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Comparative Bioequivalence Study Of Enoxaparin Sodium In Healthy, Adult, Human Subjects Under Fasting Conditions.

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ABSTRACT

An open-label, balanced, randomized, single-dose, two-treatment, two-period, two-sequence, two-way crossover, Comparative Bioequivalence study of Enoxaparin sodium Healthy, Adult, Human subjects under fasting condition. To assess the Comparative Bioequivalence study of Enoxaparin Sodium in healthy, adult, human subjects under fasting conditions. To be sure that the study is safe and tolerable topics and to keep an eye out for unexpected complications. In this study, normal healthy adult male or female subjects were recruited. Enoxaparin sodium has a high anti-Xa activity (approximately 100 IU/mg) and low anti-IIa or anti thrombin activity (approximately 28 IU/mg), with a ratio of 3.6.The test product had a significantly lower mean C_{max} than the reference product (0.85 ng/mL against 0.92 ng/mL). However, there was some variation within each group, as evidenced by the standard deviations. The test and reference products showed comparable AUC_{0-t} and $AUC_{0-\infty}$ trends. The mean AUC_{0-t} values were comparable (8.12 nghr/mL for the test product and 7.65 nghr/mL for the reference product), with similar standard deviations. Similarly, the mean $AUC_{0-\infty}$ values were very similar (8.74 ng/mL vs 8.92 ng/mL) with low standard deviations. The bioequivalence study conducted on healthy adults fasting with Enoxaparin Sodium showed no significant differences in key pharmacodynamic parameters like C_{max} and AUC. Therefore, the generic formulation of Enoxaparin Sodium is considered bioequivalent to the reference product, indicating comparable safety and efficacy profiles in fasting patients.

Keywords: anticoagulant, subcutaneous route, bioequivalence, male or female subjects.

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INTRODUCTION

Revolution of the use of generic drug increases in the last four decades in order to lower the healthcare cost. With increased availability and use of generic drug products, healthcare professionals are encountered with a large number of multisource products from which they have to select therapeutically equivalent products [1]. As noted in the constitutional definitions, BE only focus on the release of a drug substance from an active moiety and subsequent absorption into the systemic circulation. As a result, it recommended that similar approaches to measure bioavailability in a new drug application usually followed in demonstrating bioequivalence or an Abbreviated New Drug Application (ANDA) guideline. Bioequivalence is defined as the absence of a greater than allowable difference in the rate and extent to which the active ingredient or therapeutic moiety in pharmaceutical equivalents becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. Bioequivalence studies play a key role in the drug development period for both new drug products and their generic products [2]. Acceptable range of bioequivalence is generally 0.8% - 1.25% for the test or reference ratio of average values, when the parameters are logarithmically transformed. The acceptable range is generally ± 0.2 for the relative difference *in vivo* parameters between reference and test products, when the raw data are used [3]. Healthy adult human male or female volunteers participated in the study. The screening procedure includes Demographic data, Laboratory investigations & physical examination. The inclusion criteria for the study, their age should be within 18-45 years of age; Body Mass Index (BMI) should be within, 18.5-24.99 kg/m2. The volunteers should have no history of using tobacco, known history of alcoholism or drug abuse, past and present status of drug addiction, history of smoking, alcohol intake. Study participants should have no history of blood donation or history of participation in a drug research study for 90 days prior to participating in the study. Medical history, including any past and present illness, any chronic illness, persistent cough and any family history of diseases and history of any allergies (food / drug / any other) data was obtained from the volunteers. Physical and Medical examination was performed for each subjects, which includes checking of vital signs (Blood pressure (BP), pulse, temperature and respiration). Recording of ECG was performed through 12-lead electrodes for checking heart rate, rhythm and specific finding (if any). Chest X-ray (PA view), systemic examination like cardiovascular, respiratory, abdomen, nervous, musculoskeletal was done. Heart and aorta should be within normal range, lungs fields should be clean, bony cage should appear normal, diaphragm should be clear [4]. The subjects should be free from liver disease and abstained from taking any drug for two weeks prior to and during the study period. Drinking of alcoholic beverages, coffee and tea was not allowed at least one month prior to and during the entire period of the study [5]. Laboratory parameter investigation includes Complete blood count (CBC). The expected coefficient of variation of 20% and formulations differences 5% (i.e., 95-105%), with 80% power it was expected that a sample size of 20 subjects would be required to allow a decision on bioequivalence. However, considering the drop-outs, a sample size of 22 subjects is considered for the study.

Clinical Pharmacology for Enoxaparin Sodium

Mechanism of Action

Enoxaparin works by binding to antithrombin III, a serine protease inhibitor. This binding forms a complex that irreversibly inactivates factor Xa, an essential component in the blood clotting cascade [6]. As a result, thrombin, which is necessary for converting fibrinogen to fibrin and forming a clot, is unable to carry out its function effectively. While enoxaparin also directly inhibits factor IIa (thrombin), its potency in this regard is lower compared to unfractionated heparin (UFH) [7]. Overall, the cascade of effects initiated by enoxaparin binding prevents the formation of blood clots, reducing the risk of thromboembolic events [8].

Pharmacodynamics

Enoxaparin, a low molecular weight heparin (LMWH) with a mean molecular weight of approximately 4,500 Daltons, primarily exhibits high anti-Xa activity (approximately 100 IU/mg) mediated through anti-thrombin III (ATIII). It also possesses additional antithrombotic and anti-inflammatory properties, including inhibition of other coagulation factors and induction of endogenous Tissue Factor Pathway Inhibitor (TFPI) release. Enoxaparin sodium does not significantly affect activated

partial thromboplastin time (aPTT) when used prophylactically but can prolong it by 1.5 – 2.2 times the control time when used therapeutically [9].

Pharmacokinetics of Enoxaparin Sodium

Absorption: Enoxaparin sodium demonstrates close to 100% absolute bioavailability after subcutaneous (SC) injection, with a mean maximum plasma anti-Xa activity observed 3–5 hours post-injection. Intravenous (IV) bolus followed by SC administration achieves steady-state levels within 2 days of treatment. Different doses and regimens exhibit linear absorption.

Distribution: The volume of distribution of Enoxaparin sodium anti-Xa activity is approximately 4.3 liters, close to blood volume.

Metabolism: Primarily metabolized in the liver by desulfation and/or depolymerization to lower molecular weight species with reduced biological potency.

Elimination: Enoxaparin sodium has low clearance, with mean anti-Xa plasma clearance of 0.74 L/h after a 150 IU/kg (1.5 mg/kg) 6-hour IV infusion. It exhibits monophasic elimination with a half-life of about 5–7 hours. Renal clearance represents about 10% of the administered dose, with total renal excretion of active and non-active fragments accounting for 40% of the dose [10].

Indication

Enoxaparin Sodium is indicated in adults for:

Prophylaxis of Venous Thromboembolic Disease: For moderate and high-risk surgical patients, particularly those undergoing orthopedic or general surgery, including cancer surgery. Also indicated for medical patients with acute illness and reduced mobility at increased risk of venous thromboembolism.

Treatment of Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE): Excluding cases likely to require thrombolytic therapy or surgery. Also for extended treatment and recurrence prevention in

Prevention of Thrombus Formation in Extracorporeal Circulation: During hemodialysis.

Acute Coronary Syndrome Management

- For unstable angina and Non-ST-segment elevation myocardial infarction (NSTEMI), in combination with oral acetylsalicylic acid.
- For acute ST-segment elevation myocardial infarction (STEMI), including patients managed medically or with subsequent percutaneous coronary intervention (PCI).

Adverse effects

Enoxaparin common adverse effects includes hemorrhage, hemorrhagic anemia, thrombocytopenia, thrombocytosis, Allergic reaction, Headache, Hepatic enzyme increases (mainly transaminases >3 times the upper limit of normality), Urticarial, pruritus, erythema, Injection site hematoma and injection site pain.

Drug interaction

Enoxaparin sodium, a blood thinner, can interact with other medications, increasing the risk of bleeding.

Do not use Enoxaparin with

Medications affecting hemostasis: This includes high-dose aspirin, other NSAIDs (like ibuprofen), and some thrombolytic and anticoagulants.

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Use Enoxaparin with caution with

Other medications affecting hemostasis: This includes low-dose aspirin, clopidogrel, ticlopidine, dextran 40, and systemic glucocorticoids.

Medications increasing potassium levels: Monitor potassium levels closely when using these medications with Enoxaparin [11].

Laboratory Report for Volunteers

Table 1: No. of volunteers

Total number of volunteers screened for the study	60
Number of volunteers passed during screening	22
Number of volunteers failed during screening	38

In our study we screened total 60 volunteers. Out of 60 volunteers 22 volunteers passed and 38 volunteers failed because of below mentioned reason.

The present study we screened total 60 volunteers. Out of 60 volunteers 22 volunteers passed and 38 volunteers failed because some variable changes in laboratory Parameters like high plasma glucose, serum albumin was more than normal range, high LDL cholesterol, high alkaline phosphate, high blood pressure, low Haemoglobin, RBC count was low, detail of screen failure summarized in **table 2.**

Table 2: Evaluation of screen failure

Volunteers	Reason of failure
10 Volunteers	High plasma glucose
8 Volunteers	Serum albumin was more than normal range
6 Volunteers	High LDL cholesterol
3 Volunteers	High alkaline phosphate
5 Volunteers	High blood pressure
3 Volunteers	Low Haemoglobin
3 Volunteers	RBC count was low

The mean age, height, weight and BMI ± SD values for normal healthy human subjects recruited in the study and those analyzed were 28.77 ± 5.207 years, 166.915 ± 5.408 Kg, 22.075 ± 3.089 Kg/m2 respectively. The demographic data was summarized in **table 3.**

Table 3: Evaluation of Demographic and Other Baseline Characteristics

	Age (year)	**Height (cm)**	**Weight (kg)**	**BMI (kg/m2)**
Number	22	22	22	22
Median	28	167	62	22.55
Mean	28.774	166.915	61.521	22.075
Standard Deviation	5.207	5.408	8.488	3.089
Minimum	41	179	75	25.96
Maximum	20	154	16	1.51

The body temperature, respiratory rate, pulse rate for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit. Body temperature for Period I analysed: 98.12675 ± 0.106703, period II: 97.9575 ± 0.088176.Respiratory rate for Period I analysed: 15.71275 ± 0.599368, period II: 16.35825 ± 0.52555, Pulse rate for Period I analysed: 76.60075 ± 0.808824, period II: 75.6385 ± 1.221887Summarized in **table 4**

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Table 4: Evaluation of Vital Signs

Group	Body temperature (F^0) Average		Respiratory rate(/min) Average		Pulse rate(/min) Average	
	Period I	Period II	Period I	Period II	Period I	Period II
21-25 years	98.175	97.97	15.401	16.64	76.908	75.876
26-30 years	98.220	98.060	15.657	15.636	77.565	74.187
31-35 years	98.137	97.955	16.571	16.834	76.22	75.357
36-40 years	97.975	97.845	15.222	16.323	75.710	77.134

Hematology

The hematology values for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit.

Haemoglobin range for period I: 13.598 ± 0.720027(g/dl) and period II: 13.32475 ± 0.411314(g/dl).Total RBC count for period I: 4.9405 ± 0.07646132 (µL) and period II: 4.98675 ± 0.10223 (µL). Total WBC counts for period I: 8.25 ± 0.283967 (µL) and period II: 7.284 ± 0.206436 (µL) summarized in **table 5**

Differential count

The differential count values for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit. Platelet count for period I: 2.67± 0.21408254 and period II: 2.72775 ± 0.184079 (lakhs/µL). Summarized in **table 5**

Table 5: Determination and evaluation of Haematology of Study Subject

Age	21-25 Years		26-30 years		31-35 years		36-40 years	
	P I	**P II**	**P I**	**P II**	**P I**	**P II**	**P I**	**P II**
HAEMATOLOGY								
Hemoglobin (g/dL)	12.84	12.72	13.522	13.508	14.575	13.437	13.455	13.634
Total RBC count (µL)	5.036	5.091	4.968	5.003	4.886	4.846	4.872	5.007
Total leucocyte count (µL)	7.846	6.984	8.48	7.414	8.41	7.426	8.264	7.312
DIFFERENTIAL COUNT								
Platelet count (lakhs/µL)	2.782	2.774	2.516	2.533	2.467	2.643	2.915	2.961

Bio-chemistry values for the subjects recruited in the study in Period I, II were analysed according to the age of 20-40 years were within normal limit.

Glucose for period I: 89.688 ± 2.785348 (mg/dl) and period II: 94.1025 ± 8.91816(mg/dl), Urea for period I: 20.7538 ± 1.00905 (mg/dl) and period II: 19.6115 ± 0.99786 (mg/dl), Creatinine for period I: 0.9225 ± 0.05026 (mg/dl) and period II: 0.89875 ± 0.02804 (mg/dl), Cholesterol for period I: 166.986 ± 10.0169 (mg/dl) and period II: 173.146 ± 11.0269(mg/dl), Bilirubin total for period I: 0.813 ± 0.03789 (u/l) and period II: 0.61925 ± 0.09078 (u/l), Bilirubin direct for period I: < 0.04 (u/l) and period II: < 0.04 (u/l), SGOT (AST) for period I: 27.9793 ± 2.46269 (u/l) and period II: 27.7225 ± 1.60677(u/l), SGPT (ALT) for period I: 32.9128± 1.83186 (u/l) and period II: 31.5595 ± 1.23294 (u/l). Summarized in **table 6**

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Table 6: Evaluation of bio-chemical markers

Age	21-25 Years		26-30 years		31-35 years		36-40 years	
	P I	P II	P I	P II	P I	P II	P I	P II
Glucose (mg/dL)	92.635	86.51	90.653	87.682	89.465	96.555	85.999	105.665
Urea (mg/dL)	20.180	19.01	21.869	20.181	21.300	20.7	19.666	18.555
Creatinine(mg/dL)	0.881	0.864	0.966	0.921	0.966	0.922	0.877	0.888
Cholesterol (mg/dL)	153.778	162.85	165.327	166.557	171.837	187.622	177	175.555
Bilirubin total (U/L)	0.800	0.660	0.770	0.694	0.822	0.635	0.860	0.488
Bilirubin direct (U/L)	< 0.04	< 0.04	< 0.04	< 0.04	< 0.04	< 0.04	< 0.04	< 0.04
SGOT (U/L)	25.410	26.81	27.449	28.348	27.725	26.066	31.333	29.666
SGPT (U/L)	30.272	32	33.912	31.395	33.122	29.955	34.345	32.888

Clinical biochemistry of study the period (period I & period II) of the study subject was found to be within the normal limit.

The colour of urine was straw yellow and its appearance is clear for both the periods.The pH and Specific gravity period I was found to be 5.7885± 0.155412 and 1.01425 ± 0.001892969 normal. The pH and Specific gravity period II was found to be 5.595 ± 0.215242 and 1.013± 0.004082 normal.Protein, Urobilinogen, ketone, bile pigments and nitrite values in urine routine analysis were found to be negative. Summarized in **table 7**

Table 7: Determination of urine markers in study subjects

Age	21-25 Years		26-30 years		31-35 years		36-40 years	
	P I	P II	P I	P II	P I	P II	P I	P II
URINE ROUTINE ANALYSIS								
Colour	Straw yellow	Straw yellow	Straw yellow	Straw yellow	Straw yellow	Straw yellow	Straw yellow	Straw yellow
Appearance	Clear	Clear	Clear	Clear	Clear	Clear	Clear	Clear
pH	5.910	5.761	5.862	5.943	5.820	5.457	5.562	5.877
Specific gravity	1.017	1.019	1.013	1.011	1.014	1.012	1.013	1.010
Proteinmg/dl	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Glucose mg/dl	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil
Urobilinogen mg/dL	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Ketone mg/dL	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Bile pigments mg/dL	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Blood	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve
Nitrite	-ve	-ve	-ve	-ve	-ve	-ve	-ve	-ve

The serology for HIV, HBsAg, Anti-HCV, and RPR/VDRL were found to be Non-reactive Summarized in **table 8.**

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Table 8: Determination of Serology

Age	21-25 Years		26-30 years		31-35 years		36-40 years	
	P I	P II	P I	P II	P I	P II	P I	P II
HIV	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive
HBsAg	Negative	Negative	Negative	Negative	Negative	Negative	Negative	Negative
Anti-HCV	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive
RPR/VDRL	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive

The study subjects Electrocardiogram and chest X-ray were found normal. The clinical pathology of the study subjects were 100% within the normal limit. The serology report of the subjects who participated was found to be 100% non-reactive.

Urine analysis for drug of abuse of the study subjects was found to be 100% negative. Summarized in **table 9**

Table 9: Urine Analysis for Drug of Abuse

Urine analysis	Period I	Period II
Amphetamine	Negative	Negative
Benzodiazepines	Negative	Negative
Barbiturates	Negative	Negative
Cocaine	Negative	Negative
Morphine	Negative	Negative
THC	Negative	Negative

Urine analysis for drug of abuse of the study subjects was found to be 100% negative.

Period I and Period II, the check-in process was completed approximately in1 hours. In period I and period II, check- out process were completed within 30 minutes.

Table 10: Check- in and check -out timings of the study

Volunteers	Period I		Period II	
	Check-in Day 1	Check-out Day 2	Check-in Day 1	Check-out Day 2
6 **Volunteers**	4.00pm	8.15am	4.15pm	8.15am
5 **Volunteers**	4.40pm	8.30am	4.30pm	8.20am
5 **Volunteers**	5.30pm	8.40am	4.50pm	8.35am
4 **Volunteers**	5.45pm	8.45am	6.00pm	8.45am
2 **Volunteers**	7.00pm	9.00am	7.15pm	9.00am

Analysis of Efficacy

The various un-transformed mean pharmacodynamic parameters estimated for both the reference and test formulations of Enoxaparin sodium under fasting conditions.

Safety Conclusions

- on post study safety assessment, No adverse event was reported
- No serious adverse event occurred during the conduct of the study

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Safety Evaluation

Analysis of safety-related data can be considered at three levels. First, the extent of exposure (dose, duration, number of patients) should be examined to determine the degree to which safety can be accessed from the study. Second, the more common adverse events, laboratory test changes etc. Final level, should be identified, classified in some reasonable way, compared for treatment groups, and analysed, as appropriate, for factors that may affect the frequency of adverse reactions and events, such as time dependence, relation to demographic characteristics, relation to dose or drug concentration, etc.

The ln-transformed mean pharmacodynamic parameters for both the reference and test formulations

The ln-transformed least square mean and 95% Confidence interval based on least square mean obtained from ANOVA and ratio of geometric mean for the pharmacodynamic parameters C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ for Enoxaparin sodium under fasting conditions (i.e. the 95 % confidence intervals of ln-transformed parameters for Enoxaparin sodium) summarized in the **table 11.**

Table11: The ln-transformed mean pharmacodynamic parameters for both the reference and test formulations.

Pharmacodynamic Parameters	N	Test Product		N	Reference Product	
		Mean	S.D.		Mean	S.D.
C_{max} (ng /mL)	22	0.85	1.23	22	0.92	1.78
AUC_{0-t} (ng*hr/mL)	22	8.12	1.58	22	7.65	1.20
$AUC_{0-\infty}$(ng *hr/mL)	22	8.74	0.99	22	8.92	0.93

Ratio and lntra-subject variability

The ratio of geometric mean and 95% confidence interval for the un-transformed pharmacodynamic parameters C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ were found to be respectively

RESULTS

The mean C_{max} of the test product was slightly lower than the reference product (0.85 ng/mL vs 0.92 ng/mL). However, there was some variability within each group, as indicated by the standard deviations (1.23 ng/mL and 1.78 ng/mL respectively). Both the test and reference products exhibited similar trends for AUC_{0-t} and $AUC_{0-\infty}$. The mean AUC_{0-t} values were close (8.12 nghr/mL for the test product and 7.65 nghr/mL for the reference product), with comparable standard deviations. Similarly, the mean $AUC_{0-\infty}$ values were also very close (8.74 nghr/mL vs. 8.92nghr/mL) with minimal standard deviations. Pharmacodynamic Parameters like Test product and Reference product C_{max}, AUC_{0-t}, $AUC_{0-\infty}$ Concentration range of standard deviation presented in the **figure 1, 2, 3.** The reference product exhibited a slightly higher mean C_{max} (0.92 ng/mL) compared to the test product (0.85 ng/mL), although there was variability within each group (standard deviations: 1.23 ng/mL and 1.78 ng/mL, respectively).

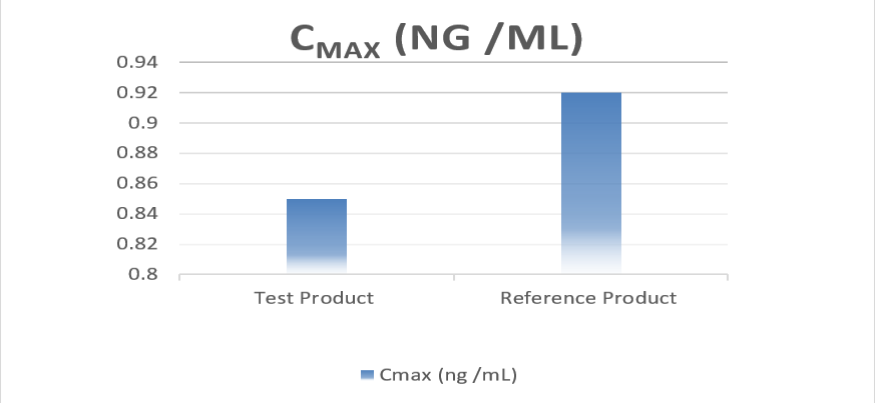

Figure 1: C_{max} (ng /mL) Test and Reference Product

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The test product showed a higher level of similarity to the reference product when considering AUC_{0-t}, indicating better bioequivalence.

Based on AUC_{0-t}, the test product appears to be more bioequivalent to the reference product.

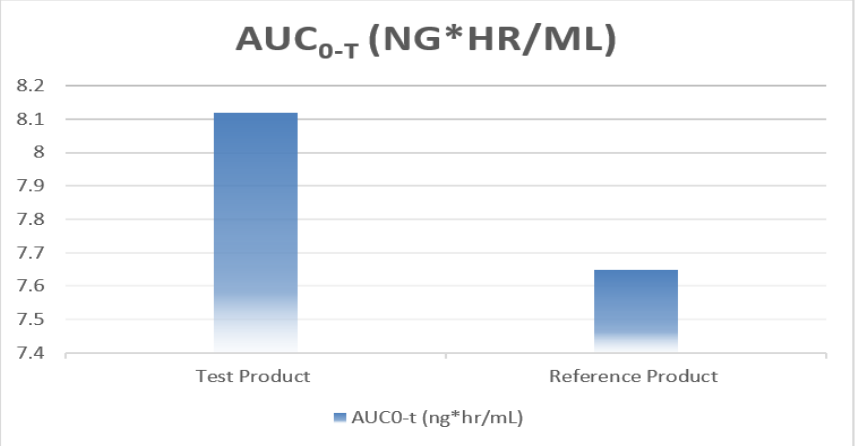

Figure 2: AUC_{0-t} (ng*hr/mL) Test and Reference Product

Both the test and reference products showed similar average $AUC_{0-\infty}$ values (around 8 nghr/mL) with very little variation, suggesting potentially similar effects.

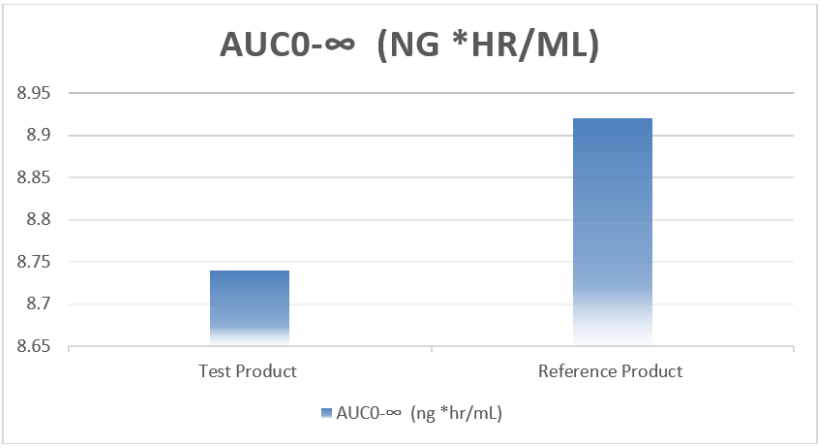

Figure 3:$AUC_{0-\infty}$ (ng *hr/mL) Test and Reference Product

The test and reference products showed very similar average values (geometric means) for C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$, with little variation across the data (narrow confidence intervals).

Table 12: The 95 % confidence intervals of ln-transformed parameters for Enoxaparin sodium.

Geometric mean, ratio and 95 % confidence interval for Enoxaparin sodium		
Pharmacodynamic Parameters	**95% upper confidence bound**	**Power**
C_{max} (ng /mL)	**99.8**	**100**
AUC_{0-t} (ng *hr/mL)	**110.8**	**81**
$AUC_{0-\infty}$(ng *hr/mL)	**109.2**	**88**

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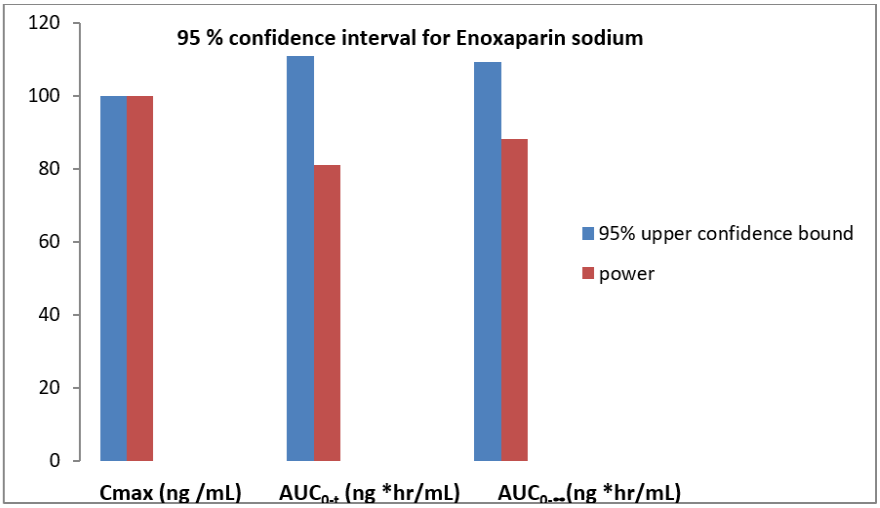

Figure 4: 95 % confidence interval for Enoxaparin sodium

Ethical Considerations

Independent Ethics Committee (Chennai Ethics Committee)

Study subjects were reviewed by the Independent Ethics Committee. Study procedures were commencing only after receipt of letter of approval is received from the committee.

DISCUSSION

Acceptable range of bioequivalence is generally 0.8% - 1.25% for the test or reference ratio of average values, when the parameters are logarithmically transformed. The acceptable range is generally ± 0.2 for the relative difference *in vivo* parameters between reference and test products, when the raw data are used [3].Two different medicinal products is said to be therapeutically equivalent when their active constituent is same, meeting same therapeutic moiety and show same clinical efficacy and safety [12].Pharmaceutical equivalence does not essentially imply therapeutic equivalence, as differences in the excipients or the manufacturing procedure and some other variables can lead to differences in product performance [13].Both BA/BE studies focusing the rate and extent to which the active pharmaceutical ingredient or therapeutic moiety was absorbed from a pharmaceutical drug product available at the systemic circulation. *In vivo* performance, in term of BA/BE, was considered to be one aspect of product quality that provides a link to the performance of the safety and efficacy. For this reason, similar approaches to measure BA in an NDA should generally be followed in demonstrating BE for an NDA For present study we screened total 60 volunteers. Out of 60 volunteers 22 volunteers passed and 38 volunteers failed because some variable changes in laboratory Parameters like high plasma glucose, serum albumin was more than normal range, high LDL cholesterol, high alkaline phosphate, high blood pressure, low Haemoglobin, RBC count.

The body temperature, respiratory rate, pulse rate for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit.

The Heamotology values for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit

The differential count values for the subjects recruited in the study in Period I, II were analysed according to the age of 21-40 years were within normal limit.

Bio-chemistry values for the subjects recruited in the study in Period I, II were analysed according to the age of 20-40 years were within normal limit.

The clinical pathology for both Periods I and Period II were found to be within normal limit and compared to be same.

Period I and Period II, the check-in process was completed approximately in1 hours. In period I and period II, check- out process were completed within 30 minutes.

CONCLUSION

The results of the comparative bioequivalence study conducted in healthy adult human subjects under fasting conditions with Enoxaparin Sodium indicate that these two formulations are bioequivalent. The comparison of several pharmacodynamic parameters, including maximum concentration (C_{max}) and area under the curve (AUC), showed no appreciable variations between the test and reference products, leading to this result. Based on these results, it can be concluded that the reference product of Enoxaparin sodium and the generic formulation of Enoxaparin Sodium are equivalent, suggesting comparable safety and efficacy profiles when given to patients while fasting.

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