CHAPTER 6.

SUMMARY & CONCLUSION
6.0 SUMMARY AND CONCLUSIONS

Generic drugs are typically less expensive than those of brand name drugs and its use is growing continuously throughout the world. While generic drug products can reduce the cost of pharmaceutical care, it is critical that these savings are not accrued at the expense of quality of health care. Substitution of generic drugs for brand-name products is highly controversial and often is met with suspicion by health care providers and patients.

Several regulatory agencies (USFDA, DCGI and EMEA) consider two products to be bioequivalent if they yield comparable bioavailability (rate and extent of drug absorption) when administered to the same individuals in the same dose and under similar conditions. The bioequivalent products are consider being therapeutically equivalent and can be interchangeable.

The present study was undertaken to check whether economical low price brands of metformin extended release tablets could substitute safely and successfully for costlier brand. Interchangeability of two low cost brand of metformin extended release tablets (Product A: Glycomet SR 500mg sustained release tablets) manufactured by USV Pharmaceuticals Ltd, India, and Product B: Bigomet SR 500mg extended release tablets manufactured by Otsira Genetica Ltd, India) were evaluated with costlier reference product (Product R: Cetapin XR 500mg sustained release tablets) manufactured Aventis Pharmaceuticals, India) by using pharmacokinetic bioequivalence method following single dose administration in eighteen healthy, adult male, human subject under fasting conditions.

The clinical study was carried out in accordance with ICH Good Clinical Practices. The study protocol (006_JAMHAM_07) and the informed consent form were approved by the Jamia Hamdard Institutional Review Board. Each of the subjects was required to understand and give his consent to participate in the study by signing the informed consent form. The signed original copy was retained and a copy was given to each study subject for record. Adequate washout period (of seven days) maintained between the each period.

The dosing was done on specified date and time in each period based on a SAS generated randomization code. Vital sign of oral temperature, blood pressure and redial pulse were found to be normal and entire subject completed the study without experiencing any adverse event during the study period.
A Liquid Chromatography Mass Spectrometry method for the determination of Metformin Hydrochloride in human plasma was developed by using the deuterated Metformin (d6-metformin) salt as an internal standard. This method was successfully used for the analysis of metformin concentrations in the human plasma samples.

The pharmacokinetic bioequivalence was assessed by measuring the pharmacokinetic parameters namely $C_{\text{max}}$, $T_{\text{max}}$, $AUC_{0-t}$ and $AUC_{0-\infty}$. 90 % confidence interval of ratios of LSM of log transformed data of $C_{\text{max}}$, $AUC_{0-t}$ and $AUC_{0-\infty}$ within 80-125 % was considered to be bioequivalent.

Dissolution profile of both test products was comparable to reference product with acceptable range of similarity factor ($f_2$) for the product A & B respectively.

Following conclusions were drawn from this study:

- Test product A (Giycomet SR) was bioequivalent to reference product R (Cetapin XR), whereas test product B (Bigomet SR) was not bioequivalent to reference product R (Cetapin XR) as per US: FDA and DCGI 80-125 % criteria.

- For product B, 90 % confidence interval (A/R) of ratios of LSM of log transformed data of $AUC_{0-t}$ and $AUC_{0-\infty}$ failed by marginal values at the upper limit.

- Both test products A & B showed a comparable dissolution profiles with that of reference product R based on same release patterns and similarity factor ($f_2$).

- The costly reference product R can be interchangeable and switchable with 30% lower cost with product A and thereby reducing the cost of therapy.

- The product A and B are not switchable even by applying wider CI range (70-133%) for $C_{\text{max}}$ in case of drugs with wider safety margins.