PREPARATION AND CHARACTERIZATION OF NABUMETONE LIPOSOMES

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Nabumetone is the effective drug for the treatment of reumatoid arthritis and osteoarthritis. The drug has a half life of 23 hrs and its oral bioavailability is only 30%. The aim of the study is to prepare 6 formulations of liposomal carrier for Nabumetone for the treatment of arthritis that is capable of delivering the drug to the specific target site by topical route by using different ratios of phospho lipid and cholesterol with a desired amount of drug by thin film hydration technique and to find out the drug release from the liposome’s of different ratios, mechanism kinetics of drug release pattern and also to find out the size distribution of liposome's of different ratios and also to increase the bioavailability and efficacy of the drug.

**Keywords:** Liposome’s, Thin Film Hydration Method, Nabumetone.

INTRODUCTION

Liposomes are colloidal particles formed as concentric bimolecular layers that are capable of encapsulating drugs. They are lipid vesicles that fully enclose an aqueous volume. These lipid molecules are usually phospholipids with or without some additives. Cholesterol may be included to improve bilayer characteristics of Liposome’s; increasing micro viscosity of the bilayer, reducing permeability of the membrane to water soluble molecules, stabilizing the membrane and increasing rigidity of the vesicle.

Liposomes are micro vesicles, whose membranes are made of phospholipids, which are bilayer having head and tail. The head group is hydrophilic and the tail group which is made of long hydro carbon chain is hydrophobic. The drug molecules can be encapsulated in aqueous space or into lipid bilayer. The exact location of the drug will depend upon its physicochemical properties and composition of lipids. The water soluble substances can be trapped inside the water sphere while fat soluble substances can be trapped inside the fat soluble opposite end of the molecule. Liposome’s give a unique delivery system for nutrients, vaccines, enzymes, or drugs. Liposomes are effective in treating diseases that affect the phagocytes of the immune system.
system because they tend to accumulate in the phagocytes, which recognize them as foreign invaders. They have also been used to carry normal genes into a cell in order to replace defective, disease-causing genes. Because of their moisturizing qualities Liposome’s are also used in cosmetics.

Liposome’s, which are vesicles consisting of one or more concentrically ordered assemblies of phospholipids bilayer, range in size from a nanometer to several micrometers. Phospholipids such as egg phosphatidylcholine, phosphatidylserine, synthetic dipalmitoyl-DL-alpha-phosphatidylcholine or phosphatidylinositol, have been used in conjunction with cholesterol and positively or negatively charged amphiphiles such as stearylamine or phosphatidic acid. Because of the multifold characteristics as drug carriers, Liposome’s have been investigated extensively as carriers of anticancer agents for the past several years. Liposomal entrapments include a variety of pharmacologically active compounds such as antimalarial, antiviral, anti-inflammatory and anti-fungal agents as well as antibiotics, prostaglandins, steroids and bronchodilators.

**MATERIALS AND METHODS**

Nabumetone drug, Soya lecithin 30% Cholesterol, Chloroform, Methanol Potassium dihydrogen phosphate, Disodium hydrogen phosphate, Sodium chloride, Acetone were used for this study.

**Methods**

**Formulation of Liposomes**

Drug: Soya lecithin: Cholesterol in different ratios was dissolved in 5 ml chloroform. This solution was taken in a 250 ml round bottom flask. The flask was rotated in rotary flash evaporator at 80 rpm for 15 minutes in thermostatically controlled water bath at 40°C under vacuum 900 mmHg. The organic solvent was slowly removed by this process such that a very thin film of dry lipids was formed on the inner surface of the flask. The dry lipid film was slowly hydrated with 5 ml of phosphate buffer ph 7.4. The fluid is allow to hydrate with phosphate buffer pH 7.4 for 2 hr Swirling the contents to yield milky white suspension. The formulation is subjected to centrifugation. The unentrapped drug is removed by centrifugation at 3000 rpm for a period of 30 minutes. The pellets are dispersed in phosphate buffer.

**CHARACTERIZATION OF LIPOSOMES**

**Drug Entrapment Efficiency**

Drug entrapment efficiency was calculated by using centrifugation method. The liposome suspension of 1ml was taken and centrifuged at 3500rpm for 15 min. The sediment obtained from the centrifugation was suspended in 100 ml of phosphate buffer pH 7.4. Then the absorbance was taken at 261 nm. From that the amount present in 1 ml of suspension was obtained. The drug entrapment efficiency was calculated from the following formula.

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\% \text{ Drug Entrapped (PDE)} = \frac{\text{Amount of Drug in the sediment}}{\text{Total amount of Drug}} \times 100
\]

**Particle Size Analysis**

The particle size of Liposome’s was determined by optical microscopy by using Perkin Elmer. All the prepared batches of Liposome’s were viewed under microscope to study their size. Size of liposomal vesicles was measured at different location on slide by taking a small drop of liposomal dispersion on it and average size of liposomal vesicles were determined.
**In Vitro Drug Release Study**

The release studies were carried out in diffusion cell having 10 ml capacity. 10 ml Phosphate buffer pH 7.4 was placed in diffusion cell. The diffusion cell contained a magnetic bed and the medium was equilibrated at 37±5°C. Dialysis membrane was taken and placed on the diffusion cell. After separation of non-entrapped Nabumetone, liposome dispersion was filled in the dialysis membrane. The dialysis membrane containing the sample was suspended in the medium. Aliquots were withdrawn (1 ml) at specific intervals, filtered, diluted with phosphate buffer and the absorbance was taken at 261 nm. Then the apparatus was immediately replenished with same quantity of fresh phosphate buffer pH 7.4 medium.

**RESULTS AND DISCUSSION**

FTIR of pure drug and physical mixture.

The drug release kinetics of prepared Nabumetone Liposomes were conducted using Higuchi’s model and Poppa’s model. Higuchi’s plot was done with square root of time in X axis and %cumulative drug in Y axis (Figure 1). The Poppa’s plot was done with log time in X axis and log %cumulative drug release in Y axis. The study of drug release kinetics showed that majority of the formulations governed by peppas model.

Results showed that F1 have a particle size of 7.994 micron and F6 have a highest value compared to other formulations. From the results of particle size analysis F1 shows satisfactory particle size (Figure 2).

According to the drug entrapment study conducted the maximum drug entrapment was shown by F1 (52±0.5).
Figure 2: In Vitro Drug Release Study of F1 to F6
CONCLUSION

Nabumetone Liposome's were prepared using soya lecithin, cholesterol and chloroform as solvent by thin film hydration method using rotary evaporator. The prepared Liposomes were evaluated by drug entrapment study, particle size analysis. In vitro drug release study and mechanism of release kinetics using Higuchi's plot and Korsemeyer Peppas plot.

The present study demonstrated the successful preparation of Nabumetone Liposomes and its evaluation. Formulation F1 showed high encapsulation efficiency with minimum particle size and drug release over a 4 hr, hence suppose to give greater bioavailability and considered as good liposomal formulation. The difference in drug entrapment and drug release was due to the different ratios of lipid to cholesterol. The drug entrapment shows decreasing when the concentration of lipid and cholesterol changes. F1 have high entrapment and satisfactory drug release within 4 hr. F1 shows least particle size from the results F1 selected as a good formulation of Nabumetone Liposomes.

REFERENCES


