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Drug Design Modelling and Molecular Virtual Simulation of an Optimized BSA-Based Nanoparticle Formulation Loaded with Di-Berberine Sulfate Acid Salt

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Abstract : Drug salting and nanoparticle-based drug delivery formulations are considered to be an effective means for rendering the hydrophobic drugs' nano-scale dispersion in aqueous media, and thus circumventing the pitfalls of their poor solubility as well as enhancing their membrane permeability. The current study aims to increase the bioavailability of quaternary ammonium berberine through acid salting and biodegradable bovine serum albumin (BSA)-based nanoparticulate drug formulation. Berberine hydroxide (BBR-OH) that was chemically synthesized by alkalization of the commercially available berberine hydrochloride (BBR-HCl) was then acidified to get Di-berberine sulfate $(BBR)_2SO_4$. The purified crystals were spectrally characterized. The desolvation technique was optimized for the preparation of size-controlled BSA-BBR-HCl, BSA-BBR-OH, and BSA-$(BBR)_2SO_4$ nanoparticles. Particle size, zeta potential, drug release, encapsulation efficiency, Fourier transform infrared spectroscopy (FTIR), tandem MS-MS spectroscopy, energy-dispersive X-ray spectroscopy (EDX), scanning and transmitting electron microscopic examination (SEM, TEM), in vitro bioactivity, and in silico drug-polymer interaction were determined. BSA (PDB ID; 4OR0) protonation state at different pH values was predicted using Amber12 molecular dynamic simulation. Then blind docking was performed using Lamarkian genetic algorithm (LGA) through AutoDock4.2 software. Results proved the purity and the size-controlled synthesis of berberine-BSA-nanoparticles. The possible binding poses, hydrophobic and hydrophilic interactions of berberine on BSA at different pH values were predicted. Antioxidant, anti-hemolytic, and cell differentiated ability of tested drugs and their nano-formulations were evaluated. Thus, drug salting and the potentially effective albumin berberine nanoparticle formulations can be successfully developed using a well-optimized desolvation technique and exhibiting better in vitro cellular bioavailability.

Keywords : berberine, BSA, BBR-OH, BBR-HCl, BSA-BBR-HCl, BSA-BBR-OH, $(BBR)_2SO_4$, BSA-$(BBR)_2SO_4$, FTIR, AutoDock4.2 Software, Lamarkian genetic algorithm, SEM, TEM, EDX
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