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### **ACCEPTED MANUSCRIPT**

## Conjugating Layered Double Hydroxide Nanoparticles with Phosphonic Acid Terminated Polyethylene Glycol for Improved Particle Stability

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#### Abstract

Conjugating nanoparticles with polyethylene glycol (PEG) is a useful strategy to improve the colloidal and biological stability of nanoparticles. However, studies on PEGylation of two-dimensional layered double hydroxide (LDH) nanoparticles are very limited. The present work reported two functionalization approaches to synthesise PEG-conjugated LDH nanoparticles by introducing phosphonic acid terminated PEG before and after LDH aging. The successful PEGylation was confirmed and suggested to be via electrostatic interaction and a ligand exchange process. Different functionalization approaches resulted in different binding types of PEG on/in LDH nanoparticles. The PEG coating maintained the dispersity of LDH nanoparticles in water and saline with the feeding mass ratio of 1:1. Further colloidal stability tests of PEGylated LDHs revealed that the PEGylated LDH dispersity was affected by the feeding mass ratio of PEG/LDH, the molar weight of PEG and anions intercalated in the LDHs. In a test to determine the extent of non-specific protein adsorption, the PEGylation was effective at resisting non-specific bovine serum albumin adsorption on LDH nanoparticles with both functionalization methods investigated. Moreover, PEGylated LDH nanoparticles had no effect on cell viability up to 500 µg/mL and demonstrated enhanced cellular uptake in a SK-MEL-28 cell culture. The results in this work indicate that conjugating phosphonic acid terminated PEG on LDH nanoparticles is a promising strategy to improve the colloidal and biological stability of LDHs for biomedical applications.

#### 1. Introduction

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