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Article

Sequential Release of Paclitaxel and Imatinib from Core–Shell Microparticles Prepared by Coaxial Electrospray for Vaginal Therapy of Cervical Cancer

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Abstract: To optimize the anti-tumor efficacy of combination therapy with paclitaxel (PTX) and imatinib (IMN), we used coaxial electrospray to prepare sequential-release core–shell microparticles composed of a PTX-loaded sodium hyaluronate outer layer and an IMN-loaded PLGA core. The morphology, size distribution, drug loading, differential scanning calorimetry (DSC), Fourier transform infrared spectra (FTIR), in vitro release, PLGA degradation, cellular growth inhibition, in vivo vaginal retention, anti-tumor efficacy, and local irritation in a murine orthotopic cervicovaginal tumor model after vaginal administration were characterized. The results show that such core–shell microparticles were of spherical appearance, with an average size of 14.65 µm and a significant drug-loading ratio (2.36% for PTX, 19.5% for IMN, *w*/*w*), which might benefit cytotoxicity against cervical-cancer-related TC-1 cells. The DSC curves indicate changes in the phase state of PTX and IMN after encapsulation in microparticles. The FTIR spectra show that drug and excipients are compatible with each other. The release profiles show sequential characteristics in that PTX was almost completely released in 1 h and IMN was continuously released for 7 days. These core–shell microparticles showed synergistic inhibition in the growth of TC-1 cells. Such microparticles exhibited prolonged intravaginal residence, a >90% tumor inhibitory rate, and minimal mucosal irritation after intravaginal administration. All results suggest that such microparticles potentially provide a non-invasive local chemotherapeutic delivery system for the treatment of cervical cancer by the sequential release of PTX and IMN.

Keywords: coaxial electrospray; core–shell microparticles; sequential release; cervical cancer; paclitaxel; imatinib

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1. Introduction

Combination therapy is widely used in clinical practice [1–4]. Many micron/nano preparations have been designed for the co-administration of different anti-tumor drugs [5–7]. However, the simple simultaneous administration of two or more drugs may not obtain satisfactory clinical outcomes, mainly because of unfavorable drug–drug interactions, differences in pharmacokinetics, and unsynchronized biodistribution [8–11].

In comparison to simultaneous administration, formulations that can precisely release different drugs in a controlled and, more specifically, sequential manner can provide maximized therapeutic efficacy and reduced adverse effects by minimizing drug–drug interactions, reducing side effects that may be associated with simultaneous co-delivery,