Design And Evaluation of Controlled Release Liposomal Film of Atenolol

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***Abstract*—The present study aimed to develop and evaluate a controlled-release liposomal film of Atenolol, a selective β_1-adrenergic blocker used in the management of hypertension. Liposomes were prepared using the thin-film hydration method and incorporated into a polymeric film matrix to achieve sustained drug release. The formulated liposomal films were characterized for physicochemical properties including thickness, tensile strength, surface morphology, drug content uniformity, and in vitro drug release. In vitro studies demonstrated a prolonged release of Atenolol, indicating potential for improved bioavailability and enhanced patient compliance compared to conventional oral formulations. The findings suggest that liposomal films can serve as an effective platform for controlled delivery of Atenolol, offering advantages in long-term cardiovascular therapy.**

***Keywords*—Atenolol, Liposomes, Controlled-release, Polymeric film, Hypertension, Drug delivery system**

I. INTRODUCTION

Hypertension is one of the most prevalent cardiovascular disorders worldwide and a major risk factor for heart disease, stroke, and kidney failure. Effective management of hypertension often requires long-term therapy to maintain blood pressure within the normal range and prevent complications. Atenolol, a selective β_1-adrenergic receptor blocker, is commonly prescribed for hypertension, angina pectoris, and certain cardiac arrhythmias. It acts by reducing heart rate, cardiac output, and renin release, thereby lowering blood pressure. Despite its effectiveness, conventional oral formulations of Atenolol face challenges such as rapid absorption, short half-life, and frequent dosing, which can negatively impact patient adherence to therapy.

Controlled drug delivery systems are designed to overcome these limitations by sustaining drug release over an extended period, maintaining therapeutic drug levels, and reducing dosing frequency. Among these systems, liposomes have emerged as a versatile platform. Liposomes are spherical vesicles composed of one or more phospholipid bilayers capable of encapsulating hydrophilic and hydrophobic drugs. They offer advantages such as biocompatibility, biodegradability, reduced toxicity, and the ability to modify drug release kinetics. Liposomal formulations can protect drugs from degradation, enhance bioavailability, and target drug delivery to specific tissues.

In recent years, polymeric films incorporating liposomes have gained attention as an innovative drug delivery approach. These films are thin, flexible, and capable of controlled drug release, making them suitable for oral, buccal, or transdermal applications. The incorporation of liposomes into polymeric matrices combines the advantages of both systems: the sustained release and protective capacity of liposomes, and the mechanical stability, flexibility, and ease of administration provided by the film.

The present study focuses on the design and evaluation of a controlled-release liposomal film of Atenolol, aiming to achieve sustained drug release, improve bioavailability, and enhance patient compliance. The study involves the preparation of Atenolol-loaded liposomes using the thin-film hydration method, incorporation into polymeric films, and subsequent characterization of the films for physicochemical properties, mechanical strength, drug content uniformity, surface morphology, and in vitro drug release. This approach has the potential to offer an effective alternative to conventional oral tablets, reducing dosing frequency and improving therapeutic outcomes in the management of hypertension.

II. MATERIALS AND METHODS

Materials

- Atenolol – obtained from Sigma-Aldrich
- Phospholipids (Phosphatidylcholine) – for liposome preparation.
- Cholesterol – for stabilizing liposomal membranes.
- Polymeric film-forming agents – Hydroxypropyl Methylcellulose (HPMC), Sodium Alginate,
- Plasticizers –Polyethylene Glycol (PEG) to enhance film flexibility.
- Organic solvents –Chloroform, Methanol, for lipid dissolution.
- Buffer solutions – Phosphate buffer (pH 7.4) for in vitro drug release studies.
- Other reagents – Analytical grade chemicals for film characterization.

Methods
Preparation of Atenolol-Loaded Liposomes

1. Thin-Film Hydration Method:

Phospholipids and cholesterol were dissolved in a suitable organic solvent (chloroform: methanol, 2:1).

Atenolol was added to the lipid solution.

The solvent was evaporated under reduced pressure using a rotary evaporator to form a thin lipid film on the flask wall.

The film was hydrated with phosphate buffer (pH 7.4) under gentle shaking to form multilamellar liposomes.

The liposomal suspension was sonicated to reduce vesicle size and achieve uniform distribution.

2. Characterization of Liposomes:

Vesicle size and polydispersity index – measured by dynamic light scattering (DLS).
Encapsulation efficiency (EE%) – determined by separating unentrapped drug and quantifying Atenolol spectrophotometrically.
Zeta potential – to assess stability of liposomes.

3. Preparation of Liposomal Film

1. Polymer Solution Preparation:

Appropriate amounts of polymer (e.g., HPMC) were dissolved in distilled water under constant stirring to form a homogenous solution.
Plasticizer (e.g., glycerin) was added to improve flexibility of the film.

2. Incorporation of Liposomes:

Prepared Atenolol-loaded liposomes were dispersed uniformly into the polymer solution under gentle stirring.

3. Casting and Drying:

The polymer-liposome mixture was poured into a leveled petri dish or mold.
The film was allowed to dry at room temperature or in a hot air oven at controlled temperature.
The dried film was carefully peeled off and cut into uniform sizes for evaluation.

4. Evaluation of Liposomal Film

1. Physical and Mechanical Properties:

Thickness – measured using a micrometer at multiple points.
Folding endurance – determined by repeatedly folding the film at the same place until it broke.
Tensile strength – using a texture analyzer or universal testing machine.
Surface morphology – examined by Scanning Electron Microscopy (SEM).

2. Drug Content Uniformity:

A portion of the film was dissolved in phosphate buffer (pH 7.4), and Atenolol content was measured spectrophotometrically at the appropriate wavelength.

3. Swelling Index:

The film was weighed, immersed in buffer for a defined period, and reweighed to calculate percentage swelling.

4. In Vitro Drug Release Studies:

Performed using a USP dissolution apparatus or dialysis method in phosphate buffer (pH 7.4) at 37 ± 0.5 °C.
Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically.
Drug release kinetics were studied by fitting data to models such as zero-order, first-order, Higuchi, or Korsmeyer-Peppas models.

III. RESULTS AND DISCUSSION

In vitro drug release from films

The films were evaluated for the drug release. The plots depicting the release of drug over time from film sloaded with liposome so with coated liposo mesare shown in Table

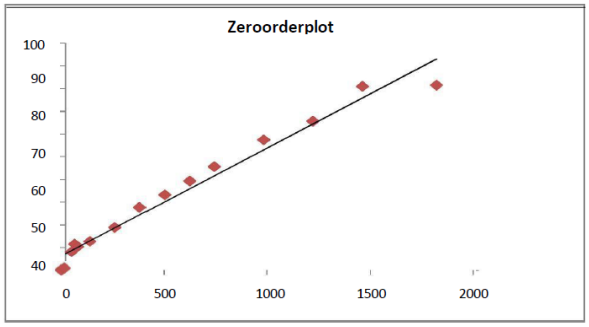

Figure 1.1: Zeroorder kinetic plot for drug release from film LF6

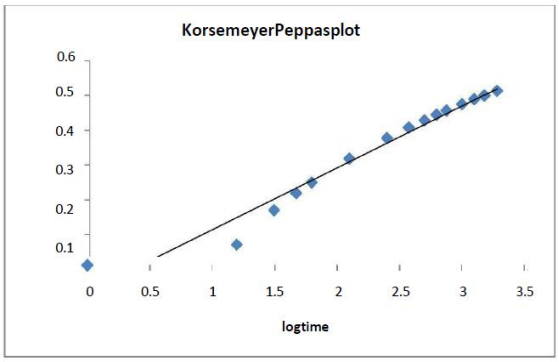

Figure 1.2: Korsemeyer-Peppas plot for drug release from filmLF6

Table 1.1 Drug release profile sfromlipo film LF6, coated lipo film LF8 and marketed product A ten 50

Time(min.)	Lipofilm	Coatedlipofilm	Marketed product
0	0± 0	0±0	0±0
15	0.72± 0.15	0.42±0.33	63.79±1.67
30	8.15± 0.54		75.42±1.42
45	9.35± 0.35	6.79±1.37	79.86±0.87
60	10.37±0.30	8.56±0.54	81.31±0.76
120	12.71±0.48	21.51±1.28	91.64±0.84
240	18.81±0.48	27.79±0.45	97.96±0.68
360	27.67±1.06	31.25±0.63	99.14±0.51
480	33.16±0.45	34.27±0.27	99.53±0.16
600	39.32±1.19	39.29±0.29	---
720	45.65±0.93	40.75±0.97	---
960	57.42±0.86	48.17±1.16	---
1200	65.68±1.24	54.84±1.03	---
1440	81.03±0.30	66.40±0.65	---
1800	81.61±0.49	76.78±1.12	---
2160	---	85.02±1.20	---
2520	---	88.8±1.24	---
2880	---	95.85±0.42	---

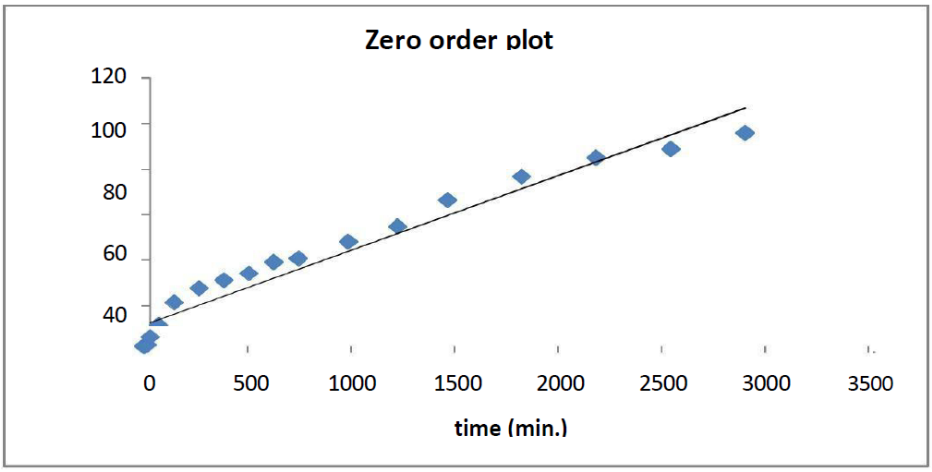

Figure 1.3: Zero order kinetic plot for drug release from film LF8

Visualization by Scanning Electron Microscopy

The surface morphology of the film loaded with liposomes and coated liposomes was observed by using scanning electron microscopy. SEM images were shown in

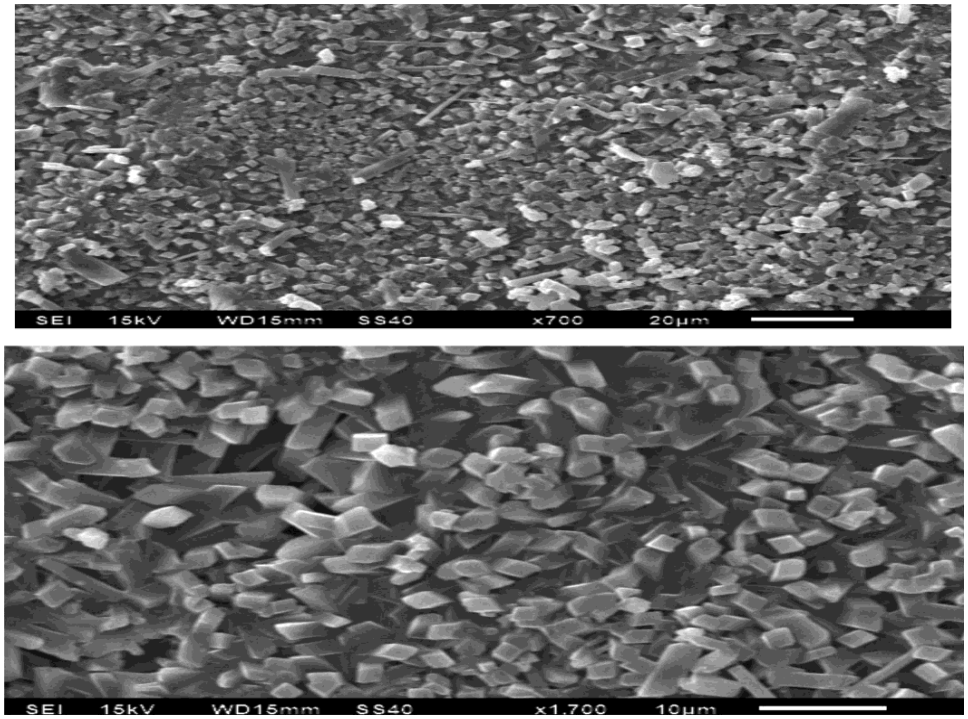

Figure 1.4: SEM image of film LF6 at different magnifications

Release plots of the films were plotted and fitted to kinetic models. Results of drug diffusion studies from films loaded with plain liposomes or with chitosan coated liposomes; both were fitted to various models as shown in Table 1.1. It was observed that the drug release followed first order kinetics where the release is concentration dependent. The mechanism of drug release from both the films is by super case II transport mechanism, where the drug release may be due to a combination of diffusion and erosion. The release patterns were also compared to the marketed product Aten 50. Aten50produced complete release of the drug over a period of 6 hours. The prepared films containing liposomes LF 6, produce controlled release of the drug over a period of 30 hours and 48 hours respectively.

IV. CONCLUSION

The present research investigation, for the first time, presented a film loaded with vesicular systems that

This new formulation is a viable alternative to conventional tablet, by virtue of its ability to sustain the drug release, and due to its ease of administration. It reduces the dosing frequency and thus is expected to help in increasing the patient compliance. The formulation of cyclosporine liposomes by Al-Meshal MA et al., support the statement that liposomal drug delivery improves bioavailability of drugs.

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