Bone-targeting delivery of alendronate for the treatment of osteoporosis

Shenmao Chen[1], Lingling Zhao[1,2] & Chaozong Liu[1]

[1] Institute of Orthopaedic & Musculoskeletal Science, University College London, Royal National Orthopaedic Hospital, Stanmore HA7 4LP, UK;
[2] Faculty of Materials Science and Chemical Engineering, Ningbo University, Ningbo 315211, China

Introduction:

Alendronate is a second-generation bisphosphonate drug for osteoporosis treatment. However, it has been limited due to its low bioavailability and gastrointestinal side effects. This work reported a novel Alen-decorated polymeric nanoparticles and their *in vitro* drug release behavior, cytotoxicity, and affinity to HAp were evaluated.

Materials and Methodology:

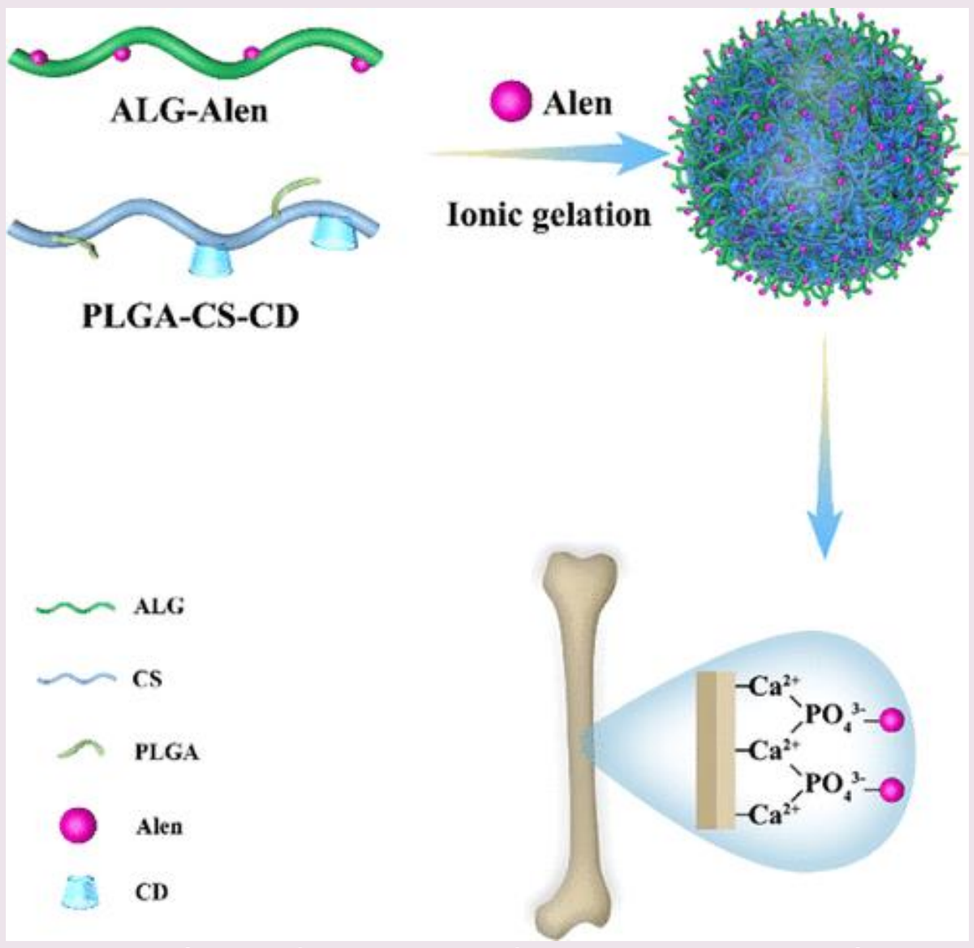
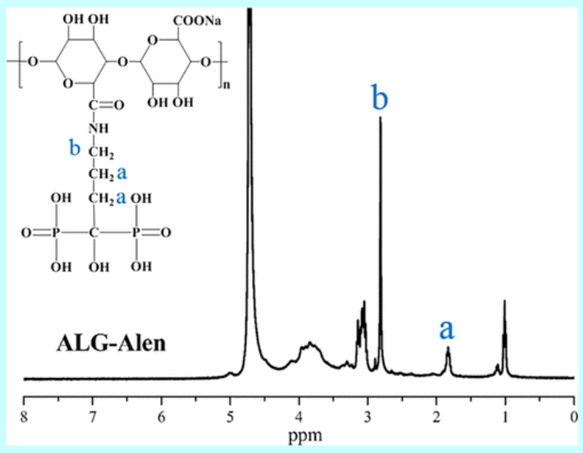


Fig 1: Alen-decorated nanoparticles were prepared through ionic cross-linking between poly (lactic-co-glycolic acid), β-cyclodextrin-modified chitosan (PLGA-CS-CD), and Alen-modified alginate (ALG-Alen) for Alen loading and bone-targeted delivery.

A dialysis method was used for *in vitro* release behavior. The cytotoxicity of nanoparticles was measured using CCK-8 assay and lactate dehydrogenase (LDH) release test

Results and discussions:

β-CD was conjugated to the CS using MA as a linker, and PLGA was grafted through the reaction between the carboxylate group in PLGA and the amino group in CS (Fig 2)



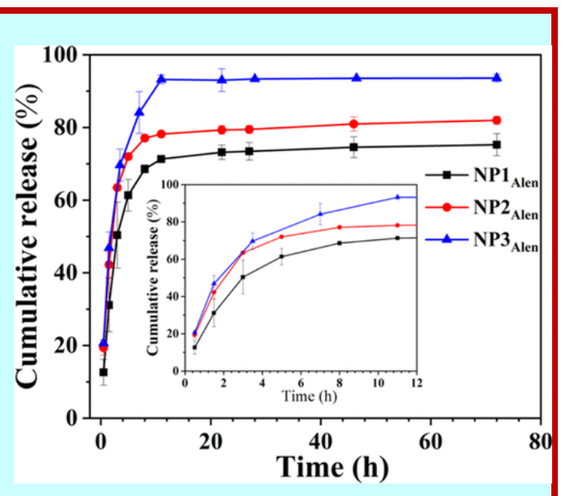


Fig 2: ^{1}H NMR spectrum of ALG-Alen

Figure 3. In vitro release profile indicated that the release profile was different depending on the PLGA-CS-CD/ALG-Alen ratio. It has a burst release in the initial stage and a prolonged release in the later stage, follows the Fickian diffusion mechanism.

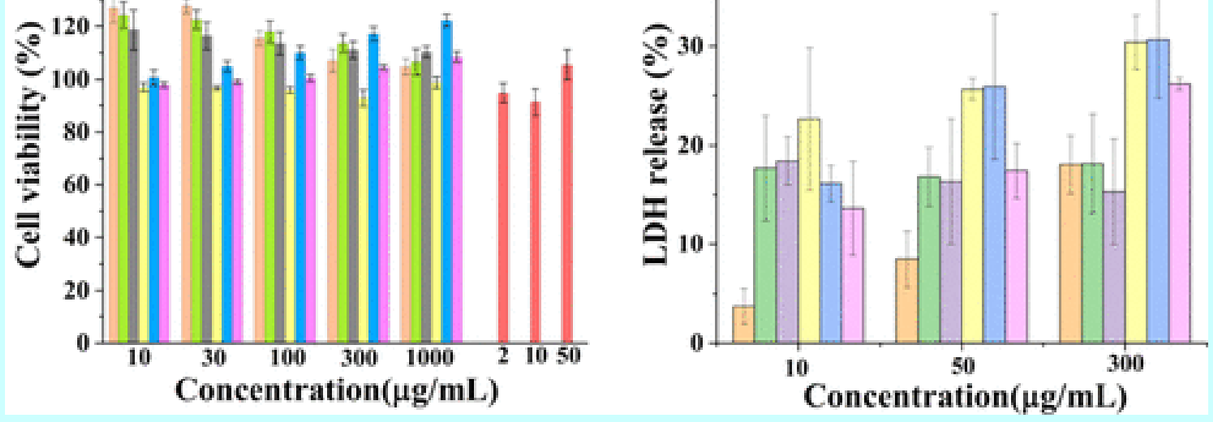


Fig 4: The nanoparticles has showed that the relative cell viability was higher than 91% for Alen at 2–50 μg mL–1, implying good biocompatibility of the drug without significant cytotoxicity to those cells. It also has a good blood biocompability.

Conclusions:

The drug release could be tuned by changing the polymer ratio. The nanoparticles had good cytocompatibility, and good blood biocompatibility a significant higher binding ratio to HAp disks compared with nanoparticles without Alen modification.

Acknowledgement:

This work was supported by the Arthritis Research UK [grant number 21160]; European Commission via H2020 MSCA RISE programme [BAMOS, grant number 734156].