ORT_03 - Evaluation of a betullinic acid nanosystem for cancer therapy

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Introduction: Betulinic Acid (BA), a pentacyclic triterpenoid derived from plants, has different biological activities including antitumor activity in different types of cancer. Its low solubility and half-life limit its effectiveness, and so far, it has not been used in clinical practice. The development of polymeric nanoparticles (PN) was used as a strategy to overcome such limitations PNs as these structures are carriers for molecules capable of modifying their physicochemical and pharmacokinetic properties being used as a targeting strategy for solid and hematological tumors.

Objectives: This study aims to incorporate BA into PNs to improve breast cancer and leukemia therapy.

Methodology: The PN production was performed by the nanoprecipitation method, using the PLGA-PEG polymer. Physicochemical characterization of NP was evaluated by the dynamic light scattering technique (average size, AS and polydispersity index, PdI) and electrophoretic light scattering (zeta-potential, PZ). The BA content loaded into PNs was determined by HPLC method. For efficient targeting to tumor cells, PNs were subjected to functionalization using a transferrin receptor binding peptide, evaluated by cell interaction assay using fluorescently labeled NP on MCF-7 and K562 cell lines, and analyzed by flow cytometry. To assess the toxicity of PN, the MTT assay was performed.

Results: BA-loaded PN showed satisfactory physicochemical characteristics with an AS of 180nm, PdI ~0.20, and PZ -6mV. Gel electrophoresis showed albumin adsorption and corona formation on the NP surface that was decreased on pegylated NP. Flow cytometry analysis of fluorescent peptide-functionalized NP, showed greater interaction with MCF-7 and K562 cell lines when compared to fluorescent non-functionalized NP, evidencing the success of functionalization and interaction with target cells. Finally, unloaded NP and BA-loaded NP, showed to be harmless to non-tumorigenic cells with viability above 70%.

Conclusion: The physicochemical characteristics of developed NP were satisfactory, with a desired low protein binding characteristic. The NP system targeting through TfR binding peptide, as expected, potentiated the interaction of NP with the target cells, and proved to be safe, not altering non tumorigenic cell viability.

Keywords: polymeric nanoparticle, cancer therapy, nanosystem