UNIVERSITI TEKNOLOGI MARA

FROM FORMULATIONS TO FUNCTIONALITY: TANNIC ACID CROSSLINKED GELATINE AS EXTENDED-RELEASE HYDROPHILIC MATRICES FOR BUCCAL DELIVERY

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ABSTRACT

Gelatine, a biopolymer known for its rapid dissolution at physiological temperature and limited mucoadhesive properties, is suboptimal as a mucoadhesive polymer for buccal film formulations with an extended mode of action. This study aimed to evaluate the potential of the gelatine films cross-linked with tannic acid (GelTA) as mucoadhesive matrices for extended buccal drug delivery. Initially, blank GelTA films were prepared using the solvent evaporation technique and evaluated for their mechanical, mucoadhesive, and dissolution characteristics. The key formulation variables included gelatine source (bovine and fish), tannic acid concentrations, the pH of the film-forming solutions, and the type and concentration of plasticisers. In the second stage, a subset of films was further analysed, exploring their antimicrobial and antioxidant properties and evaluating their stability under varying storage conditions. The final research stage focused on the evaluation of GelTA films as carriers for the model drug, cetylpyridinium chloride (CPC). After determining the solubility of CPC in selected GelTA films, they were loaded with 20% and 40% w/w CPC and subjected to comprehensive characterisation. The results demonstrated a significant enhancement in the dissolution time of GelTA films compared to non-crosslinked gelatine films, while maintaining their water-absorbing capacity. In particular, BG-TA5-GLY20-7[1] exhibited a 1.6-fold increase in mucoadhesivity compared to its non-crosslinked counterpart (BG-GLY20[2]). Additionally, blank GelTA films exhibited superior antioxidant properties compared to BG-GLY20. The solubility of CPC in GelTA films containing 2% and 5% tannic acid increased by 2 and 3 times, respectively, compared to BG-GLY20. GelTA films exhibited extended CPC release over 360 min, unlike BG-GLY20 which released CPC in less than 120 min. Based on drug release data, BG-TA2-GLY20-7 loaded with 40% w/w CPC effectively achieved the required concentration to inhibit four targeted microorganisms: *C. albicans*, *S. mutans*, *S. aureus*, and SARS CoV2. Additionally, GelTA films exhibited zero-order drug release kinetics and CPC release occurred through erosion. Regarding retention time on chicken pouch mucosa, BG-TA5-GLY20-7 and BG-TA2-GLY20-7[3] outperformed BG-TA2-GLY20-8[4]. In particular, CPC did not permeate significantly through chicken pouch mucosa membranes, supporting the suitability of these films for topical drug delivery systems. In conclusion, GelTA films prepared at pH 7 exhibited superior characteristics for extended intraoral CPC delivery, considering the CPC release profile, erodibility, and adhesion times. However, stability studies indicate the need for an oxygen-free environment during GelTA film storage.

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[1] Bovine GelTA film containing 5% w/w tannic acid, 20% w/w glycerine prepared at pH 7

[2] Bovine non-crosslinked gelatine film

[3] Bovine GelTA film containing 2% w/w tannic acid, 20% w/w glycerine prepared at pH 7

[4] Bovine GelTA film containing 2% w/w tannic acid, 20% w/w glycerine prepared at pH 8

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CHAPTER 1
INTRODUCTION

1.1 Research Background

Buccal administration involves placing a dosage form between the cheek (or lip) and the gingiva, adjacent to the teeth (Shipp et al., 2022). The buccal mucosa has gained considerable attention as an alternative route of drug delivery aimed at local or systemic effects (Nour et al., 2023; Pamlényi et al., 2023). Systemic drug delivery through the buccal route overcomes many limitations related to the peroral route, including bypassing the challenges posed by the harsh and degrading acidic environment of the stomach, enzyme activity, and first-pass metabolism (Gawas et al., 2016). Furthermore, the highly vascularised nature of the buccal mucosa adds the benefit of rapid systemic absorption, resulting in a rapid onset of drug action (Montenegro-Nicolini & Morales, 2017). Buccal administration is particularly beneficial for paediatrics, geriatrics, and patients who have difficulty swallowing or who are prone to nausea or vomiting (Pamlényi et al., 2023). Furthermore, its non-invasive nature and low level of irritability improve patient compliance compared to the parenteral route (de Carvalho et al., 2023). For localised drug delivery, the buccal route establishes direct and intimate contact between therapeutic agents and their target sites, resulting in improved treatment efficacy while minimising systemic side effects. Various therapeutic agents, such as antiseptic, anti-inflammatory, and antineoplastic agents, hold potential for local delivery to the oral cavity (Lindert & Breitkreutz, 2017).

In contrast to the sublingual route, the buccal route is preferred for sustained-release drug delivery systems (Rathbone et al., 2015). Conventional dosage forms, such as immediate-release tablets and capsules or solutions, are unable to provide sustained drug release due to their brief residence time in the oral cavity (Hebbale et al., 2017). Over recent decades, the concept of mucoadhesion has evolved, leading to the development of a diverse range of mucoadhesive dosage forms. Mucoadhesion refers to a condition in which two materials are held together for an extended duration, one of them being mucus or a mucous membrane (Pham et al., 2021). Mucoadhesive drug delivery systems prolong the retention of the dosage form at the application or