Development of novel aptamer-functionalized liposomes for oral cancer therapy

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Introduction

Conventional anticancer therapies present low specificity, leading to several secondary effects. *Pharmaceuticals* **2021**, *14*(7), 671

AS1411 is a G4 aptamer able to recognize nucleolin and is being used as an agent for anticancer drug delivery.

AS1411 derivatives have been proposed, with improved toxicity and high affinity to nucleolin.

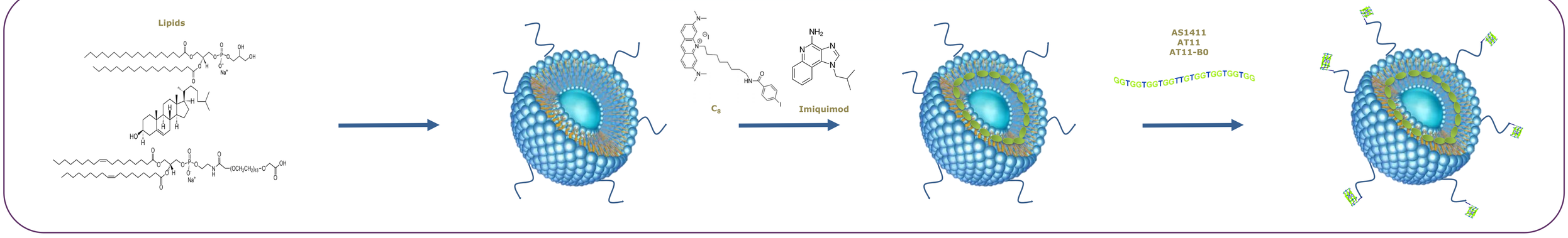
AIM: To synthesize AS1411 derivatives-functionalized liposomes to improve the selectivity of Imiquimod and C_8 into oral cancer cells.

Methodology

Liposomes Synthesis → **Liposomes Characterization** → **Biological Evaluation**

- Chloroform evaporation
- Lipidic film hydration
- Freeze/Thaw cycles
- Extrusion
- NH_2-Aptamers Functionalization

Liposomes Preparation



Results

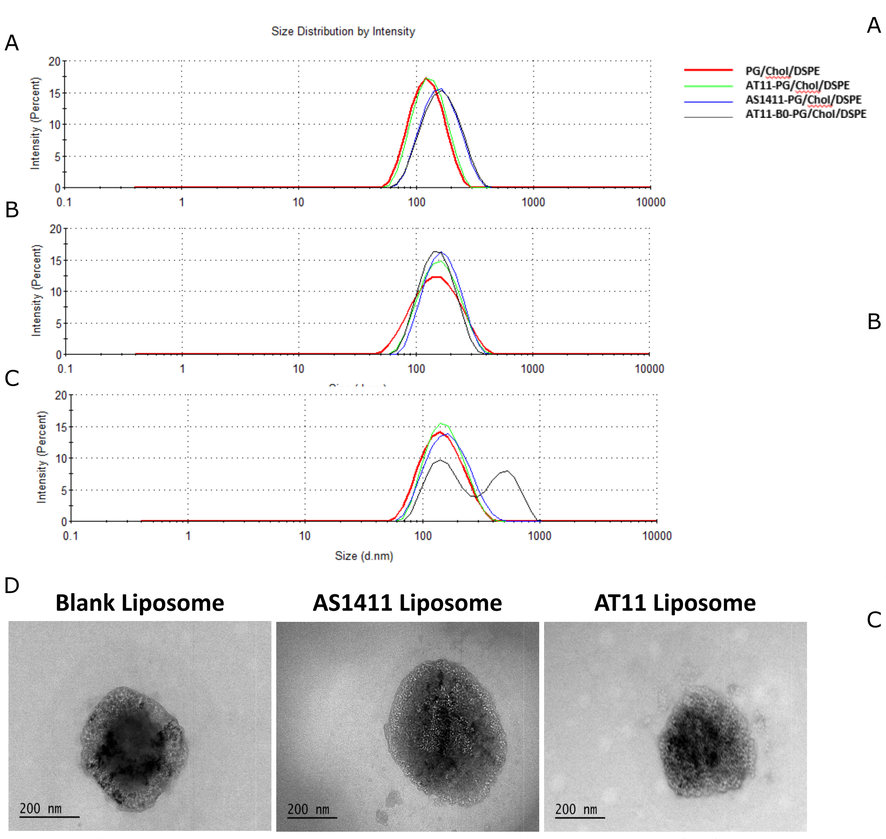


Figure 1. Dynamic light scattering size distribution of blank liposomes (red), AS1411-functionalized liposomes (blue), AT11-functionalized liposomes (green) or AT11-B0 functionalized liposomes (black) in (A) buffer solution (PBS), (B) with C_8 or (C) with Imiquimod (IQ) encapsulated. (D) Transmission electronic microscopy images of the liposomes.

A

Hydrodinamic size	Blank Liposome	AS1411 Liposome	AT11 Liposome	AT11-B0 Liposome
PBS	121.8 ± 1.253	139.3 ± 2.108	148.7 ± 0.436	150.5 ± 0.306
C_8	134.9 ± 0.827	153.2 ± 1.050	145.0 ± 0.666	140. ± 0.700
Imiquimod	136.0 ± 0.702	150.6 ± 1.498	144.2 ± 0.503	313.1 ± 25.53

B

PDI	Blank Liposome	AS1411 Liposome	AT11 Liposome	AT11-B0 Liposome
PBS	0.284 ± 0.020	0.189 ± 0.019	0.357 ± 0.016	0.133 ± 0.014
C_8	0.173 ± 0.033	0.165 ± 0.050	0.138 ± 0.003	0.122 ± 0.024
Imiquimod	0.134 ± 0.013	0.127 ± 0.021	0.138 ± 0.003	0.541 ± 0.095

C

% Functionalization yields	AS1411 Liposome	AT11 Liposome	AT11-B0 Liposome
C_8	85.83%	74.45%	79.26%
Imiquimod	87.67%	64.43%	85.64%

Figure 2. (A) Hydrodynamic size, and (B) polydispersity index (PDI) of the different liposomes. (C) Functionalization yields of liposomes with the aptamers.

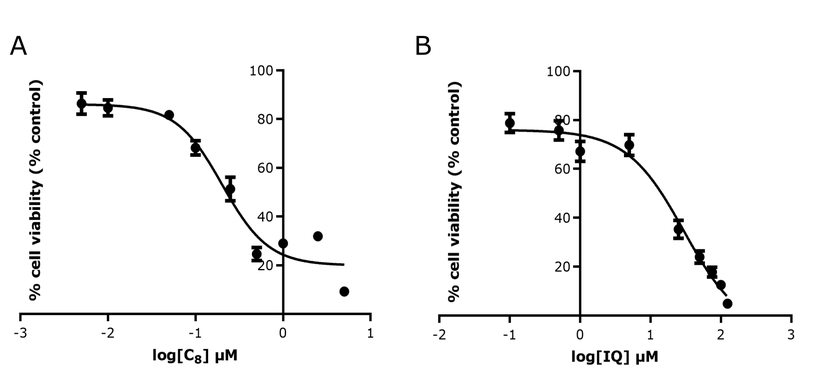


Figure 3. IC_{50} of (A) C_8 and (B) Imiquimod (IQ) in UPCI-SCC-154 oral cancer cell line after 3 days of treatment. The IC_{50} value of C_8 was 0.201 µM and the IC_{50} value of IQ was 30.11 µM.

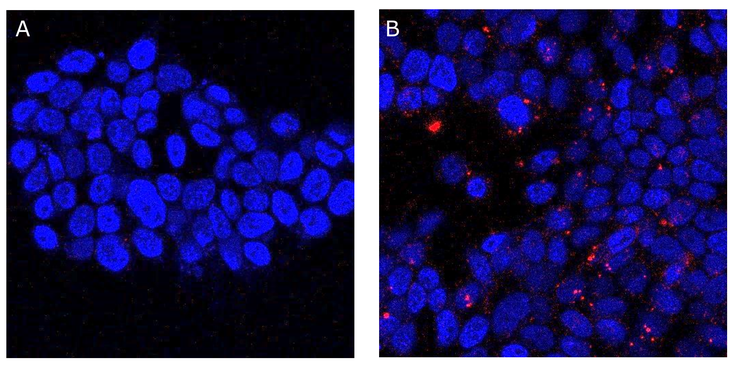
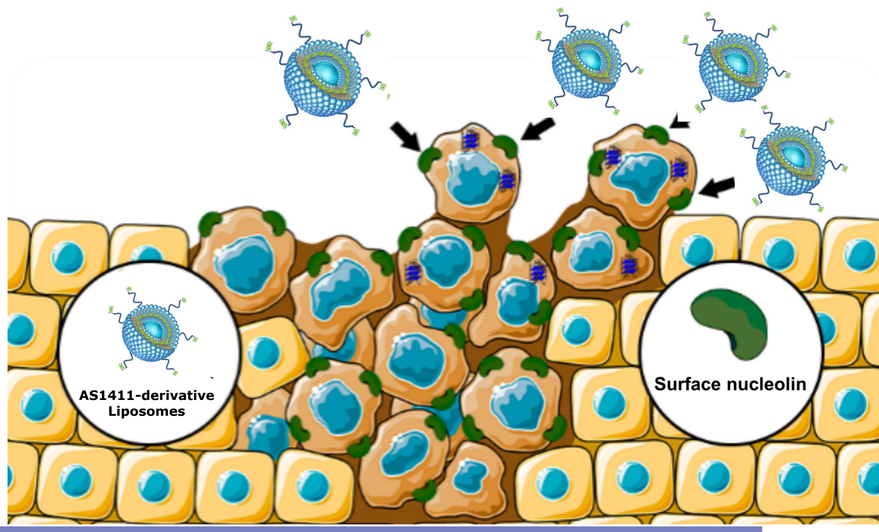


Figure 4. Confocal images of UPCI-SCC-154 cells (A) without or (B) with anti-nucleolin antibody (shown in red) incubation. Cell nuclei are stained with Hoechst 33342 (blue).

Conclusions

- ✓ **Liposomes with sizes up to 200 nm, polydispersity index below 0.4 and functionalization yields up to 85% were obtained.**
- ✓ **UPCI-SCC-154 cells express nucleolin in their surface.**
- ✓ **Through the functionalization of liposomes with the AS1411 derivatives we expect to improve the selectivity of Imiquimod and C_8 into oral cancer cells (UPCI-SCC-154 cell line) and to decrease the toxicity in normal epithelial cells (Het-1A cell line).**



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