

**BIOCOMPATIBLE CEMENT CONTAINING
REACTIVE CALCIUM PHOSPHATE
NANOPARTICLES AND METHODS FOR
MAKING AND USING CEMENT**

**CROSS REFERENCE TO RELATED PATENTS
AND PATENT APPLICATIONS**

The present application is a divisional of copending U.S. patent application Ser. No. 09/978,601, which was filed on Oct. 16, 2001, and which was a non-provisional of U.S. Provisional Patent Application Ser. No. 60/239,980, filed Oct. 16, 2000, both of which applications are hereby incorporated herein by reference in their entirety.

Work leading to this invention was supported, at least in part, by federal research grant no. N00014-97-1-0806, Department of Defense, Office of Naval Research, and the federal government may retain some rights in the invention.

BACKGROUND OF THE INVENTION

(1) Field of the Invention

The present invention relates to the production and use of cement-type materials that can be used in biological applications, and more particularly to the production and use of calcium-phosphate cement-type materials that can be used in biological applications.

(2) Description of the Related Art

To date, a wide variety of implant materials have been used to repair, restore, and augment bone. The most commonly used implants include autologous bone, synthetic polymers, and inert metals. Protocols using these materials have significant disadvantages that can include patient pain, risk of infection during operations, lack of biocompatibility, cost, and the risk that the inserted hardware can further damage the bone. Therefore, a major goal of biomaterial scientists and plastic and reconstructive orthopedic surgeons has been to develop novel bone substitutes that can be used as alternatives to these conventional techniques for skeletal repair. Ideally, treatment of such injuries as bone fractures, for example, should achieve anatomical reduction of the fracture, avoid unnecessary tissue damage, and provide temporary stability until healing occurs.

To this end, interest in the early 1980's focused on the use of hydroxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] to augment skeletal defects and for use as a coating on prosthetic implants. Sintered hydroxyapatite is a biomaterial that has attracted much interest as a substitute for injured bone and teeth due to its chemical and crystallographic similarities to the principal inorganic constituent of these hard tissues. However, sintered, preformed hydroxyapatite prosthetic devices have several disadvantages that include being difficult for the surgeon to physically shape and install, having insufficient strength to support heavy loads, and are only very slowly resorbed by the host—typically at a rate of less than 1% per year.

Bone cements, such as cements based on polymethylmethacrylate (PMMA) offer certain advantages in avoiding the use of solid implants, but also have several disadvantages. Methacrylates and methacrylic acid are known irritants to living tissues, and when PMMA-based cements are cured *in vivo*, free-radicals are generated, which can damage surrounding tissues. Moreover, the polymerization reaction for these materials is highly exothermic, and the heat evolved during curing can damage tissues.

More recently, calcium and phosphate-based bone cements (CPCs) and pastes have been the subject of much

attention as potentially superior bone substitutes because they show excellent biocompatibility and appear to be resorbed. CPCs are rapidly emerging as third generation bone substitutes and could potentially positively impact many diverse areas of orthopedic, craniofacial, and reconstructive surgery. However, current calcium phosphate-based bone cements appear to lack sufficient compressive strength and are therefore only potentially suitable for use in treating injuries to non-weight-bearing bones such as wrist fractures and in cranial/facial augmentation surgeries.

Accordingly, it would be useful to provide a material that could be used as a bone cement that was non-toxic and biocompatible with the tissue surrounding its site of use. It would also be useful if such material was self-setting—needing no irritating initiator or accelerator to promote curing, and also that the curing itself did not generate free-radicals or heat sufficient to harm surrounding tissues. It would also be useful if such material could be provided in a physical form that could be injected, flowed or applied to the site of action in a manner that would permit a minimum of invasive surgery and would allow the cement to intimately contact the parts to be joined. It would also be useful if such material could cure quickly, and to develop a high compressive strength upon curing. It would also be useful if such material was bioabsorbable by the host.

SUMMARY OF THE INVENTION

Briefly, therefore, the present invention is directed to a novel cement powder comprising reactive tricalcium phosphate nanoparticles and other ingredients required to form a cementous material.

The present invention is also directed to a novel cement paste comprising a lubricating liquid which is intermixed with a cement powder that includes reactive tricalcium phosphate nanoparticles and other ingredients required to form a cementous material.

The present invention is also directed to a novel biocompatible cured cement comprising the cured form of a cement paste comprising a lubricating liquid which is intermixed with a cement powder that includes reactive tricalcium phosphate nanoparticles and other ingredients required to form a cementous material.

The present invention is also directed to a novel method of making a cement powder containing reactive tricalcium phosphate nanoparticles, the method comprising forming the reactive tricalcium phosphate nanoparticles by precipitation from solution; and intermixing the nanoparticles with other ingredients required to form a cementous material.

The present invention is also directed to a novel method of making a cement paste containing reactive tricalcium phosphate nanoparticles, the method comprising intermixing a lubricating liquid with a cement powder that includes reactive tricalcium phosphate nanoparticles and other ingredients required to form a cementous material.

The present invention is also directed to a novel method of binding articles together comprising: providing a cement paste comprising a lubricating liquid which is intermixed with a cement powder that includes reactive tricalcium phosphate nanoparticles and other ingredients required to form a cementous material; placing the cement paste at an interface of the articles to be bound together; and curing the cement paste to form a bond between the articles.

The present invention is also directed to a novel article that is formed from a biocompatible cured cement comprising the cured form of a cement paste comprising a lubricating liquid which is intermixed with a cement powder that