



Halloysite nanotubes loaded with irinotecan; synthesis, characterization by experimental and molecular simulation methods and drug release properties evaluation

Dimitrios Papoulis (1), Eleni Gianni (1,3), Konstantinos Avgoustakis (2), Milan Pšenička (3), and Miroslav Pospíšil (3)

(1) University of Patras, Geology Department, Greece (papoulis@upatras.gr), (2) Department of Pharmacy, University of Patras, Rio, 26504, Patras, Greece, (3) Faculty of Mathematics and Physics, Charles University, Prague 2, 12116, Prague, Czech Republic

Halloysite, a tubular clay mineral biocompatible with human body could be applied for the encapsulation of many bioactive molecules, serving as a controlled drug delivery carrier. In this work, halloysite nanotubes from Utah have been examined as potential irinotecan (a semi-synthetic drug successfully used for colon cancer treatment) oral delivery system. The irinotecan-loaded halloysite nanotubes were coated with an anionic copolymer (Eudragit S100) in order to control (limit) drug release in the stomach while allowing it subsequently in the intestine. The encapsulation efficiency of irinotecan in the halloysite nanotubes reached 87 %. The average size and ζ -potential of the halloysite particles, drug-loaded and polymer-coated particles were measured (DLS). Transmission electron microscopy study provided support for the encapsulation of the drug within the halloysite nanotubes and polymer coated nanotube surfaces and Scanning Electron Microscopy showed larger aggregates when the polymer participates in higher amounts. Thermogravimetric analysis was applied in order to confirm the drug loading values obtained spectrophotometrically. The classical molecular simulation methods were applied in order to describe the interactions between irinotecan and the halloysite nanotube. The drug molecules after the structure optimization remain closer to the inner part of halloysite nanotubes. Longitudinal axes of the adjacent drug molecules are positioned along longitudinal axis of the tube. Hydrated halloysite nanotubes with the basic length of tube $a = 25.600 \text{ \AA}$ contain 5 irinotecan molecules in the calculated supercell. It was found that irinotecan release properties can be regulated by changing the halloysite:polymer ratio and that a more suitable drug release profile can be obtained with a lower amount of coating polymer.