HALLOYSITE-BASED SYSTEM FOR CONTROLLED DELIVERY OF CLINDAMYCIN PHOSPHATE

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Introduction

Halloysite (HNT) is a two-layered (1:1) aluminosilicate, chemically similar to kaolinite. It exhibits a range of morphologies, among which the predominant form is a hollow tubular structure of the submicrometer scale. HAL nanotubes are able to encapsulate low molecular weight drugs (e.g. antibiotics, anti-inflammatory agents) [1], which may be then slowly released to provide protection against inflammation or bacterial infection. The uniqueness of the HNT as a tubular carrier lies in the fact that, due to the opposite charges of its inner lumen (positive) and outer surface (negative), electrostatic interactions may be used to increase efficiency and selectivity of the entrapment of the bioactive agents.

Clindamycin is an antibiotic used to treat, among others, dental and skin infections. It is widely applied in implant sterilization and bone disease treatment, as it has high ability of penetration of the bone tissue [2]. Its positive role in the late stages of osteogenesis have been recently reported in the literature [3].

Our aim was to obtain a halloysite nanotubes based system for a controlled, prolonged delivery of clindamycin phosphate. Nanotubes were additionally etched to increase their loading ability. Such a system could be applied as a component of bone and skin regeneration materials (scaffolds, dental fillings, wound-dressings).

Materials and Methods

Halloysite nanotubes were pre-treated by etching with the 1 M acetic acid at 50°C, followed by extensive washing with water and freeze-drying. Clindamycin phosphate was dissolved in water (50 mg/ml) and then added either to the untreated (HNT) or to the etched (HNT-E) halloysite nanotubes and thoroughly mixed to obtain a stable suspension. Both nanoclays were then placed under reduced pressure (200 mmHg) to allow for the solution to be drown in into the nanotubes. The mixtures were left 15 minutes and then moved to the normal conditions to equilibrate. The cycle was repeated three times, then the sediments (HNT-Clin and HNT-E-Clin) were separated, washed with water and freeze-dried.

The morphology of the obtained nanoclay-drug systems was studied using ATR-FTIR, SEM, and TEM (FIG. 1). The release profiles for both nanoclays were studied in phosphate buffer saline (PBS) at pH = 7.4 and at 37°C. The concentration of clindamycin phosphate was measured throughout the release studies using Waters HPLC system with C18 column and UV-Vis detection. Acetonitrile:phosphate buffer (pH = 3) 20:80 mixture was used as an eluent. Encapsulation efficiency and loading of the antibiotic in the nanotubes of both untreated and etched HNT was established based on the amount of the drug released.

Results and Discussion

The SEM and TEM studies showed that the diameter of the inner lumen of the nanotubes was enlarged as a result of the etching process. SEM and ATR-FTIR studies confirmed that no unwanted processes, such as the degradation of the outer layer of the nanotubes, were observed. Clindamycin phosphate was successfully loaded into the HNT and HNT-E nanotubes. Within the first 24 h more drug was released from the HNT-E nanotubes than from untreated HNT. The long term release profile obtained for the HNT-E-Clin system showed that so-called “burst release” was observed, followed by a faster release for the first 4 hours and much slower but prolonged release of the antibiotic up to 2 days.

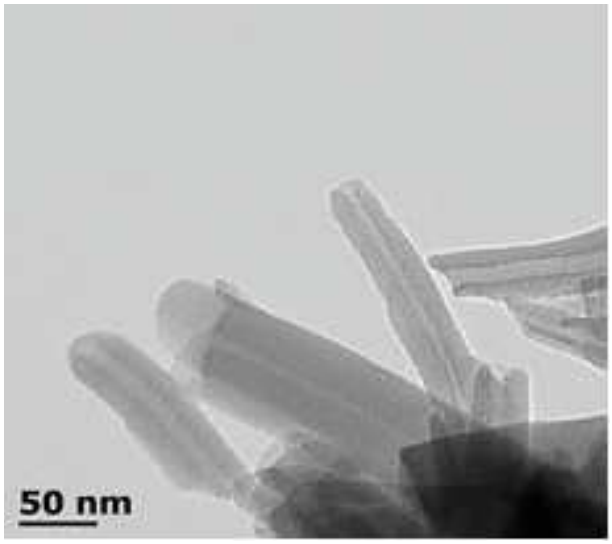

FIG. 1. TEM image of HNT-E nanotubes.

Conclusions

We have successfully loaded clindamycin phosphate into the halloysite due to the electrostatic interactions between a positively charged lumen of the nanotubes and negative charge of the drug. The proposed etching process allowed to increase the amount of drug released form the system. The obtained release profile was favourable for the proposed applications, as it provides an initial burst release of the antibiotic necessary to fight the infection, followed by e prolonged, slow release providing a long-term protection.

References

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