RESEARCH PUBLICATIONS OUT OF THE PRESENT STUDY

1. Enhancement of liposomal stability by adsorption of cross-linked bovine serum albumin.
   Indian Drugs (India)--------------------- In Press

   Journal of pharmacy and Pharmaceutical Sciences (Communicated)

3. Role of novel acyclovir gel in herpes simplex: A clinical implication
   Medical Science Monitor (Communicated).
Enhancement of liposomal stability by adsorption of 
Cross-linked bovine serum albumin

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ABSTRACT

Liposomes of acyclovir and idoxuridine were prepared with or without using cross-linked bovine serum albumin for the enhancement of their stability in terms of drug retention. A series of batches of liposomes were prepared by reverse phase evaporation method varying in cholesterol molar concentration from 0.5 to 1.3 in acyclovir and from 1.0 to 1.5 in idoxuridine liposomes keeping constant drug: lipid ratio to 1:2.5 and 1:3 respectively. The prepared liposomes were evaluated for initial drug entrapment, mean surface number diameter and drug retention on storage at 2-8°C, 25±2°C and 37°C for 3 months period. Liposomes, prepared with high cholesterol proportion caused membrane to condense with decrease in surface number diameter reflecting reduction in outer surface area, and fluidity of the bilayers of phospholipids vesicles. This resulted in minimizing the drug leakage and thus, improving drug retention on storage at room and incubation temperature for the period of three months. However, initial percent drug entrapment was decreased. On the other hand, when the outer surface of acyclovir and idoxuridine liposomes having the same compositions were rigidized by adsorbing cross-linked bovine serum albumin, confirmed by significant (p<0.05) increase in surface number diameter (d_{sn}), showed significant (p<0.01) increase in drug retention at 25±2°C and 37°C. However, it was insignificant (p>0.05) at 2-8°C. Thus, the technique of surface rigidity of liposomes by adsorbing cross-linked bovine serum albumin is useful in improving drug retention in liposomes of acyclovir and idoxuridine.

Key Words: Acyclovir, Idoxuridine, Bovine serum albumin, Percent drug retention, Surface number diameter, Liposomes
Mathematical Modelling of preparation of acyclovir liposomes: reverse phase evaporation method
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The technique of three variables at three levels ($3^3$) factorial design was used to derive simple reduced second order polynomial equation for constructing contour plots to obtain predetermined % drug entrapment (PDE) within liposomes of acyclovir (ACY) when prepared by reverse phase evaporation (REV) method. Three independent variables selected were volume of organic phase ($x_1$), volume of aqueous phase ($x_2$), and Drug/PC/CHOL in molar ratio ($x_3$). Based on factorial design, twenty-seven batches of ACY liposomes were prepared by REV method. Prepared liposomal batches were evaluated for size, lamellarity, and PDE. The PDE (dependent variable) and the transformed values of independent variables were subjected to multiple regression to establish a second order polynomial equation (full model). To simplify the equation, F-statistic was applied to reduce polynomial equation (reduced model) by neglecting nonsignificant ($p>0.05$) terms. The coefficient value for independent variable, Drug/PC/CHOL in molar ratio ($x_3$) was found to be maximum ($b_3 = 2.52$) and hence the variable $x_3$ was considered to be a major contributing variable for PDE within liposomes by REV method. The reduced polynomial equation was used to plot three two-dimensional contour plots at fixed levels of $-1$, $0$ and $1$ of major contributing variable ($x_3$) to obtain various combinations of values of two other independent variables ($x_1$ & $x_2$) at predetermined PDE. The conformity of the established equation was checked by preparing three batches three times taking values of the independent variables from the contour plots for prefixed value of PDE. Prefixed PDE value taken for designing the experiment and results obtained experimentally were compared using student ‘t’ test and difference between experimentally obtained and theoretically calculated values of PDE was found to be statistically nonsignificant ($p>0.05$). Hence, finding of this study establishes the role of the derived equation and plotted contour plots in predicting the values of independent variables for preparation of ACY liposomes by REV method having predetermined PDE.

**Keywords:** Liposomes, acyclovir, factorial design, model-dependent optimization, contour plots
Role of novel acyclovir gel in herpes simplex: A clinical implication

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