ABSTRACT

The concept of vesicular carrier system was introduced by the scientist Bingam in the year 1965 and the vesicles are named as Bingam bodies. Since three decades the interest on these vesicles is increased because of their variety applications. Enaramous research work is going on these vesicular carrier systems and the researchers introduced different vesicular carriers for different purposes. Liposomes are considred as conventional vesicular carrier systems and the same are modified to achieve desired objectives and named them differently like niosomes, ethosomes, transferosomes, pharmacosomes, bilosomes, etc. The aim of the present research work is to select the best vesicular carrier system among niosomes, ethosomes and transferosomes (primary objective) for administration of drugs across the skin to produce systemic effect. Nystatin, a polyene antifungal agent, was used as model drug in the present study. The secondary objective of the study is enhancement of bioavailability of the nystatin and to decrease the adverse effects associated with higher doses of the same by administering through skin.

 Totally 24 niosomal, ethosomal and transferosomal suspensions (eight formulations from each type of vesicular systems) were prepared. Niosomal suspensions were prepared using two different non-ionic surfactants i.e span-80 and span-60. Each surfactant used at four different concentrations (eight niosomal suspensions) was prepared. Similarly, eight transferosomal and eight ethosomal suspensions were prepared. Transferosomal suspensions were prepared using two different edge activators i.e. span-60 and span-80 at four
different concentrations whereas in preparation of ethosomal suspensions ethanol and lecithin concentrations has been changed for preparing the same (each at four different concentrations).

The prepared niosomal, ethosomal and transferosomal suspensions were evaluated by vesicles morphology (size, shape and surface texture), entrapment efficiency and in vitro drug release. The drug release data was fitted in different mathematical models such as Zero order, First order, Higuchi, Hixon-crowel, Korsmeyer-peppas to find out the order and mechanism of drug release from all formulations.

The experimental results, i.e. size, entrapment efficiency and invitro drug release results, analysed and based on the results, one optimized vesicular suspension from each type of vesicular formulation was selected.

After selecting one vesicular suspension from each type vesicular carrier suspensions, elasticity and surface charge (Zeta potential) of the vesicles present in these three optimized vesicular suspensions was studied.

Then the optimized niosomal, ethosomal and transferosomal suspensions were formulated into gels having concentration of 0.01%w/w. Along with three vesicular nystatin gels, conventional nystatin gel having same concentration was also prepared with pure nystatin drug sample for comparative study.

The prepared gels were characterized by in vitro and ex vivo drug release, skin retention and stability studies. The results showed that there is good correlation between the In vitro and ex vivo drug release data. From ex vivo drug release data of all three vesicular carrier gels, transdermal flux,
permeation coefficient and enhancement ratio was calculated and the results revealed that ethosomal gel is effective in permeation of nystatin across the dialysis membrane and skin than the other two vesicular gels.

During exvivo drug release study, amount of nystatin that retained on and accumulated in the skin was determined by performing skin retention study. The skin retention study also showed that ethosomes are efficient than other two vesicular carriers in permeation of nystatin across the skin.

In vivo study was carried out in rabbits to find out the systemic effect of all vesicular gels and conventional gel. Highest Cmax and AUC were shown by the ethosomes than other two vesicular and conventional gels. The invitro, ex vivo and in vivo characterization of three vesicular gels substantiated that ethosomal gel is effective and efficient for permeation of nystatin across the skin than the other two vesicular gels.

Our findings contribute to the evidence base for enhancing the permeability of nystatin across the skin and to produce the systemic anti fungal activity (Secondary objective). The present study demonstrates the utility of ethosomes as a tool for administration of drugs across the skin to produce the systemic effect and further studies such as clinical trials are required to conclude the same.

Key Words: transdermal drug delivery, systemic effect, localized effect, niosomes, ethosomes, transferosomes, gels.