SCIENTIFIC REPORT

Stage 1 - Year 2022

Nanovehicle fine-tuning for improved anticancer drug delivery (NanoCanTune)

Project code: PN-III-P1-1.1-PD-2021-0786
Contract no.: PD66/2022
Duration: 01/04/2022 - 31/03/2024
Total budget: 250.000,00 lei
Phase 1/2022: Liposomal nanovehicle design, development and physico-chemical characterization (WP1) Develop a protocol for liposome formulation, drug encapsulation and investigation of loading capacity and encapsulation efficiency (O1) Physico-chemical characterization of novel liposomal formulations of 5-FU (O2)
Stage 1 Budget: 71.090,00 lei

Stage 1 summary:

In this stage, which corresponds to the first 9 months of the project, 6 activities were undertaken for the purpose of designing, developing and physico-chemically characterize liposomal nanovehicles encapsulating the antitumor drug 5-fluorouracil (5-FU), according to Annex II of the funding contract. Also, two of the four objectives of the project were achieved, namely: Development of protocol for liposomal formulation, drug encapsulation and investigation of loading capacity and encapsulation efficiency (O1); Physicochemical characterization of new liposomal formulations with 5-FU (O2).

According to the work plan, 14 preliminary liposomal formulations with different lipid compositions were generated from phosphatidylcholine (PC) and dipalmitoylphosphatidylcholine (DPPC), monocomponent or with cholesterol (Chol), with or without the antitumor drug 5-FU. Liposomal suspensions were obtained through thin film hydration followed by extrusion, which was optimized through process parameter variation and the addition of a sonication step prior to extrusion in order to obtain reproducible results. The optimized protocol was then used for generating 6 liposomal formulations with various compositions from PC, DPPC and distearoylphosphatidylcholine (DSPC) that were characterized in terms of size, surface charge, encapsulation efficiency, loading capacity, as well as stability and *in vitro* controlled release properties. The formulation containing DPPC:Chol in a molar ratio of 60:40 showed the best encapsulation of the antitumor drug 5-FU in terms of estimated intravesicular concentration, but not encapsulation efficiency or loading capacity. The highest encapsulation efficiency of 5-FU was observed in the liposomal formulation with DSPC, which, however, proved to be unstable over time, possibly due to aggregation phenomena. It was also observed that PC-containing formulations provide slower 5-FU release kinetics in the first 4 hours than DPPC or DSPC formulations.

The degree of objective completion for Stage 1 is 100%.