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Formulation development and evaluation of lidocaine hydrochloride loaded in chitosan-pectin-hyaluronic acid polyelectrolyte complex for dry socket treatment

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ABSTRACT

The main purpose of this study was to assess a lidocaine hydrochloride-loaded chitosan-pectin-hyaluronic polyelectrolyte complex for rapid onset and sustained release in dry socket wound treatment. Nine formulations (LCs) of lidocaine hydrochloride (LH) loaded into a chitosan–pectin–hyaluronic polyelectrolyte complex (PEC) were assessed using full factorial design (two factors × three levels). The formulations ranged between 4 and 10% w/w LH and 0.5–1.5% w/w HA. The following physicochemical properties of LCs were characterized: size, zeta potential, % entrapment efficiency, viscosity, mucoadhesiveness, % drug release, morphology, storage stability, and cytotoxicity. The particle size, zeta potential, % EE, viscosity, and % mucoadhesion increased with increasing LH and HA concentrations. Rapid release of LH followed a zero-order model, and a steady-state percentage of the drug was released over 4 h. LCs were found to be non-cytotoxic compared to LH solution. LH loaded into PEC demonstrated appropriate characteristics—including suitable rate of release—and fit a zero-order model. Furthermore, it was not cytotoxic and showed good stability in a high-HA formula, making it a promising candidate for future topical oral formulations.

1. Introduction

Dry socket, or alveolar osteitis, is the most common complication after tooth extraction and surgical removal of the wisdom tooth (Tarakji et al., 2015; Shevel, 2018). Dry socket pain starts one to three days after extraction or surgical removal of a wisdom tooth and usually presents with metallic dysgeusia and halitosis (Shevel, 2018). The pain (which can be 7–10 on the pain scale) is a significant problem in dry socket patients (Kamal et al., 2020), requiring administration of a topical analgesic (Metin et al., 2006). The primary objective for dry socket treatment is to attenuate the pain severity until sufficient epithelium granulation occurs to cover bone and nerve. The epithelialization time is variable but may be completed within 5 to 10 days (Veale, 2015). Thus, pain remedies should relieve acute pain (within minutes) and be released over a prolonged period for pain reduction until the re-epithelialization (or wound healing process) is completed.

Lidocaine hydrochloride (LH) has long been used as a topical dental anesthetic. The onset of LH is rapid, 1 to 2 min, and it reaches its highest efficacy within 5 min (Lee, 2016). Lidocaine is widely used in dental clinics and is available over-the-counter at a concentration of approximately 2–10% w/v in solution, gel, ointment, and spray forms. The incidence of a true allergic reaction to local lidocaine anesthetic is <1%, suggesting it is safe. Lidocaine and

Abbreviations: HA, hyaluronic acid; LC, lidocaine hydrochloride loaded in chitosan-pectin-hyaluronic acid polyelectrolyte complex; LH, lidocaine hydrochloride; PDI, polydispersion index; PEC, Chitosan-Pectin- Hyaluronic acid Polyelectrolyte Complex; Zn, zinc sulphate.

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