Design and Evaluation of Naproxen Proliposomal Gels

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Abstract

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Introduction

In the past few decades, considerable attention has been focused on the development of new drug delivery system (NDDS). e NDDS should ideally ful ll two prerequisites. Firstly, it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity to the site of action. Conventional dosage forms including prolonged release dosage forms are unable to meet none of these. At present, no available drug delivery system behaves ideally, but sincere attempts have been made to achieve them through various novel approaches in drug delivery [1].

Novel drug delivery system aims at providing some control, whether this is of temporal or spatial nature or both, of drug release in the body. In recent years, vesicles have become the vehicle of choice in drug delivery. Lipid vesicles were found to be of value in immunology, membrane biology, diagnostic techniques, and most recently, genetic engineering [2-4]. Vesicles can play a major role in modeling biological membranes, and in the transport and targeting of active agents. Encapsulation of a drug in vesicular structures can be predicted to prolong the existence of the drug in systemic circulation and perhaps, reduces the toxicity if selective uptake can be achieved [5]. e phagocytic uptake of the systemic delivery of the drug loaded vesicular delivery system provides an e cient method for delivery of drug directly to the site of infection, leading to reduction of drug toxicity with no adverse e ects.

Naproxen is a non-steroidal anti-in ammatory drug with strong analgesic and lesser action on in ammation and pyrexia (fever). Naproxen half-life is 2-5 hours [6]. Naproxen is well absorbed a er oral administration peak plasma concentration is usually achieved within 2-3 hours a er its oral administration. It is highly (99%) bound to plasma protein and hence it need to be administered 2-3 times a day. Hence, there is every need for formulating a sustained release form for Naproxen to improve its therapeutic e cacy and patient compliance.

Materials and Methods

Naproxen was obtained as a gi sample from Divis Laboratories, Hyderabad. Phosphotidyl Choline, Mannitol, Cholestrol, Mannitol, Carbopol 934 were purchased from SD Fine chemicals, Mumabai. All other chemicals and reagents used were analytical grade.

Preparation of naproxen loaded proliposomes

e proliposomes containing naproxen was prepared by lm deposition on carrier method using vacuum rotary evaporator. e naproxen proliposomes was done by preparing the di erent formulations by varying the concentration of phosphatidyl choline and cholesterol. Required quantity of mannitol was placed in 100ml round bottom ask which was held at 60-70 temperature and the ask rotated at 80-90 rpm for 30 min under vacuum. A er complete drying the temperature of water bath was lowered to 20-30 . Naproxen, Phosphotidyl Choline and Cholesterol were dissolved in mixture of

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mortar and pestle, the concentration of proliposomes in the gel being 1%. All optimized formulations were incorporated into di erent carbopol gels (1% and 3%).

Characterization of proliposomes

Vesicle size and count: Average size and size distribution proliposomes was determined using optical microscope. A drop of distilled water was added to proliposome granules on a glass slide without a cover slip, and the process of liposome formulation was observed using optical microscope with 100X magni cation. Size of liposomal vesicles was measured at di erent locations on the slide. From the obtained results size distribution and average size of liposome vesicles was determined.

Surface morphology: e surface morphology of proliposomes and plain mannitol particles were examined by scanning electron microscopy (SEM) a er coating with gold. A er goldcoating of proliposome and plain mannitol particles, their surface morphology was viewed and photographed.

Drug content: Naproxen content in proliposomes was assayed by an UV-visible spectrophotometer. Proliposomes (100mg) were dissolved in 10ml methanol by shaking the mixture for 5 mins. One ml of the resultant solution was taken and diluted to 10ml with methanol. en, aliquots were withdrawn and absorbance was recorded at 323 nm using UV-visible spectrophotometer (Lab India 3200).

Entrapment efficiency: Separation of unentrapped drug from the liposomal suspension was done by centrifugation method. e entrapment e ciency of proliposomes was determined a er hydration with distilled water. 10ml of phosphate bu er (pH 7.4) was added to proliposomes granules and then subjected to sonicate for 10 mins using ultra sonicator (Citizen, India). e liposomal suspension was subjected to centrifugation on a cooling centrifuge (REMI TR-01) at 15000rpm for 30 mins for the separation of unentrapped drug. e clear supernatant (1ml) was taken and diluted to 10ml with bu er and absorbance was recorded at 323 nm using UV-visible spectrophotometer (Lab India 3200). en calculate the percentage drug in the each formulation.

Entrapment E ciency ={(Ct-Cf)÷Ct }×100

Ct – concentration of total drug

Cf – concentratin of free drug

Yield of proliposomes: A er complete drying the proliposome powders were collected and weighed accurately. e yield of proliposomes was calculated using the formula [8].

Percentage Yield= Total weight of proliposomes/ Total weight of drug+Weight of added materials*100

Characterization of gel

Gel base was evaluated for following parameters for both plain gel and gel loaded with proliposomes.

Physical appearance: All prepared proliposomal gel formulations have been observed for their visual appearance, such as transparency, colour, texture, grittiness, greasiness, stickiness, smoothness, sti ness, tackiness and clarity was determined by using clarity chamber with black and white background.

pH of formulation: pH measurement of the gel was carried out of the formulation was measured by using a digital pH meter (Lab India SAB 5000), dipping the glass electrode completely into the gel system. e observed pH values were recorded for all formulations (F1-F9) in triplicates.

Rheological properties

e rheological properties of prepared gels were estimated using a Brook eld viscometer. Sample holder of the Brook eld viscometer was lled with the gel sample, and then spindle was inserted into sample holder. e spindle was rotated at 100 rpm. All the rheological studies were carried out at room temperature. A viscosity measurement was done in triplicate. Viscosity of 1, 2 and 3% carbopol gel was determined and selected the optimized formulation.

Drug Content

For determination of drug content, accurately weighed quantity (1gm) of gel equivalent to 10 mg of naproxen was dissolved in phosphate bu er (PH 7.4) and analyzed by UV-Vis Spectrophotometer at 323 nm and the drug content was calculated.

In itro studies

Franz di usion cell was used for the in vitro drug release studies. Semi permeable membrane was placed between donar and receptor chamber of di usion cell. Receptor chamber was lled with freshly prepared 30ml 7.4 PH phosphate bu er. Proliposomal gel equivalent to 1gm was placed on semi permeable membrane. e franz di usion cell was placed over magnetic stirrer with 500rpm and temperature was maintained at 37±10C. 5ml of samples were withdrawn periodically and replaced with fresh bu er. e withdrawn samples were periodically diluted and analysed for drug content using UV visible spectrophotometer (Lab India 3200) at 323 nm.

Results and Discussion

A positive correlation was observed for both variables phospholipid and cholesterol in case of liposome vesicle size. us, with increase in the concentration of phospholipid and cholesterol vesicle size was

In vitro drug release

e result of In vitro release of naproxen from the gel formulation clearly shows that the gels have ability to retain the drug for prolonged