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Abstract

Design of Nanoplatforms for Targeted Delivery of Irinotecan †

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1. Introduction

Irinotecan is an antineoplastic used for the treatment of different types of cancer and solid tumors (rectal, colon, ovarian and glioblastoma) [1,2]. However, its use is currently associated with serious side effects, such as neutropenia and severe diarrhea that determines significant dehydration and could potentially lead to death [2]. An ideal drug delivery system for antitumoral agents needs to be designed to significantly improve the classical treatment, possessing protective action to prevent drug degradation, which is related to an increased drug concentration that enriches the tumoral sites. Moreover, the nanoparticles should be synthesized to ensure a selectivity towards the accumulation in tumoral cells to reduce side effects on healthy cells [3]. The aim of this study was to assess the influence of the support on the irinotecan release from developed systems, an investigation of how the carrier modification (folate moiety binding or ulvan deposition) can lead to a modulation of irinotecan release kinetics from the proposed mesoporous silica-type carriers in correlation with their biological activity.

2. Materials and Methods

The mesoporous supports and cytostatic agent-loaded supports were characterized by specific techniques: XRD, FT-IR spectroscopy, N2 adsorption–desorption isotherms and thermal analysis. The cell viability of irinotecan-loaded supports was tested on tumoral colon cells (Caco-2 and HT-29). The cell cycle analysis was performed using flow-cytometry (HT-29) for irinotecan alone or loaded on ulvan-silica supports in comparison with the corresponding nanoplatforms.

3. Results

A modulation of irinotecan release from the proposed carriers was obtained, and slower release kinetics was observed from the pristine SBA-15 carrier or that modified with folate moiety (up to 40% in 52 h in PBS pH 5.7), while a faster release of the cytostatic agent was obtained from silica-ulvan-type carriers for which a complete release of the antineoplastic agent was achieved in 8 h in PBS at a pH of 7.6. For irinotecan-loaded silica-ulvan supports, significant toxicity was noticed against tumoral cell line HT-29. Irinotecan-loaded ulvan-silica nanoplatforms influenced the cell cycle (HT-29) at 250 μg/mL. It was

observed that the cells are trapped in a higher proportion in the synthesis stage; therefore, a reduction in cell growth is observed.

4. Conclusions

Iri@SBA-NH-folate system would be recommended for a targeted antitumoral action, with diminished side effects, while if a complete delivery of the cytostatic agent in a shorter time is desired, a silica-ulvan-type nanoplatform could be used for Irinotecan.

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