0-inf}$ )	Treat	B	2208.24	A	2307.36	104.49	100.74	108.38	100.00	9.72	Yes



**Fig 03 Mean plasma concentration (ng/mL) vs Time Profile Graph of Test Product (A) Vs Reference Product (B) of Cetirizine HCL Extended Release Tablets USP 5 mg under fasting condition.**

**2.2.4 Pseudoephedrine**

Eighteen subjects were available for pharmacokinetic evaluation. The pharmacokinetic parameters used to assess the bioequivalence of the test formulation versus the reference were AUC<sub>0-t</sub>, AUC<sub>0-∞</sub> for the extent of the absorption and C<sub>max</sub> and t<sub>max</sub> for the rate of absorption. Descriptive statistics of the pharmacokinetic parameter for pseudoephedrine test and reference are summarized in Table 6 where the mean values for the AUC<sub>0-t</sub>, AUC<sub>0-∞</sub>, C<sub>max</sub> and t<sub>1/2</sub> values obtained for each formulation are shown. The pharmacokinetic characteristic t<sub>max</sub> was presented as median values. For pseudoephedrine, the mean obtained values for test and reference products were 360.84 and 383.60 ng/mL for C<sub>max</sub>; 5404.37 and 5492.67 ng.h/mL for AUC<sub>0-t</sub>; 5497.52 and 5571.35 ng.h/mL for AUC<sub>0-∞</sub>. The median t<sub>max</sub> for both formulations was 5.00 h.

**Table 2.2.4 Pharmacokinetic Data for the Test Product (A) and Reference Product (B) - Pseudoephedrine**

Subj ect	Se q	C <sub>max</sub>		AUC <sub>0-t</sub>		AUC <sub>0-∞</sub>		T <sub>max</sub>		K <sub>el</sub>		T <sub>half</sub>		AUC Extrapolated	
		Test	Ref	Test	Ref	Test	Ref	Tes	Ref	Tes	Ref	Tes	Ref	Tes	Ref
		A	B	A	B	A	B	t A	B	t A	B	t A	B	t A	B
N		41	41	41	41	41	41	41	41	41	41	41	41	41	41
Mean		360.84	383.60	5404.37	5492.67	5497.52	5571.35	5.5	5.3	0.1	0.1	5.9	5.8	1.73	1.4
SD		87.9	85.9	1455.5	1529.5	1469.5	1540.5	1.6	1.5	0.0	0.0	0.9	0.7	0.72	0.5
1		1	9	42	52	48	12	8	2	2	2	7	7		7
Min		232.62	251.15	2829.24	3179.01	2850.22	3231.30	2.5	3.0	0.0	0.0	3.1	4.6	0.74	0.4
62		15		24	01	22	30	0	0	9	9	2	6		5



<b>Median</b>	<b>339.</b> <b>46</b>	<b>369.</b> <b>93</b>	<b>5106.</b> <b>17</b>	<b>5177.</b> <b>91</b>	<b>5245.</b> <b>08</b>	<b>5267.</b> <b>30</b>	<b>5.0</b> <b>0</b>	<b>5.0</b>	<b>0.1</b> <b>2</b>	<b>0.1</b> <b>2</b>	<b>5.7</b> <b>9</b>	<b>5.6</b> <b>5</b>	<b>1.62</b>	<b>1.3</b> <b>5</b>
<b>Max</b>	<b>630.</b> <b>85</b>	<b>759.</b> <b>78</b>	<b>9271.</b> <b>62</b>	<b>9447.</b> <b>88</b>	<b>9423.</b> <b>88</b>	<b>9490.</b> <b>17</b>	<b>8.0</b> <b>0</b>	<b>8.0</b> <b>3</b>	<b>0.2</b> <b>2</b>	<b>0.1</b> <b>5</b>	<b>7.8</b> <b>2</b>	<b>7.6</b> <b>6</b>	<b>4.10</b>	<b>2.9</b> <b>6</b>
<b>CV%</b>	<b>24.3</b> <b>6</b>	<b>22.4</b> <b>2</b>	<b>26.93</b>	<b>27.85</b>	<b>26.73</b>	<b>27.64</b>	<b>30.</b> <b>21</b>	<b>28.</b> <b>57</b>	<b>20.</b> <b>56</b>	<b>12.</b> <b>62</b>	<b>16.</b> <b>38</b>	<b>13.</b> <b>22</b>	<b>41.7</b> <b>4</b>	<b>39.</b> <b>66</b>

### PK Ratio

Only 40 subject data are calculated because of subject No 09 withdraw from the study in period-II due to personal reason.

Pre-dose concentration (>5%) was observed in Subject number 25 in both period-I and period-II.

Hence as per study protocol subjects No 09 & 25, excluded from pharmacokinetic and statistical analysis

**Tables no 2.2.5 PK Ratio (A With B) of Pseudoephedrine HCL for Parameters  $C_{max}$ ,  $AUC_{0-t}$ ,  $AUC_{0-inf}$**

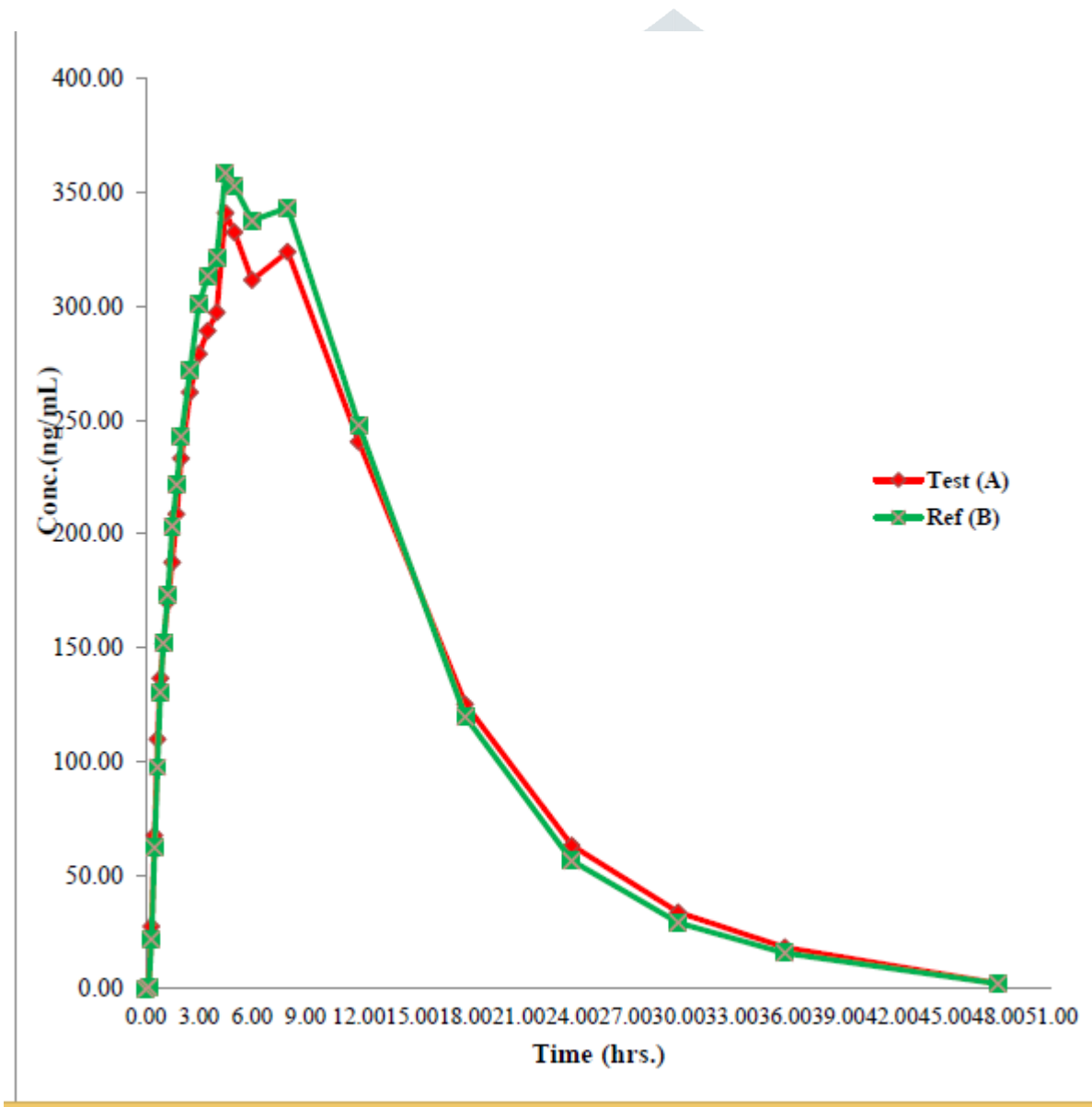
<b>PK Ratio (A With B) of Pseudoephedrine for Parameters <math>C_{max}</math>, <math>AUC_{0-t}</math> and <math>AUC_{0-inf}</math></b>			
<b>Subject</b>	<b><math>C_{max}</math></b>	<b><math>AUC_{0-t}</math></b>	<b><math>AUC_{0-inf}</math></b>
<b>N</b>	<b>40</b>	<b>40</b>	<b>40</b>
<b>Mean</b>	<b>95.53</b>	<b>100.49</b>	<b>100.76</b>
<b>SD</b>	<b>19.95</b>	<b>20.03</b>	<b>19.97</b>
<b>Min</b>	<b>58.90</b>	<b>62.21</b>	<b>63.48</b>
<b>Median</b>	<b>93.91</b>	<b>104.10</b>	<b>103.80</b>
<b>Max</b>	<b>157.67</b>	<b>154.30</b>	<b>154.75</b>
<b>CV%</b>	<b>20.89</b>	<b>19.93</b>	<b>19.82</b>

### 2.2.6 Statistical Analysis

The result obtained from the statistical analysis to establish bio-equivalence in the 42 subjects and Cetirizine hydrochloride and Pseudoephedrine Hydrochloride in both test and reference products that were performed for the estimation of least square mean difference in the test and reference formulation. log-transformed pharmacokinetic parameters  $C_{max}$ ,  $AUC_{0-t}$  and  $AUC_{0-\infty}$  of Cetirizine hydrochloride and Pseudoephedrine Hydrochloride and the 90% confidence intervals also are given in following table.

**2.6 Table No Average Bioequivalence for the log transformed data : Pseudoephedrine HCL, A = Test Product, B= Reference Product**

Dependent	Form Var	Form_ Ref	RefGeo LSM	Form_ Test	TestGeo LSM	Ratio (%)	CI_90		Power (%)	SCV %	Bio equivalence
							Lower	Upper			
Ln (C <sub>max</sub> )	Treat	B	376.14	A	351.38	93.42	88.76	98.32	100.00	13.81	Yes
Ln (AUC <sub>0-t</sub> )	Treat	B	5311.90	A	5217.61	98.22	93.95	102.70	100.00	12.01	Yes
Ln (AUC <sub>0-inf</sub> )	Treat	B	5390.08	A	5309.20	98.50	94.28	102.91	100.00	11.81	Yes



**Fig 03 Mean plasma concentration (ng/mL) vs Time Profile Graph of Test Product (A) Vs Reference Product (B) of Pseudoephedrine HCL Extended Release Tablets USP 120 mg under fasting condition.**

## DISSCUSION

Bioequivalence study of the Test Product: Cetirizine hydrochloride And Pseudoephedrine hydrochloride Extended Release Tablet USP 5 mg/ 120 mg of Aurobindo Pharma Limited, India, with Reference Product: ZYRTEC-D 12 HOUR (Cetirizine hydrochloride and Pseudoephedrine hydrochloride 5 mg /120 mg) Extended Release Tablet of McNeil Consumer Healthcare, Division of MCNEIL-PPC, INC, USA. was conducted with high accuracy and precision .This study as an open-label, balanced, randomized, two-treatment, two-sequence, two-period, single dose, two-way crossover design under fasting condition The study was conducted in compliance with the current ICF,GCP,GLP guidelines and all the requirement of current version of the Declaration of Helsinki.42 healthy male human subjects were screened, recruited and analyzed for the study. The final pharmacokinetic and statistical analysis was performed on sample collected from all 40 Subjects.(Except 09 & 25) subject No 09 withdrew from the study in period-II due to personal reason. Pre-dose concentration (>5% of the Cmax) was observed in Subject number 25 in both period-I and period-II. Hence as per study protocol subject no 09&25 data was excluded from pharmacokinetic and statistical analysis. There was no protocol deviation in study. All the post dose samples was collected with in the planned sampling time in each study period (except for ambulatory samples). There was no adverse events reported during the study on post study safety assessment adverse event were not reported for any subject number. Sample analysis perform with LCMS-MS and in house SOPs requirements. Descriptive statistical analysis was presented for all primary and secondary Pharmacokinetic parameter (Cmax, AUC<sub>0-t</sub> AUC<sub>0-inf</sub> ,AUC<sub>0-t</sub> /AUC<sub>0-inf</sub> t<sub>max</sub>, Kel and t<sub>1/2</sub>). The Pharmacokinetics parameters,90% confidence interval for the ratio of the in-transformed mean of the test product T and reference product R was found to be within Acceptable Range of BE (80-125%) Hence it indicates that the Test product A is Bioequivalent to Reference product

## CONCLUSION

The study of Cetirizine hydrochloride and Pseudoephedrine hydrochloride Extended Release Tablets was performed with high accuracy and with compliance of all the regulatory Requirement. Base on the statistical analysis Test Product Cetirizine hydrochloride And Pseudoephedrine hydrochloride Extended Release Tablet USP 5 mg/ 120 mg of Aurobindo Pharma Limited, India.is Bioequivalent to Reference product ZYRTEC-D 12 HOUR (Cetirizine hydrochloride and Pseudoephedrine hydrochloride 5 mg /120 mg) Extended Release Tablet of McNeil Consumer Healthcare, Division of MCNEIL-PPC, INC, USA.in adult healthy male human volunteers under fasting condition. Also it was observed that both test & reference products were well tolerated & found to be safe in adult human volunteers under fasting condition.

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