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Abstract

Development and Evaluation of AT11-Guided Liposomes for Human Papillomavirus Cancer †

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Abstract: Conventional anticancer therapies present low specificity, leading to several secondary effects. To improve these drawbacks, aptamers able to fold into G-quadruplex (G4) are being used to promote drug accumulation in cancer cells. AS1411 is a G4 aptamer able to recognize nucleolin, a protein overexpressed on cancer cells' surfaces. This aptamer was tested in clinical trials, but it showed low response rates and suboptimal pharmacokinetics. Nevertheless, AS1411 is being used as a targeting agent. Moreover, AS1411 derivatives were developed, with improved toxicity and high affinity to nucleolin. Thus, we propose to use AT11, an AS1411 derivative, to functionalize liposomes and improve the selectivity of C_8 (a potential anticancer drug) into oral cancer. Therefore, we produced liposomes (blank or C_8-associated) by the ethanol injection method to, then, we functionalized them with AT11-TEG-Cholesteryl. The resulting liposomes were characterized by DLS. C_8 association was determined by UV/vis spectroscopy, and the AT11 functionalization was determined by SDS-PAGE. The effect of blank and C_8-associated liposomes on oral cancer and healthy cells' viability was determined by MTT, and its internalization of was visualized by confocal microscopy. Liposomes with hydrodynamic diameters of 148–168 nm were obtained, and C_8 was efficiently associated (~100%). When the cells were treated with blank liposomes, cell viability was almost unaffected. After treating with C_8-associated liposomes, both cell lines showed a dose–response effect. Additionally, we observed that AT11-liposomes can internalize and reach the cytoplasm of cells. Overall, these findings suggest that the tested liposomes are promising drug carriers for oral cancer therapy.

Keywords: aptamer; liposomes; oral cancer

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