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Imiquimod-Loaded Chitosan-Decorated Di-Block and Tri-Block Polymeric Nanoparticles Loaded In Situ Gel for the Management of Cervical Cancer

Aliyah Almomen [1], Mohamed Badran [2], Adel Ali Alhowyan [2] , Musaed Alkholief [2], and Aws Alshamsan [2]
[1]Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University,
Riyadh 11495, Saudi Arabia
aalmomen@ksu.edu.sa; mbadran@ksu.edu.sa
2 Department of Pharmaceutics, College of Pharmacy, King Saud University
, Riyadh 11495, Saudi Arabia
adel-ali@ksu.edu.sa; malkholief@ksu.edu.sa; aalshamsan@ksu.edu.sa

Extended Abstract

Cervical intraepithelial neoplasia (CIN) is a condition that precedes cervical cancer, the second most common cancer in women worldwide [1]. The primary causes of CIN and invasive cervical cancer are the human papillomavirus (HPV) virus strains 16 and 18. Current treatments for high-grade CIN involve surgical excision, associated with recurrence rates and increased risk of spontaneous abortion [2]. Non-surgical alternatives, such as imiquimod (IMQ), are needed for managing CIN. IMQ induces the expression of cytokines and activates T-cells, leading to a tumor-directed immune response associated with HPV clearance [3-5]. However, IMQ's poor water solubility and side effects may limit its effectiveness [6]. Polymeric nanoparticles (NPs) are being researched for targeted drug delivery due to their advantages, such as sustained drug release and improved local availability [7]. Polylactic acids (PLAs) and polycaprolactone (PCL) have gained attention for their biodegradable properties and potential for biomedical applications.[8] Mucoadhesive polymeric systems like chitosan (CS) have been used to improve the residence time of vaginal drug delivery systems[9, 10]. Poloxamer in situ gel-forming systems have gained attention for their ability to transform from a liquid formulation into a gel-like state at the target site [9, 10]. As a result, this study aims to improve the efficacy and reduce the side effects of IMQ by developing a local vaginal drug delivery system based on the loading of IMQ into NPs coated with CS and loaded in an in-situ hydrogel.

Method: IMQ nanoparticles were created using polylactic-co-glycolic acid (PLGA), polycaprolactone (PCL), poly lactide-co-caprolactone (PLA-PCL), and poly L-lactide-co-caprolactone-co-glycolide (PLGA-PCL). The mucoadhesive properties of chitosan (CS) were then added to the surfaces of the IMQ NPs. The NPs were then mixed with poloxamer hydrogels. The size and morphology of the NPs, as well as their encapsulation efficiency (EE), in vitro drug release, gel characterization, ex vivo drug permeation, and in vitro safety and efficacy, were all studied.

Results: IMQ NPs and CS-coated NPs (CS-IMQ NPs) were prepared in two batches. In general, both types of NPs were uniformly spherical in shape, with average particle sizes of 237.3 4.7 and 278.2 5.4 nm, respectively, and EE% of 61.48 5.19% and 37.73 2.88 for IMQ NPs and CS-IMQ NPs. In comparison to free IMQ, both systems reduced the production of inflammatory cytokines by at least 25%.

Conclusion: IMQ and CS-IMQ NP in situ gels improved drug stability and release, as well as IMQ penetration through vaginal tissues. Furthermore, the new systems increased IMQ's cytotoxic effect against CC cells while decreasing inflammatory responses. As a result, these systems could be a viable alternative to commercial IMQ systems for CC management.

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