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Short communication

Preparation and characterization of nimesulide-loaded liposomes for dermal application

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Introduction

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID) with preferential cyclooxygenase-2 inhibition and well-documented analgesic and anti-inflammatory activity (Singh et al., 2005). Its oral use is limited by slow absorption and dose-dependent gastrointestinal side effects, making dermal administration an attractive alternative for the local treatment of painful and inflammatory conditions; however, the stratum corneum strongly limits the percutaneous absorption of lipophilic, poorly water-soluble molecules such as nimesulide. Liposomes as vesicular phospholipid-bilayer systems, are efficient carriers for dermal delivery, improving stability, controlled release and skin penetration, and their incorporation into a gel further improves local retention (Torchilin, 2005; Singh et al., 2005). The aim of this work was to prepare nimesulide-loaded liposomes by thin-film hydration and to characterize their encapsulation efficiency, particle size, zeta potential and drug–excipient interactions, as a basis for a gel with liposomes loaded with nimesulide.

Materials and methods

Materials

In the preparation of the liposomes were used cholesterol (Aldrich, Germany), soybean phosphatidylcholine (Vitalia, North Macedonia), Tween 80 (Merck, Germany), Chloroform (Carlo Erba, Italy) and nimesulide, kindly donated by Replek AD, North Macedonia. All other chemicals were of analytical grade and used as received.

Preparation of liposomes

Nimesulide-loaded liposomes were prepared by the thin-film hydration method. Two formulations containing 100 mg nimesulide and 700 mg soybean phosphatidylcholine were prepared, differing in cholesterol/Tween 80 ratio: F1 (250/50 mg) and F2 (70/150 mg). The components were dissolved in chloroform, evaporated under reduced pressure to form a thin lipid film, hydrated with phosphate buffer (pH 7.4) to a final volume of 10 mL, and homogenized using an Ultra-Turrax (9500 rpm, 5 min). Empty liposomes were prepared without nimesulide.

Determination of encapsulation efficiency

Encapsulation efficiency (EE%) was determined by direct and indirect UV–Vis spectrophotometric methods following centrifugation (4000 rpm, 20

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min). Quantification of nimesulide was performed using calibration curves prepared in phosphate buffer (pH 7.4) for the indirect method and in chloroform:methanol (2:1) for the direct method. For the indirect method, the supernatant was diluted and analyzed to determine the amount of non-encapsulated drug. For the direct method, the pellet was dissolved in a chloroform:methanol (2:1) mixture and analyzed to determine the amount of encapsulated nimesulide.

Particle size and zeta potential

Particle size was determined by laser diffraction (Mastersizer 2000, Malvern Instruments Ltd., UK), while zeta potential was measured by dynamic light scattering (Zetasizer Nano-ZS, Malvern Instruments Ltd., UK) after appropriate dilution.

FTIR spectroscopy

Drug incorporation and potential drug–excipient interactions were evaluated by FTIR-ATR spectroscopy. Spectra of pure nimesulide, excipients, empty liposomes, and drug-loaded liposomes were recorded in the 650–4000 cm^{-1} range. For liposomal samples, a drop of the dispersion was placed on the ATR crystal, dried at room temperature, and analyzed as a dried film. The spectra were compared to assess the incorporation of nimesulide into the vesicles and to identify any potential interactions between the drug and formulation components.

Results and discussion

Encapsulation efficiency determined by the indirect method was high for both formulations, reaching 90.3% (F1) and 97.1% (F2), indicating efficient incorporation of nimesulide into the lipid vesicles. Direct determination yielded a comparable value for F1 (88.7%), while a lower value was obtained for F2 (42.6%), likely due to incomplete disruption of the liposomal pellet or extraction-related losses.

The liposomes exhibited micrometer-sized vesicles characteristic of multilamellar systems obtained by thin-film hydration. Drug-loaded liposomes showed larger mean particle sizes (7.81 µm for F1 and 10.20 µm for F2) than the corresponding empty liposomes, indicating successful drug incorporation. F2 produced larger and more polydisperse vesicles, suggesting that the higher Tween 80 content influenced vesicle formation. Both formulations displayed near-neutral zeta potentials (+0.12 mV for F1 and −0.15 mV for F2), consistent with sterically stabilized phosphatidylcholine-based liposomes.

FTIR spectra of the drug-loaded liposomes showed no significant shifts in the characteristic bands of nimesulide or the excipients, indicating the absence of major drug-excipient interactions. The intensity of the characteristic nimesulide bands, particularly the aromatic nitro stretching band at 1515 cm^{-1}, was markedly reduced compared to the pure drug, suggesting successful incorporation of nimesulide into the lipid matrix and a low amount of surface-associated crystalline drug.

Conclusion

Nimesulide-loaded liposomes were successfully prepared by the thin-film hydration method, achieving high encapsulation efficiencies (>90% by indirect determination). Drug incorporation resulted in an increase in vesicle size compared with the corresponding empty formulations, while both systems exhibited near-neutral zeta potentials characteristic of phosphatidylcholine-based liposomes. FTIR analysis showed no significant drug–excipient interactions and confirmed the incorporation of nimesulide within the lipid matrix. These findings demonstrate the suitability of the developed liposomal systems as carriers for nimesulide and support their further development as liposomal gel formulations for dermal delivery.

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