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Development of Antibody-Conjugated Arsenite Embedded Nanoparticles (Nps) With Potential to Target Primary, and Chemo and Radio Resistant Nasopharyngeal Carcinoma

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ABSTRACT

Nasopharyngeal carcinoma (NPC) is a clinical, biological and histological entity that stands out from other carcinomas of the head and neck by its relationship with the Epstein Barr virus (EBV), Although radiotherapy (RT) and the radiotherapy-chemotherapy combination remain the therapies of choice for non-metastatic forms and advanced cases compared to chemotherapy alone, cases of tumor recurrences characterized by the expression of the major oncogene of viral origin (LMP1). To cope with these forms of therapeutic resistance, we are working on the preparation of a nanometric tool capable of encapsulating radio-sensitizing anticancer molecules by targeting tumor cells.The targeted addressing of the molecule allows its accumulation in the target site expressing the surface oncogene of EBV by reducing its exposure to healthy tissue. Our aim is to design a nano-vector, by simple emulsion, based on two biopolymers (sodium alginate and gelatin) to encapsulate sodium arsenite.

Keywords: nanoparticles, nasopharyngeal carcinoma, sodium arsenite, biopolymers.

1. Introduction

Nasopharyngeal carcinoma (NPC) is a highly metastatic carcinoma of the head and neck which is often associated with Epstein Barr virus (EBV) infections. It represents one of the most important cancers in our country, with an ASR of 3.5 [1]. Although radiotherapy (RT) and the radiotherapy-chemotherapy remain the therapies of choice for non-metastatic forms and advanced cases, chemo and radio resistance and tumor recurrence will affect 30% to 50% of the affected cases [2, 3].To cope with these forms of therapeutic resistance, we developed a nanometric tool capable of encapsulating arsenite and addressing the cytotoxic drug [4] in a targeted fashion to tumor acidic tissues expressing the surface oncogene of EBV. To this aim, we here designed a nano-vector, by simple emulsion, based on two biopolymers (sodium alginate and gelatin) to encapsulate arsenite.

2. Experimental

DLS, SEM and TEM were used to evaluate size and confirm the generation of nanoparticles (NP). Zeta sizer and DSCwere used to evaluate NP stability and melting point. EDXRF, was used for drug encapsulation assessment. DLS and Zeta potential test were used to confirm antibody conjugation.

3. Results and Discussion

The optimization of the morphological aspects of the arsenite-alginate-gelatin nanoparticles (NP) was characterized by DLS, SEM and TEM. Our results indicate that spherical shape NP were obtained with a size of 120.43 ± 8.64 nm. The produced NP showed to be highly stable products with ζ =-63,8 mW and have melting point that varied between 270 and 320°C as tested by Zeta sizer and DSC. The rate of arsenic encapsulation, analyzed by EDXRF, showed to be of 60% ± 10%. Analysis of the drug release in tumor mimicking environment (pH: 5.5 vs pH: 7.4) showed that arsenite release was improved in an acidic milieu. Finally, we functionalized our nano-administration system by specific antibody (anti-LMP1) to target a specific viral protein expressed on tumor cells. This event increased the mean NP size and modified its zeta

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potential thereby confirming the successful antibody-nanoparticles conjugation.

4. Conclusions

All together our results indicate that we developed antibody-conjugated arsenite embedded nanoparticles (NPs) with potential to detect LMP-1+ tumors, as a mean to eliminate primary and chemo and radio resistant nasopharyngeal carcinoma tumors.

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