SUMMARY AND CONCLUSION

The present work was an attempt to formulate and evaluate antifungal topical herbal drug delivery system. Vidang was chosen as an antifungal herbal drug to formulate topical drug delivery system. Embelin is the major constituent of the Vidang which is used to prevent and treat fungal skin infections. In the present study, two topical formulations containing Vidang extract viz. gel and cream were prepared to achieve higher local drug concentration and to avoid the adverse effects of systemically administered formulations.

In the present study, Powder of Vidang fruit was extracted using n-Hexane by continuous soxhlet extraction method. Vidang extract was used to formulate topical drug delivery system.

The Vidang topical gel formulations were prepared by using carbopol 934 as a gelling agent (1.2, 1.6 and 2%) and propylene glycol (PG) as a co-solvent (8, 12 and 16%). Carbopol 934 prolongs the contact time of drug with infected part by increasing the viscosity of the topical gel formulations while propylene glycol increases the solubility of poorly aqueous soluble Vidang drug. Total nine topical gel formulations (F1-F9) were prepared using 3^2 factorial design and evaluated for physical appearance, pH measurements, viscosity measurements, spreadability, drug content, *in vitro* diffusion study through cellophane membrane.

A 3^2 randomized full factorial design was utilized for the optimization of formulation. The two factors amount of carbopol 934 (X_1) and amount of propylene glycol (X_2) were selected as independent variables. The three parameters viscosity, time required for 50% release of drug ($T_{50\%}$) and drug release at 1 hr (DR_1) were selected as depended variables. The statistical analysis of factorial design batches was performed by multiple linear regression analysis using Microsoft Excel 2003.

The results of the all topical gel formulations F1-F9 showed that drug content complied with the official standards as per Indian Pharmacopoeia, 1996 and pH suitable for application on the skin. Viscosity and spreadability of the F1-F9 formulations were found in the range of 39200 $\pm$ 140 cps to 63700 $\pm$ 220 cps and 13.11 $\pm$ 1.10 to 23.62 $\pm$ 1.23 gm$*$cm/sec respectively. The results of *in vitro* diffusion profiles of the F1-F9 formulations showed that formulations containing 1.2 % carbopol 934 (F1-F3) had higher release rate while formulations containing 2 % carbopol 934 (F7-F9) had slower release rate. The release rate from formulations containing 1.6 % carbopol 934 (F4-F6) was found to be satisfactorily and near to expected values as compare to formulations containing 1.2% and 2% of carbopol 934.

The viscosity (Y_1), $T_{50\%}$ (Y_2), and DR_1 (Y_3) were found to be significant with R^2 value of 0.994, 0.985, and 0.999 respectively. Surface response analysis reveals that viscosity and $T_{50\%}$ were increased and DR_1 was decreased by increasing the amount of carbopol 934 and/or by decreasing the amount of propylene glycol.

On the basis of % similarity with maximum desirability of dependant variables, formulation containing 1.6% carbopol 934 as a gelling agent with 12% propylene glycol as a co-solvent was selected as an optimized formulation (OF) and evaluated for *Ex vivo* permeation study through hairless skin and *in vitro* antifungal study using cup-plate method.

The data of *Ex vivo* permeation profiles of optimized formulation (OF) clearly indicate that Vidang extract was readily permeated through hairless skin because of both profiles of diffusion and permeation study are overlapping to each other. Concerning the data of MDT and f_2 value, it is evident the release profile of Vidang extract from cellophane membrane and hairless skin are similar. Optimized formulation (OF) exhibited

satisfactory antifungal activity against the cultures of *Candida Albicans, Trychophyton Rubrum* and *Microsporum Canis*. There was no antifungal activity found in DMSO solution which is considered as a control during the study. The data of *in vitro* antifungal study clearly indicate that antifungal activity was found only due to the presence of optimized formulation in the plate. Hence, it was concluded that the optimized formulation gave a promising results with maximum desirability.

Stability studies for optimized formulation (OF) were carried out at 25^0C/60% RH and at 40^0C/75% RH for three months as per ICH guidelines, Q1C: "Stability testing of new dosage forms". There was no significant variation found in general appearance, drug content, pH, viscosity and *in vitro* diffusion profile of optimized formulation (OF).

Secondly, the Vidang topical cream formulations were prepared by using stearic acid (2, 6 and 10%) and propylene glycol (PG) (2, 7 and 12%). Stearic acid gives proper emulsification and consistency of the cream formulation while propylene glycol increases the solubility of poorly aqueous soluble Vidang drug. Total nine topical cream formulations (C1-C9) were prepared using 3^2 factorial design and evaluated for physical appearance, pH measurements, viscosity measurements, spreadability, drug content, *in vitro* diffusion study through cellophane membrane.

A 3^2 randomized full factorial design was utilized for the optimization of formulation. The two factors amount of stearic acid (X_1) and amount of propylene glycol (X_2) were selected as independent variables. The three parameters viscosity, time required for 50% release of drug ($T_{50\%}$) and drug release at 1 hr (DR_1) were selected as depended variables. From the results, it was concluded that pH of the all topical cream formulations was found similar to the pH of skin and also drug content complied with the official standards given in Indian Pharmacopeia, 1996. Viscosity and spreadability of the C1-C9

formulations were found in the range of 398000 ± 4910 cps to 920000 ± 6190 cps and 11.06 ± 0.97 to 23.96 ± 1.76 gm∗cm/sec respectively. The results of *in vitro* diffusion profiles of the C1-C9 formulations showed that formulations containing 2 % stearic acid (C1-C3) had higher release rate while formulations containing 10 % stearic acid (C7-C9) had slower release rate. The release rate from formulations containing 6 % stearic acid (C4-C6) was found to be satisfactorily and near to expected values as compare to formulations containing 2% and 10% of stearic acid with varying amount of propylene glycol.

The viscosity (Y_1), $T_{50\%}$ (Y_2), and DR_1 (Y_3) were found to be significant with R^2 value of 0.999, 0.996, and 0.998 respectively. Surface response analysis reveals that viscosity and $T_{50\%}$ were increased and DR_1 was decreased by increasing the amount of stearic acid and/or by decreasing the amount of propylene glycol.

On the basis of % similarity with maximum desirability of dependant variables, formulation containing 6% stearic acid with 10% propylene glycol was selected as an optimized formulation (OC) and evaluated for *in vitro* diffusion study through cellophane membrane, *Ex vivo* permeation study through hairless skin, *in vitro* antifungal study using cup-plate method and other measurable parameters.

The data of *Ex vivo* permeation profiles of optimized formulation (OC) clearly indicate that Vidang extract was readily permeated through hairless skin because of both profiles of diffusion and permeation study are overlapping to each other. Concerning the data of MDT and f_2 value, it is evident the release profile of Vidang extract from cellophane membrane and hairless skin are similar. Optimized formulation (OC) exhibited satisfactory antifungal activity against the cultures of *Candida Albicans, Trychophyton Rubrum* and *Microsporum Canis*. There was no antifungal activity found in DMSO

solution which is considered as a control during the study. The data of *in vitro* antifungal study clearly indicate that antifungal activity was found only due to the presence of optimized formulation in the plate. Hence, it was concluded that the optimized formulation give a promising results with maximum desirability.

Stability studies for optimized formulation (OC) were carried out at 25^0C/60% RH and at 40^0C/75% RH for three months as per ICH guidelines, Q1C: "Stability testing of new dosage forms". There was no significant variation found in general appearance, drug content, pH, viscosity and *in vitro* diffusion profile of optimized formulation (OC).

Thus, the objective of present study to develop topical delivery of Vidang extract by using various formulation approaches can be successfully fulfilled.

In summary, gel and cream based herbal formulations were prepared to obtain topical delivery of Vidang extract. The efficient formulation approach enables us to develop functional formulations to achieve higher local drug concentration and to avoid the adverse effects of systemically administered formulations.