Fabrication and characterization of porous hydroxyapatite ocular implant followed by an in vivo study in dogs

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Abstract. Porous hydroxyapatite ocular implant was fabricated by a novel and simple method using hydroxyapatite powder synthesized in the laboratory. The porosity and pore size of the implant were controlled to make it light in weight as well as suitable for rapid vascularization after implantation. The implant was characterized by X-ray diffraction studies, infrared spectra and chemical analysis for phase purity and chemical composition. The pore morphology and pore size distribution of the samples were investigated by scanning electron microscope (SEM). Thereafter, efficacy of the implant was examined by in vivo study in dogs. Clinical, haematological and radiological studies indicated the suitability of the implant for replacement of the lost eye of human patients.

Keywords. Bio-ceramics; hydroxyapatite; porous implant; ocular implant; in vivo study.

1. Introduction

Hydroxyapatite (HAp) is the principal inorganic constituent of bone and teeth. The chemical similarity of this material with bone and teeth as well as its excellent biocompatibility and bioactivity has attracted the attention of medical professionals. For the last several years, hydroxyapatite ceramics in different forms (block, granules, coating) are being used widely in the field of orthopaedics (Uchida et al 1990; Aoki 1991; Lavernia and Schoenung 1991; Ozawa and Kasugai 1996; Dorozhkin and Epple 2002) and dentistry (Legeross 1988; Passi et al 1991; Ichikawa et al 1996). The extensive research on biological and physico-chemical properties of this material has widened its scope of application and in recent years it has found promising application in other areas of medicine (Aoki et al 1987; Grote 1987; Shin et al 1992) also.

The use of hydroxyapatite as an ocular implant is a relatively new development (Perry 1990, 1991; Dutton 1991; Shields et al 1991; Ferrone and Dutton 1992). When an eye of a person is damaged due to disease or injury, the surgeon removes the eyeball from the orbit to avoid the risk of life or risk to the other eye of the patient. The lost eye can be mechanically replaced by an ocular implant to fill-up the orbital volume lost after enucleation or evisceration to achieve better cosmesis and rehabilitation of the anophthalmic patient. In the past, many materials have been tried for this purpose but with little success. Until the 19th century, artificial eyes were made of metal, which were soon discarded as they were expensive, heavy and painful to wear. In 1884, Mules (1885) was the first to introduce hollow glass sphere as an implant. This sphere offered some support for the upper eyelid but was unable to relieve the chronic downward pressure on the lower lid which is essential to alleviate the lid sag characteristic of long term anophthalmic patients and therefore, the search was on for more suitable material. Subsequently numerous materials like gold, cartilage, xenogeneic animal eyes, silver, aluminium, silicone and glass beads were used to fill irregular cavities in the orbit. Most of the implants composed of these materials were found unsuitable due to various reasons and were discarded one after another. In 1941, an acrylic based, partially exposed orbital implant was introduced by Ruedemann (1946). Since this implant had to be manufactured before each operation and further secondary strabismus procedures were often required to correct late position problems, this implant was also eventually abandoned. There have been many variations in the designs of orbital implants (Gougelmann 1976) after the Ruedemann eye. The partially exposed implants imparted good motility to the artificial eye, but were prone to infection and extrusion. Buried implants were then developed (Gougelmann 1976) to provide motility through special contours on the anterior aspect of the implant which matched corresponding contours on the posterior aspect of the eye.

In recent years, porous ocular implants composed of hydroxyapatite (HAp) are widely accepted for recon-
struction of the artificial eyes after enucleation and evisceration surgery. Porous implants capable of sustaining fibrovascular growth are termed as integrated implants. Porous implants have the advantage of becoming infiltrated by fibrovascular tissue, thereby providing resistance to infection, migration and extrusion (Rosen 1991; Shields et al 1993; Christmas et al 1998).

Currently available coralline derived HAp implants (Dutton 1991) provide excellent fibrovascular in-growth. But, these implants have a rough outer surface that sometimes abras the overlying conjunctiva and Tenon’s capsule resulting in exposure of the implant. There are also concerns about human immunodeficiency virus (HIV) infection and the need for an additional surgery to harvest a donor sclera. The availability of the starting material i.e. coral, from commercial sources is irregular and the chemical composition of the coral varies widely due to the presence of ions such as magnesium, sodium, chloride and fluoride in seawater. This affects the sintering parameters and the biological response and thereby, the control of process parameters becomes difficult. So, the need for an ocular implant material with a smoother implant surface is a necessity to reduce abrasion on the orbital tissues during and after implantation. The smoother surface is expected to facilitate deeper placement of the implant in the orbit and reduce intra-operative time because the implant may not need to be surrounded by an additional coating. In a very recent publication, Munoz et al (2001) have reported the preparation of eyeball prosthesis from HAp ceramic powder by gel-casting method. The pore size distribution of the prosthesis was in the range of 10–40 μm.

The objective of the present study is to provide a novel and simple process for the production of porous ocular implants from synthetic calcium hydroxyapatite and to examine its efficacy by an in vivo study in dogs.

2. Experimental

2.1 Powder preparation

The HAp powder was prepared by precipitation between Ca(OH)₂ and H₃PO₄ according to the following reaction:

\[ 10 \text{Ca(OH)}_2 + 6\text{H}_3\text{PO}_4 = \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 18\text{H}_2\text{O} \]

An aqueous solution of H₃PO₄ was added very slowly to a suspension of Ca(OH)₂. During reaction, temperature of the suspension was maintained at 80°C and pH 11–12. The resulting precipitate was aged, dried and calcined at 800°C. The calcined powder was ground in a planetary mill and characterized for phase purity, chemical composition and particle size analysis. The details of powder synthesis and its characterization have been described elsewhere (Sinha et al 2000), which is also schematically shown in figure 1.

2.2 Fabrication of ocular implants

The HAp powder calcined at 800°C was used for the fabrication of implant. The powder was intimately mixed with appropriate quantity of naphthalene powder (300 μm size) by repeated sieving. The powder mix was inserted into rubber bag and compacted at a pressure of 160 MPa by cold-isostatic pressing (EPST NV; SO 10036, Belgium) to form cylindrical shape (diameter 25 mm and length 115 mm) which was subsequently machined to fabricate the ocular implant. By heating at 80°C, the naphthalene was driven off from the green implant and great care was taken at this stage to prevent cracking. Finally, the implant was sintered at 1250°C for 3 h to improve the mechanical properties. Figure 2 schematically outlines the method for fabrication of ocular implant.

2.3 Implant characterization

The implant was characterized by X-ray diffraction (Philips PW1710) using monochromatic Cu Kα₁ radiation at

![Figure 1. Scheme of the HAp powder preparation.](image-url)