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Fabrication of novel niclosamide-suspension using an electrospray system to improve its therapeutic effects in ovarian cancer cells *in vitro*

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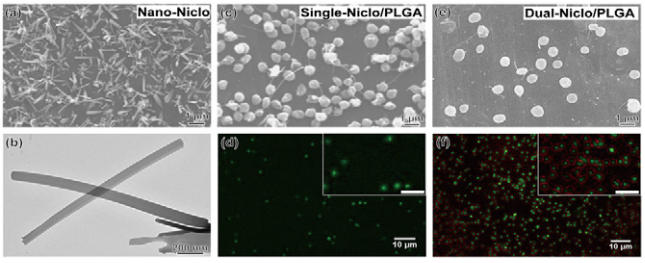
HIGHLIGHTS

- Niclosamide, a hydrophobic drug, was found to show inhibitory activity against human ovarian cancer.
- We utilize the electrospray system to produce a series of niclosamide-suspension.
- Niclosamide shows stronger inhibitory activity against the CP70 cell than that on SKOV-3 cell.
- Compared to conventional formulation, our suspension shows better anti-proliferative ability.
- The effectively inhibitory concentration of niclosamide-suspension is also reduced

GRAPHICAL ABSTRACT



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ABSTRACT

This work describes the feasibility of using a single- or dual-capillary electrospray (ES) system to produce a series of novel niclosamide suspensions. Analytical results indicate that the ES system generates a homogeneous suspension of pure niclosamide or niclosamide-encapsulated poly(D,L-lactic-*co*-glycolide) (PLGA) particles in phosphate buffer saline (PBS). Also, the suspension solution remains stable for several months. SEM images reveal that the pure niclosamide particles all have a rod-like shape (transversal length: 105 ± 21 nm, longitudinal length: 493 ± 151 nm) and the niclosamide-encapsulated PLGA particles are spherical with a diameter of approximately 584–662 nm. Additionally, qualitative and quantitative analyses are performed using UV–vis spectroscopy, which yields two characteristic absorption peaks that are attributed to niclosamide (336 nm and 376 nm, in PBS medium). Based on use of this information as an index, a standard curve is established for quantification. Raman spectra analysis indicates that the generated pure niclosamide or niclosamide-encapsulated PLGA particles are all composed of niclosamide monohydrate instead of an anhydrous form of niclosamide. According to *in vitro* cell studies, this novel suspension of niclosamide with or without PLGA encapsulation exhibits a better anti-proliferative ability against CP70 and SKOV-3 ovarian cancer cells than that of conventional formulation. In particular, the anti-proliferative ability of niclosamide-encapsulated PLGA particles against CP70 cells is better than that of pure niclosamide suspension, which is likely caused by the more efficient intracellular delivery.

1. Introduction

Niclosamide (Niclo) was originally developed as an anthelmintic drug that is active against most tapeworms (Fig. 1a). To date, several research groups have reported its use in human antitumor

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