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DSL403

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Electrostatic Nano-Stitches for DNA: Atomistic Simulations of Ca-Mediated Adsorption of DNA on Phospholipid Membranes

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Formation of supramolecular complexes of DNA and zwitterionic phospholipids is important from the point of view of the development of non-toxic gene delivery vectors and DNA-based nanodevices interacting with cell membranes. While experimental studies have shown that divalent cations can promote adsorption of negatively charged double helixes of DNA on zwitterionic (neutral) phospholipid membranes, the underlying molecular mechanism of such adsorption as well as the microscopic structure of the resulting supramolecular DNA-membrane complexes are still unknown. To address this problem, here we employ atomic-scale molecular dynamics simulations to probe interactions between DNA and phospholipid bilayer membranes in aqueous solution with and without CaCl2 salt. The state-of-the-art atomistic force-fields AMBER parmbsc0 and AMBER Lipid14 were used to describe a double helix of DNA and phospholipid molecules, respectively. We carried out microsecond-long molecular dynamics simulations which allowed us to evaluate a wide range of dynamic and structural characteristics of DNA-membrane systems. Overall, our results provide compelling evidence that Ca ions are largely responsible for attractive interactions between DNA and phospholipid membranes on a nanoscale: We demonstrate that divalent calcium cations serve as nano-stitches between phosphate groups of DNA and lipid molecules, stabilizing thereby DNA-lipid complexes.
The simulations were performed on the Lomonosov supercomputer at the Moscow State University and on the computer cluster of the Institute of Macromolecular Compounds RAS. This work was partly supported by the Presidium of the Russian Academy of Science through the grant program ”Molecular and Cellular Biology” and also by the Russian Foundation of Basic Research through Grant No. 14-03-01073.

DSL406

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Use of Pseudoboehmite Nanoparticles for Drug Delivery System of Glucantime®

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The incidence of American Cutaneous Leishmaniasis (ACL) has, in recent years, growing in Latin America, especially Brazil, where from 1980 to 2005 605,062 cases were recorded. The drug Glucantime ® whose active principle is the meglumine antimoniate (or meglumine antimonate), is used in the treatment of leishmaniasis, its toxicity is due mainly to the presence of antimony in its structure, thereby determining the control of the doses as an essential factor in the treatment. Drug delivery systems are currently the focus of many studies before its effectiveness in treating disease and favorable performance compared to conventional methods. Due to some advantages, they can avoid repeated doses, also the substantial decrease the amount of drug intake, which not only enhance the therapeutic effect, but also reduces the risks of plasma concentration reaches toxic levels. Synthetic nanomaterials have attracted great interest for applications in pharmaceutical technology focused, so that control of their size and composition allows the best performance in interaction with the drug and its release. Pseudoboehmite is a synthetic aluminum compound precursor of alumina[1], with the same structure of boehmite and active groups in their structure[2], which characterizes it as an excellent adsorbent material. In the present work, pseudoboehmite prepared by sol-gel process for use as an excipient. The incorporation of pseudoboehmite in Glucantime® performed in the processing of tablets. The tablets were characterized by nitrogen adsorption isotherm, X-ray diffraction (XRD), Differential thermal analysis, thermogravimetry analysis (TG), Scanning Electron Microscopy (SEM) using secondary electron detector and EDS detector. The release profile obtained by UV/Vis spectroscopy for in vitro simulation. The results showed that there was no reaction between the drug and excipient.

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DSL412
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Drug Transport in Charged Polymeric Hydrogels for Drug Delivery

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The ability to provide tunable drug delivery rates represents one of the most promising medical approaches of the last years. In this framework, hydrogels are widely investigated polymeric scaffolds due to their ability to mimic living tissues together with their high biocompatibility. Here the interpretation of transport phenomena is a key step, but nevertheless within these systems is still controversial and a comprehensive theory lacks [1,2]. We investigated a promising agarcarbomer (AC) hydrogel library loaded with ethosuximide (ESM), an anticonvulsant drug. The self-diffusion coefficient of ESM in AC formulations was measured using two methods: a direct measurement with pulsed field gradient spin-echo (PFGSE) method, using an NMR spectrometer equipped with High Resolution Magic Angle Spinning (HRMAS) probe, and an indirect one fitting in vitro drug delivery data [1]. Starting from experimental data a complete overview on ESM transport properties was provided, considering the contribution of drug concentration. In particular a mathematical model that describes and rationalizes the differences between gel and water environments regarding ESM adsorption and diffusion within hydrogel pores was taken into account. The competition between these two mechanisms causes two different regimens. At low drug concentration, on one hand, adsorption prevails with a consequent diffusivity in gel lower than in water. On the other hand for high drug concentration, where all adsorption site are saturated, the diffusion in gel is similar to water solution. This study may pave the way toward the development of models able to encompass the simultaneous effect of different phenomena on diffusion for a better device design.

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