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BSA Nanoparticles with Parvifloron D for Pancreatic Cancer Treatment

Introduction: Pancreatic cancer is the thirteenth most common cancer and the eighth leading cause of cancer death worldwide. An improvement in the outcome of patients with pancreatic cancer is strongly dependent on the development of more effective therapies [1]. Nanotechnology can play a crucial role by targeting the drugs to the malignant cells [2]. In another hand, medicinal plants, as an example, *Plectranthus* species, have exhibited cytotoxic and antiproliferative activities against human tumor cells, like the present abietane diterpenoid, Parvifloron D [3]. The aims of this work were to isolate Parvifloron D from *P. ecklonii* and to prepare and characterize albumin nanoparticles using different processes. **Material & Methods:** Parvifloron D was obtained by extraction through an acetone ultrasound-assisted method and isolated by a chromatography column over silica gel using mixtures of increasing polarity eluents. Albumin nanoparticles were produced through desolvation method [4]. The formulation was optimized using different cross-linking processes (glutaraldehyde, glucose, glucose with UV light and UV light), albumin concentrations (30, 50 and 150mg), cross-linking times (30min and 24h) and organic solvents (DMSO, acetone, ethanol and hexane). Resultant particles were then characterized in terms of stability, particle size by photon correlation spectroscopy, zeta potential by laser Doppler anemometry, cross-linking efficacy by Bradford method and shape and size by atomic force microscopy (AFM). Parvifloron D was encapsulated in the optimized formulation and then characterized by using the same techniques. Encapsulation efficacy (%) was determined by measuring the non-encapsulated drug lost in the

supernatant (i.e., indirect quantification) by HPLC analysis. **Results & Discussion:** Extraction was carried out as previously described [5]. A yield of 28.54 g was obtained and subjected to successive chromatographic processes and 0.882 g of Parvifloron D was isolated (0.45% (w/w) of the dry plant). The particle size range obtained was between 90 and 520nm. Some agglomerates were visible in some of the methods. All nanoparticles showed a negative zeta potential, independently of the different production conditions. In terms of morphology, nanoparticles were spherical and AFM confirmed the particle size. Different cross-linking efficacies in the methods were observed and ranged between 43.8% and 99.6%. Then, Parvifloron D was encapsulated in the chosen formulation. Particle size was around 95nm and nanoparticles maintained a negative zeta potential. The cross-linking efficacy was up to 85% and the encapsulation efficacy was 91.2%. **Conclusions:** This study confirms the feasibility of producing uniform and well-defined albumin nanoparticles, encapsulating Parvifloron D. Further ligand-attachment onto the nanoparticle surface and efficacy studies against tumor cells will be performed.

References

- [1] N. Silvestris, et al., *Curr. Med. Chem.*, 21 (2014) 948–965
- [2] C. Silva, et al., *Int. J. Pharm.*, 493 (2015) 1-2
- [3] H. Niknejad, et al., *Iran J. Pharm. Res.*, 14 (2015) 385-394
- [4] W. Qi, et al., *Mol. Pharm.*, 12 (2015) 675-683
- [5] M. Simões, et al., *Phytochem. Lett.*, 3 (2010) 234–237