Local application of bisphosphonates cross-linked by glutaraldehyde on bovine hydroxyapatite - gelatin composite scaffold

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Introduction

Bisphosphonates are widely used in the treatment of bone disorders characterized by osteoclast-mediated bone resorption such as Paget's disease, fibrous dysplasia, myeloma, bone metastasis and osteoporosis[1]. Among bisphosphonate, alendronate (Ale) is commonly used that effectively inhibiting bone resorption by preventing recruitment and differentiation of osteoclasts. In recent study, alendronate stimulate proliferation and differentiation osteoblasts, thereby facilitating for bone regeneration. In oral administration, alendronate has poor bioavailability (1% -5%). Because of this, the local administration through scaffold composite is a favourable way to deliver alendronate to the bone tissue [2,3].

Hydroxyapatite (HA) is an inorganic component that naturally present in bone tissue. Bovine hydroxyapatite (BHA) is natural version of HA derived from bovine bone. BHA has a higher porosity than synthetic HA, which makes BHA has osteoconductivity. Gelatin is a natural polymer which is similar to the organic components of the bone. Because of this, BHA and gelatin composite is widely used as scaffolds for bone regeneration [4].

However, scaffold composed of BHA and gelatin can easily degrade because of the insufficient chemical/physical bonds present on the composite [5]. Therefore, on the scaffold formulation, it is necessary to add glutaraldehyde (GA) as crosslink agent [6].

Objective

The objectives of this study were to prepare and characterized scaffold of alendronate using hydroxyapatite-gelatin and cross-linked by GA.

Materials and Methods

1. The BHA-GEL-ALE scaffold composed of 0%, 0.5%, 0.75%, and 1% GA was made by direct compression.
2. Mechanical test of scaffold was investigated through compression strength measured using an autograph.
3. Density is calculated based on the ratio of dry mass to volume, while the porosity is the ratio between the difference in wet mass and dry mass divided by the volume of the sample.
4. Swelling ability and weight loss test was carried out by immersing the sample in PBS in order to mimic the body fluids in vivo. Weight loss is the changes in scaffold’s dry weight after immersion and initial weight before immersion. Swelling ratio is the scaffold’s swollen weight divided by the dry weight of scaffold.
5. The MTT assay is used to determine the viability of cells using 21 fibroblast cell.

Conclusion

We successfully prepared bovine hydroxyapatite gelatin scaffold with bisphosphonates with varying concentrations of glutaraldehyde. Increase concentration of GA increases the porosity, which causes a decrease in compressive strength. In the swelling ratio and in vitro degradation (weight loss) is inversely proportional to the increase in GA. All samples were non-toxic based on cytotoxic assays. Based on these results the presence of glutaraldehyde in bovine hydroxyapatite gelatin composite with bisphosphonates are safe and suitable candidate for bone regeneration.

References