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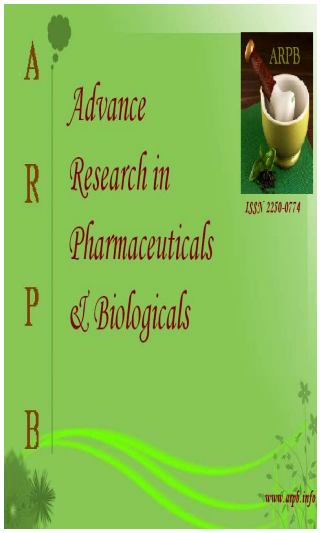

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BIOCERAMIC AS DRUG DELIVERY SYSTEM IN ORTHOPEDIC GRAFT

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ABSTRACT:

Ceramic substances are in the market as bone substitutes, which include calcium phosphate ceramics like Tricalcium phosphate (TCP) and Hydroxyapatite (HAp). Calcium phosphate based bioceramics have been used in medicine and dentistry for nearly 30 years. Applications include dental implants, percutaneous devices and joint replacements. Different phases of calcium phosphate ceramics are used depending weather a resorbable or bioactive material is required. The material used for this study was a Calcium phosphate (Biphasic) granule, consisting of different ratios of relatively stable Hydroxyapatite and more soluble Tricalcium phosphate phases, thereby controlling the resorbability of the bioceramic for drug release. The drug used for encapsulation and subsequent release is Teriparatide

KEYWORDS: Tricalcium Phosphate, Hydroxyapatite, Calcium Phosphate (Biphasic), Osteoconduction, Osteoinduction, Teriparatide

INTRODUCTION

The porous structure of biomaterials plays a critical role in improving the efficiency of biomaterials in tissue engineering. Here we fabricate successfully porous bioceramics with accurately controlled pore parameters, and investigate the effect of pore parameters on the mechanical property, the cell seeding proliferation and the vascularization of the scaffolds[1]. Ceramic substances are in the market as bone substitutes, which include calcium phosphate ceramics like Tricalcium phosphate (TCP) and Hydroxyapatite (HAp). The interconnections in a porous biomaterial are the pathways between the pores. They conduct cells and vessels between pores. Thus they favour bone in growth inside ceramics[2]. Calcium phosphate based bioceramics have been used in medicine and dentistry for nearly 30 years. Applications include dental implants, percutaneous devices and joint replacements. Different phases of calcium phosphate ceramics are used depending weather a resorbable or bioactive material is required.

The main aim of the current research is to develop a bioceramic based drug delivery system. The material used for this study was a Calcium phosphate (Biphasic) granule, consisting of different ratios of relatively stable Hydroxyapatite and more soluble Tricalcium phosphate phases, thereby controlling the resorbability of the bioceramic for drug release. The drug used for encapsulation and subsequent release is Teriparatide[3]. Teriparatide is a recombinant form of parathyroid hormone, used to increase the proliferation of osteoblasts and promote osteoconduction and osteoinduction at the site of fracture of the bone. The scaffold prepared using such materials would help in accelerating the bone growth, remodeling and binding of the fragments at the site of fracture. The materials would be synthesized by microwave processing, which is the quickest route for the production of Calcium phosphate (Biphasic) granules. This method has enormous potential for large scale commercial production of Calcium phosphate (Biphasic) granules.

MATERIALS AND METHODS

The materials used for the drug delivery study were Calcium phosphate (Biphasic) granules and Teriparatide (drug).

Synthesis of Calcium phosphate in Biphasic form:

The Calcium phosphate (Biphasic) granules were synthesized by the microwave route. Calcium hydroxide and Diammonium Hydrogen ortho Phosphate were used as raw materials. The amounts of reactants used for the reaction were calculated based on the Ca/P molar ratio of 1.58. Weighed amounts of the starting granules were dissolved in water and the Diammonium Hydrogen ortho Phosphate solution was added to the calcium hydroxide

solution. The solution is then exposed to microwave irradiation in a microwave oven.

Pellet formation:

The pellets of pure Calcium phosphate (Biphasic) granules and with flour were formed by compaction under a pressure of 80 MPa to form a pellet of about 2-3 mm thicknesses in a hydraulic press. The flour used plays a dual role. It acts as a binder, as well as a pore-creating medium. Thus by varying the flour content the porosity of each pellet can be varied. Four types of pellets were made by varying their flour content. The pellets were then sintered in a box furnace at 1000°C for about 2 hours in air and furnace cooled. Four types of pellets were made by varying their flour content and the details are listed in the Table 1.

Table 1: List of Pellet Composition

Pellet Designation	Composition
Pellet A	Calcium phosphate (Biphasic) granules
Pellet B	Calcium phosphate (Biphasic) + 10% flour
Pellet C	Calcium phosphate (Biphasic) + 20% flour
Pellet D	Calcium phosphate (Biphasic) + 40% flour

Drug Encapsulation:

Encapsulation of Teriparatide into the granules and pellets were carried out separately by Interfacial cross-linking method[4]. The encapsulation is done in a phosphate buffer solution, having a pH of 7.4, at room temperature. The drug to Calcium phosphate (Biphasic) granules ratio for loading is maintained at 1:1. About 100 mg of granulised Teriparatide is transferred into a beaker containing about 10 ml of 7.4 pH sodium phosphate buffer solution. Percentage of drug loading is calculated using the equation:-

Percentage drug loading = ((AB)/A)*100

Where, A - Initial drug concentration of buffer solution

B - Final drug concentration of buffer solution

RESULTS AND DISCUSSION

The comparison between Teriparatide release profiles from the granules and pellets showed that the release was faster if Teriparatide was directly incorporated in granules than absorbed through the pores in pellets. However the Calcium phosphate (Biphasic) pellets provides a suitable drug delivery system which can be used to modulate the rate of release of a therapeutic agent. In-vivo studies were carried out on few rabbits. Maximum and accelerated bone growth was observed within four months of implantation. Calcium phosphate (Biphasic) granules seem to act as a scaffold and encourage host bone growth.The rate of release of the drug can be controlled by varying the pore size and morphology of the pellet. Microwave processing of this material has enormous potential for large scale commercial production of Calcium phosphate (Biphasic) granules. Calcium phosphate (Biphasic) granules seem to increase the proliferation of osteoblasts and

promote osteoconduction and osteoinduction at the site of fracture of the bone, thereby decreasing the fracture healing time.

CONCLUSIONS:

Calcium phosphate (Biphasic) granules based bioceramic drug delivery systems for delivering drug were developed[5]. The drug used was Teriparatide. The drug release profiles for different systems were studied. The Calcium phosphate (Biphasic) granules have a shorter drug release time. Pellet based systems have a longer drug release time (Fig.1). The drug loading seem to depend on porosity, pH conditions and morphology of the drug carrier. The pellet with the highest porosity had the longest drug release time. The present paper has shown the feasibility of developing and using a Calcium phosphate (Biphasic) granules based drug delivery system and the drug release profiles can be modified by changing geometry as granules or pellet form or by varying pore size as in case of the pellets. However the appropriate release profile can be optimized in consideration with the clinicians and other available data.

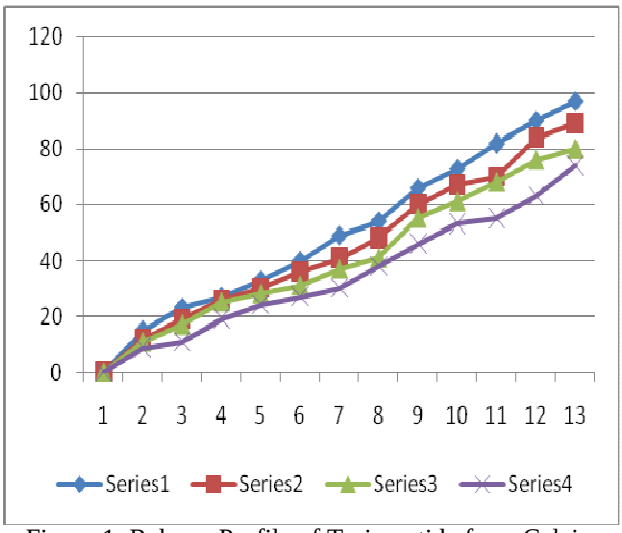

Figure 1: Release Profile of Teriparatide from Calcium phosphate (Biphasic) granules and Pellets

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