INTRODUCTION
Bioequivalence focus on the release of a drug substance from its dosage form and subsequent absorption into the systemic circulation. For this reason, similar approaches to measuring bioavailability should generally be followed in demonstrating bioequivalence.

Bioequivalence studies should be conducted for the comparison of two medicinal products containing the same active substance. Esinhart (1996). The studies should provide an objective means of critically assessing the possibility of substituting one for the other. Two products marketed by different licensers, containing same active ingredient(s), must be shown to be therapeutically equivalent to one another in order to be considered interchangeable. Several test methods are available to assess equivalence, including comparative bioavailability (bioequivalence) studies, in which the active drug substance or one or more metabolites is measured in an accessible biological fluid such as plasma, blood or urine. To help contain drug costs, virtually every state has adopted laws and/or regulations that encourage the substitution of drug products. The 90% confidence interval for the difference in the means of the log-transformed data should be calculated using methods appropriate to the experimental design. Population Bioequivalence. Analysis of BE data using the population approach should generally be used in measuring bioavailability should generally be followed in demonstrating bioequivalence.

METHODOLOGY
STUDY DESIGN
A randomized, open label, balanced, two-treatment, two-period, two-sequence, single dose, crossover, oral bioequivalence study under fasting conditions. The proposed bioequivalence study was conducted after the approval of Independent Ethics Committee and Drug Controller General of India.

SELECTIOE OF SUBJECTS:
Subjects aged between 18-55yrs. Physician certified medically healthy subjects with clinically acceptable laboratory profiles. Only subjects willing to give written Informed Consent to participate in the study. At the discretion of the physician-in-charge, subjects can be included in the study within 28 days from the date of screening.

EXCLUSION CRITERIA
Subjects who are pregnant. Medically unfit subjects who have any present illness of cough / chest pain / palpitation / dyspnoea / pyrexia / vomiting / anorexia / headache / giddiness. Subjects who have any history of presence of significant Cardiovascular, Pulmonary, Hepatic, Renal, Hematological, Gastro Intestinal, Endocrine, Immunologic, Dermatologic, Neurological or Psychiatric diseases. Subjects who have any history of chronic illness / surgery / blood transfusion / blood donation within past 3 months. Any clinically significant abnormality in the pre-study screening. Intake of any OTC preparations (like NSAIDS). Subjects who have participated in any other research study within 92 days (3 months) of the study start. More specifically, history or presence of significant: Systolic BP <90 and >130 mmHg, Diastolic BP <60 and >80 mmHg and Pulse Rate <60 and >100pm. Alcohol dependence, alcohol abuse or drug abuse. Smoking or consumption of tobacco products (pan masala or gutkha). Asthma, urticaria or other allergic type reaction after taking aspirin. Ulceration or history of gastric and/or duodenal ulcer. Allergy to Omeprazole.

SAMPLE SIZE
Sample size is based on estimates obtained from reported literature. Assuming a formulation ratio (T/R) ranging from 0.87 – 1.03 and low intra-subject variability, a sample size of 24 subjects would be sufficient to show bioequivalence with a power of at least 80%. Hence a sample size of 26 subjects (2 standby subjects) were used in the study, between 18 - 55yrs of age, within the BMI ranging between 18 – 26 kg/m² (accepted normal range).

PREMATURE WITHDRAWAL OF SUBJECTS FROM THE STUDY
Subjects were informed that they were free to withdraw from the study at anytime without stating the reason. The investigator could withdraw a subject from the study if he experiences Serious Adverse Effects (SAE) and withdrawal would have been the best interest of the subjects.

TREATMENT SEQUENCE (a) TWO TREATMENT
I. Omeprazole 20mg Powder for suspension-Treatment formulation
II. Omeprazole 20mg Powder for suspension-Reference formulation

The order of receiving the test and reference product for each subject during the 2 periods in both the fast study were determined according to the randomization schedule which was balanced. The duration of the study was approximately 4 months enroled in quest life sciences pvt.ltd, Chennai, Tamilnadu.

SEPTEMBER - Protocol preparation and designing
OCTOBER - Recruitment of subjects for fast study
NOVEMBER - Conduction of the fast study; Biological samples were analyzed and pharmacokinetic parameters were estimated.

DECEMBER - Documentation of study for fast.

c) DOSAGE AND ADMINISTRATION
After an overnight fast (for at least 10 hours), one of omeprazole 20mg powder
for suspension test or reference product was administered to each subject orally at the start of an experimental day with about one (240ml) of water at per the randomization schedule.

e) BLOOD SAMPLING

Before and during each study period, subjects were Allowed water as desired except for 1 hour before and after drug administration In each of the study periods. 21 blood samples of 5ml each were collected from subject including the predose sampling from an ante-cubital vein or a fore-arm vein using an indwelling intravenous cannula. The predose sample of 5ml was collected with 4 hours prior to dosing. The post dose samples (5ml each) were collected at the time specified. Before each blood sample was drawn between 0.00 to 16.00 hours, 0.5ml of blood was discarded so as to avoid haemolyzing of plasma from interfering with the analysis. Blood samples were collected in pre-labeled vacutainers, which contained KEDTA as an anticoagulant and after centrifugation (at 4000rpm and 4°C for 10 minutes), plasma were transferred to RIA vials and were kept frozen at or below -70°C until analysis.

Analytical Method

In human plasma using liquid chromatography – tandem mass spectrometry. The assay is based on protein precipitation with acetonitrile and reversed phase liquid A rapid, sensitive and reliable method was developed to quantify omeprazole chromatography performed on an octadesylsyla column (35 mm x 3mm, 3 µl particles), the mobile phase consisted of methanol –10mM ammonium acetate (60:40, v/v). Omeprazole and lensaprazole the internal standard. Quantification was through positive ion mode and selected reaction monitoring. The lower limit of quantification was 70.56 ng/ml using 0.25 ml of plasma and linearity was observed from 500 to 5000 ng/ml. Within-day and between-day precision expressed by relative standard deviation was less than 5% and inaccuracy did not exceed 12%. The assay was applied to the analysis of simultaneous determination of omeprazole and 5 hydroxyomeprazole in human plasma is described. Isolation of the analytes from plasma was achieved via solid-phase extraction using a polymeric sorbent based cartridge. The analytes were chromatographed under reversed-phase conditions on a Zorbax XDB- C8 column (50 x 4.6 mm). The HPLC mobile phase consisted of a mixture of acetonitrile-water (21.79 v/v) containing 10mM ammonium hydroxide. The apparent pH of the mobile phase was adjusted to 8.5 with formic acid prior to use. A Sciep API II + tandem mass spectrometer equipped with a heated nebulizer atmospheric pressure chemical ionization interface was used as a detector and was operated in the positive ion or with other drugs.

OBSERVATIONS AND MEASUREMENTS

(a) Assessments performed before start of the study: Demographic data (age, sex, weight, height, BMI) and other symptoms and physical examination findings were recorded in the Case Report Form (CRF) at the time of screening. Hematological examinations (like Hb, RBC, WBC, PCV, PC, DC, ESR, B.G.) and other evaluations like ECG, X-ray, urine analysis (including drugs of abuse – opioids, amphetamines, benzodiazepines, barbiturates, cannabinoids), RBS, hepatic functions, [Bili (T and Dia), SGPT, SGOT, alkaline phosphatase, total protein (albumin/globulin), renal function (serum creatinine, serum uric acid, BUN, sodium, potassium, chloride), serum cholesteryl and serological tests (VDR, HIV, HBsAg, HCV) were done during screening.

(b) Assessments performed during the study

Blood samples were collected at 0.00 hours (pre dose), and post dose samples were collected 0.25hrs, 0.50, 0.75, 1.00, 1.25, 1.50, 1.75, 2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 5.00, 6.00, 8.00, 10.00, 12.00 and 16.00 hours after dosing and centrifuged. The plasma samples were separated and stored in the deep freezer. The safety was assessed by checking the vital signs (oral temp, pulse rate and BP) at 2hrs, 4hrs, 8hrs and 24hours post dose. Hematological examinations (like Hb, WBC, PC, RBS / FBS, hepatic functions [Bilirubin (T and Dia)], SGPT, SGOT), renal functions (BUN and creatinine) were done at the end of the study.

c) Statistical Analysis:

Statistical analysis (90% confidence interval and ANOVA) was performed for the pharmacokinetic parameters. ANOVA and the 90% confidence interval were done by using Kinetica version 4.3 for windows. ANOVA was performed for the log-transformed pharmacokinetic parameters using Type III sum of squares, and ANOVA with the main effects of sequence, period, and formulations as fixed effects and subjects nested within sequence as random effect. The sequence effect was tested at the 0.10 level of significance.

RESULT

The Demographic of subject who had participated in the fasting study. A Total number of 26 male subjects completed both the periods of study. The pharmacokinetic parameter is shown. The individual and mean pharmacokinetic parameter of test and reference formulations of omeprazole powder for suspension. The table two statistical analysis for test and reference formulation ratio are 92.83% with 90% CI value the Lower limit are 87.3992 and upper limit 98.6150 for AUCmax ng/ml and non significant different and AUC∞, ng/l that lower limit 86.8154 and upper limit 98.9403 respectively confidence interval 92.4803% Respectively 95.0241% Confidence interval and Lower limit 87.4522 and upper limit 103.2520. The reference and test omeprazole are differ significantly AUCmax the p value of omeprazole test is (>0.10) value and respectively test p value is (<0.01)and the AUC∞ infinity the p value are (>0.10) of test and reference value (p<0.10) respectively significantly differ significantly and C max of both formulations for test (>0.10) and reference value (<0.10)obtained.

DATA ANALYSIS

The plasma for pharmacokinetic parameter have been estimated including the observed maximum plasma concentration the time to reach Cmax ( T max) the area under curve from 0 hrs to time t AUC∞ the area under the plasma concentration time curve O hrs to nifty AUC∞ and maximum plasma concentration Cmax and the time to reach Cmax were obtained directly from the plasma concentration time profile AUC∞ was calculated by kinetic version 4.3 software. The Area under the plasma concentration curve AUC∞ and AUC∞ = C/Keq with Ct defined as the last measurable concentration at the time the t Level of statistical significance between the groups were assessed using the ANOVA test and t-test significant differences were judged at (P<0.05)

DISCUSSION

The aim of study was assess the bioequivalence of two formulation of omeprazole sodium bicarbonate 20mg powder for suspension to reference and test product comparative study performed. The plasma levels and pharmacokinetic data of all subject of omeprazole suspension. The pharmacokinetic data of each subject were excluded separately. The recruitment of pharmacokinetic data of all subject of omeprazole suspension. The table two statistical analysis for test and reference formulations

- **Table 1**: Summary of Pharmacokinetic parameters of Omeprazole
- **Table 2**: Statistical Analysis for Test & Reference Formulations

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**Fig.1.** mean plasma concentration curve

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± Standard Deviation</th>
<th>Reference</th>
<th>Coefficient of Variation (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUCmax (ng/ml*h)</td>
<td>1545.99 ± 1335.388</td>
<td>1726.70 ± 1666.122</td>
<td>86.7755</td>
<td>96.5146</td>
</tr>
<tr>
<td>AUC∞ (ng/ml)</td>
<td>1710.47 ± 1484.839</td>
<td>1802.74 ± 1796.77</td>
<td>86.8097</td>
<td>94.9222</td>
</tr>
<tr>
<td>Cmax (ng/ml)</td>
<td>944.29 ± 538.245</td>
<td>998.29 ± 436.823</td>
<td>78.3028</td>
<td>87.4522</td>
</tr>
<tr>
<td>t1/2 (h)</td>
<td>0.4262 ± 0.2064</td>
<td>0.4712 ± 0.1550</td>
<td>47.8069</td>
<td>45.9865</td>
</tr>
<tr>
<td>t0.5 (h)</td>
<td>1.1550 ± 0.7617</td>
<td>1.2000 ± 0.7861</td>
<td>37.3028</td>
<td>37.0228</td>
</tr>
<tr>
<td>tmax (h)</td>
<td>0.7808 ± 0.1550</td>
<td>0.7861 ± 0.1550</td>
<td>37.3028</td>
<td>37.0228</td>
</tr>
<tr>
<td>KEL (h)</td>
<td>0.8390 ± 0.3744</td>
<td>0.8768 ± 0.3744</td>
<td>47.8069</td>
<td>45.9865</td>
</tr>
</tbody>
</table>

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**Table 2**: Statistical Analysis for Test & Reference Formulations

<table>
<thead>
<tr>
<th>Parameter</th>
<th>T/R (%)</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUCmax (ng/ml*h)</td>
<td>92.83%</td>
<td>87.3992-103.2520</td>
</tr>
<tr>
<td>AUC∞ (ng/ml)</td>
<td>92.84%</td>
<td>87.3992-103.2520</td>
</tr>
<tr>
<td>Cmax (ng/ml)</td>
<td>95.02%</td>
<td>87.4522-103.2520</td>
</tr>
</tbody>
</table>


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adverse drug reaction during the study. The study was the AUC_{0} and AUC_{0-\infty} for two treatment and two product (test and reference) are non significant different respectively.

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