8 SUMMARY:

To summarise the project it can be concluded that a successful GRDDS of Mosapride citrate dihydrate has been formulated.

The gastro retentive drug delivery is suitable for the controlled release of the drugs with absorption window in stomach and proximal part of small intestine. As it holds the drug delivery above the absorption window and release the drug at a controlled rate. To achieve the desired therapeutic profile with maximum drug utilization and improve patient compliance, the present study was undertaken to develop a gastro retentive drug delivery system (GRDDS) for model drug Mosapride. Commercially it is available as conventional dosage form like Immediate release 5mg (Mosadac-Zydus Cadila).

This study reveals successful application of Factorial design and optimization technique for the development of GRDDS.

In the present study a Floating Matrix Drug Delivery System of Mosapride Citrate (using dihydrate form) was formulated using the non aqueous wet granulation technique and compression of the granules to result in a sustained release gastroretentive drug delivery system (GRDDS).

The active drug was profiled using analytical techniques described under 4.1.

The drug excipients compatibility was studied using a novel approach of $3^4/3^2$ Factorial design module details of which are described under 5.4, 5.5, and 5.6. The results of the compatibility study showed which excipients have the least or no interaction with the drug and the polymer and excipients were selected based on these observations.

From the literature survey of excipients, characteristics of floating matrices and requirements of a GRDDS, it was envisaged that the factors controlling the floating properties and release patterns of this formulation would be the binder and the polymer. Thus a $3^2$ Factorial Design Module was selected for this work. Details of this Factorial
Design Module are explained under 6.1.4 and Tables 16, 17 and 18. A $3^2$ Factorial Design gives 9 different formulations (Table 18)

Oral of 9 different preparations were made and evaluated. Out of the 9 set of the results the formulation F5 (Refer Table no. 18) complied to all the parameters was selected for the purpose of validation. As F5 gave the best results for the critical parameters of release profile, FLT, FT and matrix integrity and was also in compliance with the rest of the evaluation parameters, it was selected as the desired GRDDS formulation.

Thus, three validation batches AF5, BF5 and CF5 were prepared using the same formulation and process used for F5 and the tablets thus prepared were evaluated for all the parameters which were applied for the $3^2$ Factorial design (9 batches). The results for these three batches comply with those of F5.

All throughout the experimental work and the validation of the process, it was observed that the following were critical parameters which have to be strictly monitored to achieve reproducibility of results for every batch manufactured.

1. Sieving parameters
2. Granulation time
3. Correct quantity of binding solution
4. Granule size
5. Thickness of tablets

The dissolution profile showed that the formulation F5 followed the Korsmeyer Peppas kinetics of drug release as the ‘r’ value for F5 is 0.9995 and the ‘n’ value of 0.5611 indicates anomalous diffusion or non-fickian dissolution. Thus, the release from F5 is by anomalous diffusion and erosion.

This was confirmed by the results of the same analysis for the validation batches AF5, BF5 and CF5 (Table no.32)

The conclusion drawn from the present work are:
A $3^2$ full factorial design can be used to achieve the desired release of Mosapride from the floating tablets, by careful selection and monitoring of formulation variables.

The success of the $3^2$ factorial design for the experiments was confirmed by the 3 validation batches which produced consistent results.

A $3^4/3^2$ factorial design was successfully used for the compatibility study of drug and excipients which simplified the excipient selection and used a mathematical model for cutting down on number of experiments required for such a study.

The statistical approach for formulation optimization is a useful tool, because two or more variables can be evaluated simultaneously.

The formulation F5 matrix tablets releases the drug appropriately as per design. The cumulative drug release at the end of 24hrs. from F5 was 97.83% and this was confirmed by the 3 validation batches AF5, BF5 & CF5 which gave a cumulative drug release for 24hrs. as 98.79%, 99.12% & 99.72% respectively.

It can be concluded that a once daily GRDDS matrix tablet of Mosapride Citrate Dihydrate, having a short half life was found to exhibit a satisfactory sustained release profile which may result in improved bioavailability, increased therapeutic efficacy and better patient compliance.

On the basis of comparison of the AUC$_{0-t}$ for MOSAPRIDE SR after single dose administration, the relative bioavailability of the Test preparation of MOSAPRIDE SR 15mg was 89.77% of that of the Reference preparation, Tablet MOZA -5.

On the basis of the pharmacokinetic parameters studied, it can be concluded that the Test preparation of MOSAPRIDE SR 15mg is bioequivalent with the Reference preparation of MOSAPRIDE 5mg, Tablet MOZA -5 mfd. by INTAS PHARMACEUTICALS LTD.