Diffusion in Defect Free, Rigid Multi-walled Nanotubes

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Abstract: Nanotubes show exceptional properties that make them promising candidates for applications that require the transport of fluids or the storage of Molecular systems. Halloysite clay nanotubes are utilized as tubular multi-walled nano containers with the aim of producing a vehicle for sustained release of molecules with low risk for instant release. The effect of the pH of the surrounding media on the rate of release of encapsulated molecular species is studied studied experimentally and reproduced computationally.

Keywords: Diffusion, Nanotubes, Sustained Release, Zeta Potential, Time Quantified Monte Carlo.

1. Introduction

Many interesting applications have been designed and developed using nanotubes. Applications like the sustained and selective delivery of specific quantities of drugs to specific cell types,[1, 2] self-healing composites,[3] and the prolongation of rust coatings on metal surfaces in extremely hazardous environments,[4] require the controlled diffusion of molecules. A sustained release dosage form can overcome the problem of the need for frequent intake of medication for it to be therapeutically effective. Such a dosage form normally contains the drug dose required to maintain a therapeutic concentration of the drug in the body for long durations. A sustained release method will also help design self-healing "smart" polymeric composite materials. These are nothing but polymeric material doped with clay nanotubes filled with healing and anticorrosion agents. The healing agents loaded into the nanotubes are slowly released in the damaged locations (such as cracks) to suppress the defect propagation, over 20 to 50 hours. Doping loaded clay nanotubes into polymeric matrix provides a ceramic "skeleton" within the coating layer; these "bones" are loaded with functional chemicals (like real bones are loaded with marrow). This skeleton also improves the coating strength and adhesiveness. Existing sustained release drug delivery systems are based either on patches or on infusion pumps. One possible application is to create oral-ingestion-based sustained release drug delivery system. With most drugs there is a high risk if dose-dumping occurs, dose dumping is the release of the entire dosage in a short span of time and can cause severe and sometimes lethal side effects. The probability of dose dumping is dependent on the environment surrounding the delivery container, for example, the variation of pH and enzymatic activity within the gastrointestinal tract associated with intake of food. Furthermore, crushing of the drug container (voluntary or involuntary) can also potentially initiate dose dumping. An efficient orally ingestible sustained release product could potentially lower

cost on the health care system. It is our endeavor in this paper to present a time quantified Monte Carlo based computational model to predict the release-rate of healing and anticorrosion agents from clay nanotubes. This work utilizes multi-walled Halloysite nanotubes to design sustained release platforms for a wide variety of molecules and applications. Naturally occurring Halloysite clay tubes are aluminum-silicate hollow cylinders with a length of 1 μm, an outer diameter of 50 nm, and a lumen of 15 nm[5]. The molecules are loaded into the nanotubes that have the property to release contents slowly in the desired locations potentially suppressing dose dumping. When the length scale of a system is down to micro- or nanometers, interfacial phenomena become very important. Electric double layer (EDL) interfacial phenomena play a fundamental role in the liquid flow mechanism through micro and nano channels. Electro kinetic flow has become one of the most important non-mechanical actuating techniques in micro fluidics, widely used for pumping, mixing, and separating, because of its excellent scalability, low dispersion, and ease of control. In this study the approach has been to study the effect of a number of interactions between particles and nanotube on the out diffusion of molecular species. Experiments are conducted and results used to validate the simulations. Simulations will be used to guide the experiments to a more efficient release of particles from single and multi-walled nanotubes.

Simulations

Ref [6] describes a study where clay nanotubes (Halloysite) are used for loading and sustained release of Fentanyl. In that work it is demonstrated that the nanotubes entrap Fentanyl in the inner lumen and release them in media of different pH's (1 - 6.8). Molecules may be retained inside the tubes for extended periods of time. Longer release times can be achieved through the addition of tube opening stoppers[7]. We study the mechanisms of slowing the release from halloysite in terms of pH of the surrounding media and tube length. By the variation of external fluidic properties and the creation of smart caps at the tube's ends, it is possible to develop a wide range of release rates. A Monte Carlo model implementing a forced random-walk algorithm is used to model the diffusion of particulate entities from the nanotubes. In this study the diffusion of particles in tubular nanostructures is modeled as a function of the interaction between particles and the nanotube walls; it is hypothesized that the delay in the diffusion rate is dependent on particle-particle interaction in the confined interiors of nanotubes and a strong interaction between the nanotube walls and the particles. Our algorithm generates combinations of the most probable motion of the particles in the nanotubes which are then streamlined to predict the diffusion paths and times. The overall energy of the system is calculated with contributions from particle-wall and particle-particle interactions. The wall-particle interactions are modeled by summing up the contributions from dipole-charge interactions, shielded Columbic interactions, coupled with Van Der Waals interactions at short distances. Particle-particle interactions are modeled primarily by taking into consideration columbic interactions, Van Der Waals contributions are also considered. The shielding is introduced by implementing a modified Debye-Huckel screening model. A novel method is used to introduce time into the Monte Carlo simulations. The mean free path of the molecules is taken to be the maximum hop distance (the mean free path is predicted by the Knudsen flow model for free molecular gas flow). The velocity of the particles during hops is taken to be the velocity derived by solving a system of equations utilizing the Poisson- Boltzmann equations governing electro kinetic flow near EDL surfaces, the equation for electrolyte flow, the conservation of

species and the conservation of mass equations. Elapsed time per time step is then calculated by dividing the total mean displacement of all particles in that time step by our derived velocity. The results from the experiments conducted on halloysite nanotubes are presented in the results and discussion section. As can be seen there is a delay in diffusion or release of the encapsulated molecules from the nanotubes.

2. Results and Discussions

Electro kinetic Phenomenon is present due to the electric double layer which forms as a result of the interaction of ionized solution with static charges on the dielectric surface. The extent of the EDL is predicted by the Debye length which is the distance from the dielectric wall at which the electro kinetic potential or zeta potential is equal to the thermal energy. The Debye length and therefore the zeta potential depend on the concentration of ions present and the dielectric constant of the solvent, this implies the zeta potential is dependent on the pH of the solution. Figure 1a depicts the variation of the zeta potential of Halloysite with respect to pH, the zeta potentials for silica and alumina are detailed in the graph, and these represent the behavior of the outer and innermost layers of a Halloysite nanotube. The zeta potential of Halloysite lies in between those of silica and alumina. Figure 1b depicts a typical nanotube loading process for molecules. Fentanyl was loaded into halloysite nanotubes using a similar vacuum impregnating technique.

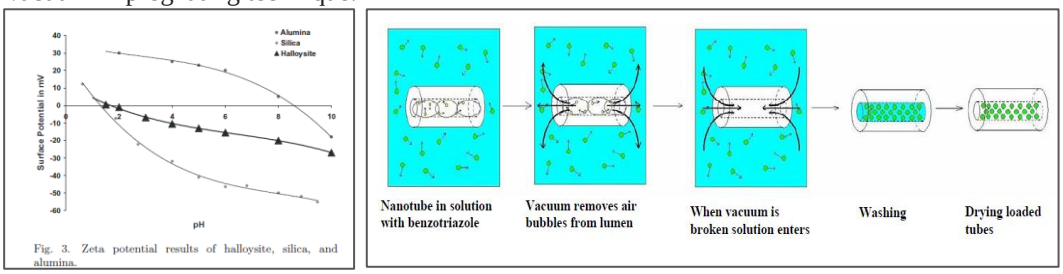

Fig.1. **(a)** Zeta potential results of Halloysite, silica, and alumina [8], (b) Loading halloysite nanotubes with molecule of intrest [4].

Figure 2a show the release profile of Fentanyl from crushed (Halloysite tubes with shortened length to simulate swallowing with chewing of Fentanyl loaded Halloysite capsules) and uncrushed (intact/full) halloysite nanotubes at pH 6.8 Figure 2b.shows the sustained release profiles of the opiod Fentanyl from uncrushed halloysite at two different pH (6.8 and 1). A sustained release of three to four hours was obtained in all studied solutions from intact Halloysite nanotubes, whereas crushed nanotubes released the drug content somewhat faster due to the shorter length of the nanotubes. The findings suggest that Halloysite nanotubes demonstrate a sustained release of the drugs, and are therefore a promising material in future developments of new opioid containing oral tablets.

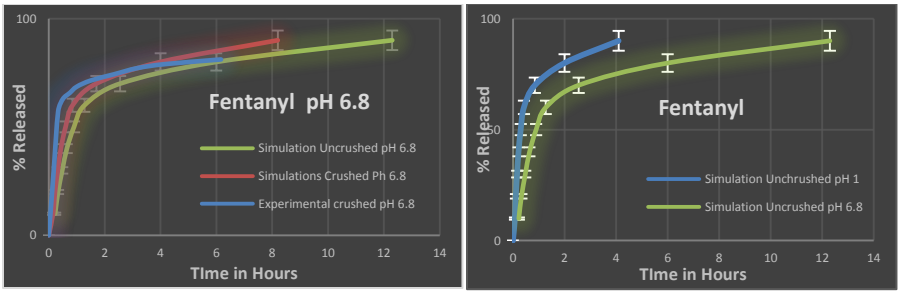

Fig.2. (a) Release profiles of Fentanyl from intact and crushed nanotubes at Ph 6.8. (b) Release profiles Fentanyl release curves from intact nanotubes in two different solutions of pH 6.8 and 1.

The release process from intact nanotubes at pH 1 differs from the release or release in pH 6.8 because of the pH dependence of the zeta potential. The velocity of Fentanyl inside the nanotube is directly related to the zeta potential. Also at pH 1 the Halloysite surface does not carry a negative net charge any longer (the zeta-potential is positive) and thus, the number of available sites for electrostatic attraction of Fentanyl cations are fewer. The attractive forces between the Fentanyl molecules and the nanotube wall are so weak that the molecule-molecule repulsion dominates and the Fentanyl molecules are propelled outwards.

3. Conclusion

Experiments corroborated with simulation results show that a sustained release of Fentanyl can be achieved when it is administered encapsulated within Halloysite nanotubes. Dose dumping/ instant release that is normally associated with direct oral ingestion of Fentanyl can thus be avoided. Simulation studies show that a pH-dependence exists and that pH of the surrounding media can be used as a control parameter to vary the rate of diffusion of molecular species from multi-walled nanotubes. Simulation results show good qualitative agreement with the experiment but more work needs to be done for a better quantitative agreement.

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