FORMULATION AND EVALUATION OF LIPOSOMES CONTAINING FAMOTIDINE

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ABSTRACT

In the present study liposomal formulations containing Famotidine were prepared and studied. Liposomal formulations were evaluated for drug entrapment, surface characterization and in-vitro drug release studies. Drug excipient compatibility was determined by using spectral studies. Liposomal suspensions were prepared using film hydration technique by varying concentrations of ingredients and optimize the ideal combination for required drug release. The prepared liposomes were rigid, intact and fulfilled all official requirements. The results of in vitro drug release studies showed that release from liposomal formulation was slow and sustained for more than 8 hrs period. Thus the liposomal suspensions of Famotidine were successfully formulated and established for their quality control parameters.

KEY WORDS: Liposome, Drug Release, Formulation, Famotidine.

INTRODUCTION

Liposome defined as a spherical vesicle of lipid bilayers enclosing an aqueous compartment. Their size ranges from 25 to 5000 nm. The lipid most commonly used is phospholipids, sphingolipids, glycolipids and sterols. Liposomes may be formulated with a range of characteristics including different size, charge and drug retention, which can be tailored for a given drug and target site. They are used as a delivery system for drugs, genes and vaccines in therapeutics. Liposomes can also be actively targeted to specific cells or sub cellular
regions using targeting ligands attached to their surface or by modification of the bilayer to
give triggered release under appropriate conditions [1-4].

Famotidine is a histamine H₂-receptor antagonist. It is widely prescribed in gastric ulcers,
duodenal ulcers, Zollinger-Ellison syndrome and gastro-esophageal reflux disease. In the
management of benign gastric and duodenal ulceration the dose is 40 mg daily by mouth at
bedtime, for 4 to 8 weeks. In the Zollinger-Ellison syndrome the initial dose by mouth is 20
mg every 6 hours, increased as necessary; dose up to 80 mg daily have been employed. The
low bioavailability and short biological half life following oral administration of Famotidine
motivate many researchers to improve its pharmacokinetics profile and many researchers
made attempts in this direction like development of a sustained release formulation and
utilization of other techniques which improve release profile of drug. [5, 6]

MATERIAL AND METHODS
Famotidine was obtained as a gift sample in the form of crystalline powder. All other
chemicals/reagents used were of analytical grade, available commercially and used as such
without further processing.

PREPARATION OF LIPOSOMES
Liposomes were prepared by thin film hydration technique. Accurately weighed quantities of
phosphatidylcholine and cholesterol were dissolved in chloroform-ethanol mixture in
different ratios in a round-bottomed flask. BHT, equivalent to 2% of the total lipids as an
antioxidant, was added in the organic phase in the flask. The chloroform-ethanol mixture was
evaporated by rotating the round bottom flask on the palms. After complete evaporation of
organic solvents, hydration of the thin film was carried out. The various formulation variable
considered in this research have been presented in Table 1.

Table 1: Composition of lipids for preparation of liposome

<table>
<thead>
<tr>
<th>S. No</th>
<th>Formulation</th>
<th>Phosphatidylcholine (moles)</th>
<th>Cholesterol (moles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L1</td>
<td>5.5</td>
<td>4.5</td>
</tr>
<tr>
<td>2</td>
<td>L2</td>
<td>6.5</td>
<td>3.5</td>
</tr>
<tr>
<td>3</td>
<td>L3</td>
<td>7.5</td>
<td>2.5</td>
</tr>
<tr>
<td>4</td>
<td>L4</td>
<td>8.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>
EVALUATIONS OF DIFFERENT PARAMETERS

Estimation of Entrapped Drug

Drug entrapped within the liposomes was estimated after removing the unentrapped drug, which was separated by collecting the supernatant after subjecting the dispersion to centrifugation in a cooling centrifuge at 1000 rpm. The pellets of liposomes were washed again to remove any unentrapped drug, and the washing was combined with the supernatant and analyzed for drug content at 265 nm.

Surface Characterization

The SEM studies for formulated liposomes were conducted, and the pictures were shown in

![Fig. 1: SEM of liposomes](image)

![Fig. 2: Drug release profiles of formulations](image)
In Vitro drug release study
The United States Pharmacopoeia basket-type dissolution rate test apparatus was used for all the in vitro release studies. A weighed quantity of the material was suspended in 900 mL of 0.1 mol HCL of pH 1.2. The dissolution medium was stirred at 100 rpm and maintained at constant temperature (37±0.5°C). At present time intervals 5 mL aliquots were withdrawn and replaced by an equal volume of fresh pre-warmed dissolution medium maintaining sink condition throughout the experiment. After suitable dilution, the samples were analyzed for drug quantification at 265 nm using Double beam UV-VIS Spectrophotometer [7].

RESULTS AND DISCUSSION
The liposomes formulation were prepared and evaluated for various characterstichs; the result of IR spectral study shows characteristic peaks due to the pure Famotidine and peaks appeared in the spectra of Liposomes without any remarkable change in the position and comparable with standards. Liposomes with varying proportions as per shown in Table 1 were prepared using hand shaking method. Drug entrapped efficiency were found to be from 77-89 % which indicates desirable consideration of drug dosing. The result of SEM studies for surface characterization reveals the uniform spherical size of liposomes with optimum ranges of size (Figure 1). Release profiles indicated that L4 showed 80%, L3 showed 73.2%, L2 showed 68.7%, L1 showed 62% for 8 hr of release study. Release of drug from all the formulated liposomes followed sustained release profile which was desirable to overcome the solubility problem of drug (Figure 2). All the prepared formulations follows diffusion controlled release mechanism. Hence release of Famotidine from the prepared liposomal formulation follows zero order kinetics by utilizing diffusion as a controlled release mechanism [8].

CONCLUSION
The prepared liposomal formulations using different lipid cholesterol molar ratios were developed and evaluated. The evaluation studies concluded that higher the concentration of cholesterol rigidity of the bilayer will be more and showed better controlled release of drug. Hence the combination used in formulation were found to be optimum for achieving better controlled release thus the liposomal formulation of Famotidine would be a suitable means to produce more uniform release profile.
REFERENCES


