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Short communication

Formulation, characterization and comparison of mucoadhesive alginate biofilms loaded with dexamethasone delivery carriers

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory disorder of the oral mucosa characterized by recurrent lesions and an unclear etiology. Currently, no definitive cure exists, and management is primarily symptomatic, with topical corticosteroids representing the main therapeutic option (Didona et al., 2022). However, effective drug delivery to the oromucosal environment remains challenging due to rapid salivary clearance, enzymatic activity, and limited mucosal retention.

Therefore, the aim of this study was to develop and characterize bioadhesive sodium alginate/sodium carboxymethylcellulose (SA/CMC) biofilms incorporating advanced drug delivery systems, namely nanostructured lipid carriers (NLC) and microsponges (MS), loaded with dexamethasone (DEX), to enhance local retention and sustained drug delivery at the site of application.

Materials and methods

Materials

Sodium alginate and sodium carboxymethylcellulose (Aldrich), dexamethasone (Alkaloid AD), ethyl cellulose (Sigma) and Poloxamer 407 (BASF) were used. All other reagents were of analytical grade.

Methods

Preparation of MS: MS were prepared using quasi-emulsion solvent evaporation. Ethyl cellulose (100 mg) and DEX (20 mg) were dissolved in dichloromethane:methanol (9:1, *v/v*). This organic phase was emulsified into 25 mL of 0.2% PVA under high-speed homogenization (3600 rpm, 15 min), followed by stirring at 100 rpm until solvent evaporation. The obtained MS were sonicated for 5 min prior to use.

Preparation of NLC: NLCs were prepared using a hot emulsification–solvent evaporation method. An ethanol based organic phase consisted of oleic acid: Phospholipon 90H (1:1.15, *w/w*) and DEX (100 mg) was mixed with an aqueous phase containing 3% Tween 80 and Poloxamer 407 (30 mg) at 65°C under stirring (250 rpm). The organic phase was added dropwise, followed by homogenization at 9500 rpm for 5 min and cooling at 4 °C overnight.

Preparation of biofilms: Biofilms were prepared using a modified solvent casting method. SA and CMC (0.3:0.01, *w/w/w*) were dissolved in 30 mL distilled water at 60°C under stirring (300 rpm) until complete dissolution. Glycerol (0.3 mL) was added as a plasticizer, followed by dropwise addition of 0.6

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mL of 4% $CaCl_2$ under stirring at 500 rpm. The mixture was stirred for 18 h and cast to dry for 96 h. Drug-loaded systems were incorporated into the films as follows: NLC-loaded films: 5:1 mass ratio; MS-loaded films: 5:2.5 mass ratio; Control films: SA/CMC film with 10% DEX solution.

Particle size and particle size distribution was measured using laser diffraction (Mastersizer 2000), with refractive index and absorption index for MS/NLC set to 1.52/0.1 and 1.348/0.001 respectively.

Encapsulation efficiency was determined indirectly by quantifying free drug after separation using Vivaspin ultrafiltration units (100 kDa MWCO) via centrifugation (4000 rpm, 25°C, 25 min, 4 cycles). The supernatant was analyzed using UV-Vis spectrophotometry at 243 nm.

In vitro drug release was evaluated using an *in vitro* membrane dialysis method (MEMBRA-CEL® dialysis tubing, MWCO 7000 RC, Serva Feinbiochemica GmbH, Germany) in phosphate buffer (pH 6.8) at 37°C under stirring (100 rpm). Samples were withdrawn at predefined intervals up to 5 h and analyzed at 243 nm.

Mechanical properties were assessed using oscillatory rheometry (MCR 92, Anton Paar). Amplitude sweep tests (37°C, 1 Hz, 0.01–10% strain) and creep–recovery tests (3 and 10 Pa stress, 300 s) were performed to evaluate viscoelasticity, deformation, and structural recovery.

Results and discussion

NLCs exhibited a mean particle size (D50: 0.161 µm; Span: 0.284), while MS showed a larger size (D50: 2.582 µm; Span: 1.904), indicating a uniform particle distribution in both systems. The nanoscale size of NLCs may favor improved interaction with the mucosal surface and enhanced drug availability, whereas MS are more likely to remain within the mucosal matrix, contributing to prolonged local retention. Both systems demonstrated high dexamethasone encapsulation efficiency (NLC: 97%, MS: 93%), confirming efficient drug loading.

Drug release studies showed that both carrier-loaded films provided more controlled and prolonged release during the examined period of 5 h compared to the free drug film due to the additional diffusion barriers of the polymer matrix and the presence of embedded carriers as well as the carriers (NLC - 34.91% and free MS - 79.11%). MS-loaded films exhibited an initial burst release (3.6%), followed by a slower and sustained release up to 20.02% at 5 h. In contrast, NLC-loaded films showed a faster but still controlled release, reaching 28.87% at 5 h. The control film exhibited the highest overall release (35.78%), reflecting the absence of encapsulation systems. This sustained release behavior is advantageous for oral mucosal application, as it maintains prolonged local dexamethasone availability, which is essential for the management of oral lichen planus.

Rheological analysis confirmed viscoelastic, shear-thinning, and predominantly elastic behavior of all films. However, incorporation of MS and NLC altered the mechanical properties of the polymer network, resulting in improved flexibility and spreadability. These properties are important for uniform application over the oral mucosa and adaptation to dynamic oral movements. Creep–recovery tests showed reduced elastic recovery for MS (14.28%) and NLC (10.81%) compared to the control (38.69%), indicating increased deformability, which may support better mucosal adaptation and prolonged residence time.

Conclusion

Overall, the integration of advanced drug carriers into bioadhesive SA/CMC films significantly influenced structural, mechanical, and release properties. These modifications enabled tunable drug release profiles and prolonged residence behavior, which are essential for maintaining local drug availability in the challenging oromucosal environment.

References

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