Preparation and Evaluation of Triamcinolone Acetonide-loaded Hydrogel using an Electron Beam

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ABSTRACT SUMMARY

A triamcinolone acetonide-loaded hydrogel was prepared by electron beam irradiation and evaluated for use as a buccal mucoadhesive drug delivery system. A poloxamer modified to have vinyl end groups was used to prepare the hydrogel via an irradiation cross-linking reaction. Carbopol was introduced to improve the mucoadhesive properties of the hydrogel. The in vitro release of triamcinolone acetonide from the hydrogel was examined at 37°C. To investigate the topical therapeutic effect of triamcinolone acetonide on wounded rat skin and buccal mucosa, the appearance and histological changes were evaluated for 15 days after treatment with saline, triamcinolone acetonide solution, triamcinolone acetonide hydrogel, and blank hydrogel.

INTRODUCTION

Radiation-induced cross-linking offers several advantages, including a lack of need for cross-linking agents, initiators, and the removal of unreacted materials, as well as simultaneous sterilization through the cross-linking process, which makes the product suitable for medical applications. Common cross-linking processes require long reaction times, while cross-linking by irradiation takes only a short time. As physical properties are controlled by modulation of the strength of irradiation and hydrogel forms are prepared using molds of various types and shapes, radiation technology has been used for biomedical materials and other industries.

Here, we prepared a triamcinolone acetonide-loaded hydrogel by radiation-induced cross-linking to overcome the gel’s weak physical strength and mechanical properties. The release of triamcinolone acetonide from the hydrogel and histological changes in wounded skin and the buccal mucosa were investigated.

EXPERIMENTAL METHODS

Thermoreversible hydrogels were prepared using the cold method [1]. Briefly, diacrylated poloxamer (D-Pol) and triamcinolone acetonide were dissolved in distilled water as described previously [2]. The D-Pol was synthesized by the addition of an acryloyl group to poloxamer 407 according to a previously reported method [2]. To increase the mixture’s mucoadhesive properties, carbopol was added to the D-Pol solution.

In vitro drug release from the hydrogel was investigated at 37°C for 48 h using a Franz diffusion cell (Logan Instruments, Somerset, NJ). At predetermined time points, 1 mL of sample was withdrawn from the acceptor compartment, and the sampled volume was replaced with PBS (pH 7.4). The withdrawn samples were filtered and analyzed.

For the skin model, the dorsal skin samples were excised and removed with surgical scissors and forceps [3]. For the buccal model, Ulceration was induced by excision of the mucosal membrane using a biopsy punch 4 mm in diameter on the left cheek [4]. Over 3 days, the wounds were dressed with normal saline (control), 0.1% triamcinolone acetonide solution, 0.1% triamcinolone acetonide-loaded hydrogel, or blank hydrogel for 8 h daily under moist and sterile conditions. Lesions from the dorsal skin and oral cavity obtained by necropsy were fixed in formalin and embedded in paraffin for routine histological processing. Sections (4-μm thick) obtained from each paraffin block were stained with hematoxylin and eosin.

RESULTS AND DISCUSSION

Triamcinolone acetonide was released constantly from the gel formulation at 37°C and reach 100% at about 48 h (Fig. 1). No initial burst was observed, which may be useful in achieving a prolonged therapeutic effect.
To visualize the changes in skin regeneration by triamcinolone acetonide, dorsal rat skin of samples were treated with the triamcinolone acetonide hydrogel after wounding a biopsy punch 6 mm in diameter. The time course of changes in the wounded skin is shown in Fig. 2. There were no significant differences in gross observation among the groups on day 1 or 2. Hyperemia, hemorrhage, and edema were observed around the wound, and there were no pustules and no recovery.

The histological appearance of the buccal mucosal regions in the control and experimental groups is shown in Fig. 3. On day 2, there were no significant differences among the groups in terms of the histopathological observations, inflammatory cells, hyperemia and/or hemorrhage, or fibrin found scattered in the wound. The wound space was filled with granulation tissue, and fibroblast infiltration into the tissue with fibrin deposition and inflammatory cell infiltration were seen under the epithelial tissue in the wound site. However, the inflammatory reaction in the group treated with the triamcinolone acetonide loaded hydrogel was milder than in the other groups. On day 8, the wound surface was largely covered by an exudate, blood clots, and fibrin, and regeneration of the epithelium was observed along the sides of the wound. The inflammatory cell number in the wound site was increased. The inside of the scar tissue was filled with fibrin, connective tissue, and inflammatory cells, and the tissue was full of regenerated vessels. In the group treated with the triamcinolone acetonide-loaded hydrogel, the inflammatory reaction was milder than in the other groups and the wound surface was completely covered with regenerating, hyperkeratotic, thickened epithelial cells.

CONCLUSION
Our results indicate that the triamcinolone-acetonide hydrogel showed sustained drug release behavior, while causing no significant histopathological changes in buccal and skin tissues. Therefore, this hydrogel system may be a powerful means of drug delivery for buccal administration with controlled release and no tissue irritation.

REFERENCES