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Simulation study of the mechanism of uptake of cell penetrating peptides in cancer cells

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It is somehow easy to understand why it is still so controversial the mechanisms of cellular uptake of cell-penetrating peptides (CPP). Although there is evidence that these peptides are capable of directly crossing the plasma membrane without any intermediate step, still several researchers claim that endocytosis is an intermediate step required for entry into the cells. It is well known that ionic interactions play a critical role for the binding to the plasma membrane and translocation of CPPs. A simulation of the interaction between arginine-glycine (RG)5 and histidine-glutamic acid (HE)5, as well as with DOPC of the lipid bilayer was conducted in order to calculate the free binding energy. The results supported the data obtained in the in vitro release, cell uptake and cytotoxicity studies. The absolute value of binding energy of (RG)5 with (HE)5 was the highest, however a decrease in the pH was found to diminish this strong bond. Interestingly, the conjugation of (RG)5 to PEG-PLA copolymer increased the binding energy to DOPC. In summary, the peptides tend to interact with the cell membrane which facilitates the uptake in an energy and receptor independent manner as postulated by many researchers.

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Challenges and advances in solid lipid nanoparticle drug delivery systems

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In recent decades, a variety of pharmaceutical research projects have been conducted to develop new dosage forms, but the field of drug development experiences very low success rates with regards to drugs that enter the market, also it has become more and more evident that the development of new drugs alone is not sufficient to ensure progress in drug therapy. Exciting experimental data obtained in vitro are very often followed by disappointing results in vivo. Main reasons for the therapeutic failure include poor drug solubility leading to lowered bioavailability, insufficient drug concentration, high fluctuation of drug plasma levels, toxicity of the therapeutic compounds and thus reduced efficacy. Various approaches have been explored to address these challenges with little success. Scientific community believes that nanotechnology based drug delivery system offers new ways to address residual scientific concerns for the treatment of many diseases. In nanotechnology based drug delivery system, the Solid Lipid Nanoparticles (SLNs) are a new form of interesting nano particulate or lipid based drug delivery carriers in addition to the more conventional ones such as liposomes, lipid emulsions and polymeric nanoparticles. The potential advantages include: the possibility of controlled, sustained or prolonged drug release and drug targeting, increased drug stability, high drug payload, non-biotoxicity of the carriers, avoidance of organic solvents, suitability for large scale production and sterilization. Moreover, SLN promotes the oral absorption of poorly water soluble lipophilic drugs and enhances the bioavailability. The addition of PEGylation molecules prevents immune-protein adsorption and minimizes phagocytic uptake by macrophages, thus increasing blood plasma circulation time. An additional advantage involves the production of SLN in a powder form, which may be loaded into pellets, capsules or tablets for further enhancement of drug delivery.

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