Review Article

The Composite of Hydroxyapatite with Collagen as a Bone Grafting Material

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Abstract:
Bone substitutes allow repair mechanisms to take place, by providing a permanent or ideally temporary porous device (scaffold) that reduces the size of the defect which needs to be mended. This paper aims to discuss the hydroxyapatite composites (e.g., hydroxyapatite plus collagen derivatives) that have been developed to mimic biochemical and biomechanical properties of natural bone in order to enhance osteointegration and graft healing for potential biomedical applications.
Keywords: Hydroxyapatite, Collagen, Graft.

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INTRODUCTION

Bone is a dynamic biological tissue composed of metabolically active cells that are integrated into a rigid framework. The healing potential of bone, whether in a fracture or fusion model, is influenced by a variety of biochemical, biomechanical, cellular, hormonal, and pathological mechanisms. A continuously occurring state of bone deposition, resorption, and remodeling facilitates the healing process.[1] Bone is the most implanted tissue after blood. The major solid components of human bone are collagen (a natural polymer, also found in skin and tendons) and a substituted hydroxyapatite (a natural ceramic, also found in teeth). Although these two components when used separately provide a relatively successful mean of augmenting bone growth, the composite of the two natural materials exceeds this success.[2] Bone substitutes allow repair mechanisms to take place, by providing a permanent or ideally temporary porous device (scaffold) that reduces the size of the defect which needs to be mended.[3] The ideal bone graft should be: 1) osteoinductive and conductive; 2) biomechanically stable; 3) disease free; and 4) contain minimal antigenic factors. These features are all present with autograft bone. The disadvantages of autografts include the need for a separate incision for harvesting, increased operating time and blood loss, the risk of donor-site complications, and the frequent insufficient quantity of bone graft.[4]

TYPES OF BONE GRAFTS

Autologous bone remains the gold standard, but requires a second surgical site that can result in additional pain and complications, is limited in quantity and increases the cost of the procedure.[5] However it is widely considered for a number of reasons, including osteogenic, osteoconductive, and osteoinductive properties and the lack of disease transmission or of immunogenicity. But the use of autograft may be at risk of major drawbacks, such as limited availability and variable quality of the graft, hematoma, infection, increased operative time and bleeding, chronic donor site pain, and additional cost.[6] Allograft bone, either fresh-frozen or demineralized freeze dried bone allograft (DFDBA) has also been used, but the rapid resorption can make it less than ideal for some larger defects. The advantages of allografts include the absence or minimization of donor site morbidity and the unlimited choice of graft shape and size. In human medicine, allografts are commonly used, although their expanded use is limited by the supply of bone and the potential for disease transmission. These limitations have spurred interest in substitute materials. Recent therapeutic technologies concerning bone substitutes and alternatives to biocompatible scaffolds include growth factor, calcium phosphate, hydroxyapatite, tricalcium phosphate, type I collagen, bioactive glasses, and synthetic polymers. Now-a-days, these xenograft materials have been used quite frequently as bone graft substitutes with good success in recent years.[5]

A COMPOSITE OF COLLAGEN AND HYDROXYAPATITE

Collagen as an osteoinductive material is due to its osteoconductive property and when it is used in combination with osteoconductive carriers like hydroxyl-apatite or tricalcium phosphate. These composites are mixed with autologous bone marrow which subsequently provides osteoprogenitor cells and other growth factors.[7] Hydroxyapatite is a biocompatible ceramic produced through a high-temperature reaction and is highly crystalline form of calcium phosphate. The nominal composition of this mixture is Ca10 (PO4)6 (OH) 2 with a calcium-to-phosphate atomic ratio of 1.67. The most unique property of this material is chemical similarity with the mineralized phase of bone; this similarity accounts for their osteoconductive potential and excellent biocompatibility.[7] Hydroxy-apatite is available in various physical forms. Bone formation, graft incorporation varies with each. HA in ceramic and crystalline form is slow in resorption and bone formation, where as non ceramic, non crystalline form is fast in resorption and in bone formation. Collagen is added to hydroxyapatite to give mechanical strength.[8] Bones comprise mainly of collagen and carbonate substituted hydroxyapatite, both are osteoconductive components. Thus, an implant manufactured from such components is likely to behave similarly, and to be of more use than a monolithic device. Indeed, both collagen and hydroxyapatite were found to enhance osteoblast differentiation[9] but combined together, they were shown to accelerate osteogenesis. A composite matrix when embedded with human-like osteoblast cells, showed better osteoconductive properties compared to monolithic HA and produced calcification of identical bone matrix. In addition, Col-HA composites proved to be biocompatible both in humans and in animals.[2] These composites also behaved mechanically in a superior way to the individual components. The ductile properties of collagen help to increase the poor fracture toughness of hydroxyapatites. The addition of a calcium/ phosphate compound to collagen sheets gave higher stability, increased the resistance to three-dimensional swelling compared to the collagen reference[10] and enhanced their mechanical ‘wet’ properties.[2] Recently, Surgiwear has developed xenograft in the name of G-Graft. It is natural Hydroxyapatite with natural collagen and with naturally occurring trabecular pattern. It is very useful for bone repair and replenishment. G-Graft is made of natural low crystalline Hydroxyapatite with collagen. It is available in form of granules, dowels and blocks. The shape can be changed by using Gigli saw and bone nibblers.[11] Wahl DA et al. proposed that, the composite of Hydroxyapatite & Collagen (G-Graft) may lead to earlier bone regeneration & greater density of the mature bone.[2] Araujo M et al. in a study also found that de novo hard tissue formation after 3 months, particularly in the cortical region of the extraction site using of hydroxyapatite /collagen composite (Bio-Oss Collagen) on healing of an extraction socket of dogs.[12] Johnson KD et al, in a study reported that Collagen-hydroxyapatite composite was better in comparison to tricalcium phosphate and hydroxyapatite used alone , in healing 2.5 cm bony defect created surgically in a canine radius model.[13] Although hydroxyapatite is the most widely studied stiff scaffold material, the frequency of its clinical use is less than 10% of all bone grafting procedures due to its unstable fixation and insufficient interaction with host tissues. Instead, hydroxyapatite composites (e.g., hydroxyapatite plus collagen derivatives) have been developed to mimic biochemical and biomechanical properties of natural bone in order to enhance osteointegration and graft healing for potential biomedical applications. The rapidly evolving technology enables the development of biomimetic nanocomposite biomaterials that fulfill the current requirements of an improved bone scaffold.[14]

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