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REVIEW ARTICLE

ARTIFICIAL BONE- AN OVERVIEW

Balveer Singh*, Vivek Daniel, Kratika Daniel, Sarika Sharma

Department of Pharmaceutical Chemistry, Mandsaur Institute of Pharmacy, Mandsaur (M.P), India

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Abstract

Replacement of extensive local bone loss is a significant clinical challenge. There are a variety of techniques available to the surgeon to manage this problem, each with their own advantages and disadvantages. It is well known that there is morbidity associated with harvesting of autogenous bone graft and limitations in the quantity of bone available. Alternatively allografts have been reported to have a significant incidence of postoperative infection and fracture as well as the potential risk of disease transmission. During the past 30 years a variety of synthetic bone graft substitutes has been developed with the aim to minimize these complications. The benefits of synthetic grafts include availability, sterility and reduced morbidity. The present article examines the relevance of synthetic bone graft substitutes, their mechanical properties and clinical application.

Keywords: Allograft; autogenous; bone graft substitute; future

INTRODUCTION

Bone

Bones are rigid organs that form part of the endoskeleton of vertebrates. They function to move, support, and protect the various organs of the body, produce red and white blood cells and store minerals. Bone tissue is a type of dense connective tissue. Because bones come in a variety of shapes and have a complex internal and external structure they are lightweight, yet strong and hard, in addition to fulfilling their many other functions. One of the types of tissue that makes up bone is the mineralized osseous tissue, also called bone tissue that gives it rigidity and a honeycomb-like three-dimensional internal structure. Other types of tissue found in bones include marrow, endosteum and periosteum, nerves, blood vessels and cartilage. There are 206 bones in the adult human body and 270 in an infant. The largest bone in the human body is the femur. [1]

Artificial bone

It refers to bone-like material created in a laboratory that can be used in bone *grafts*, to replace human bone that was lost due to severe fractures, disease, etc.

Bones are rigid organs that serve various functions in the human body including mechanical support, protection of soft organs, blood production (from bone marrow), etc. Bone is a very complex tissue: strong, elastic, and self-repairing. Damaged bone can be replaced with bone from other parts of the body (autografts), from cadavers (alograft), or with various ceramics or metallic alloys. [1]

A Review on Artificial Bone

Scientists have developed "injectable bone", a soft substance which hardens in the body. They won the Medical Futures Innovation Award for their discovery, and it is planned to test this material in clinical trials. Researchers at Columbia University have grown an anatomically correct human jawbone from stem cells, though it was solid bone without the normal accessory tissues such as bone marrow, cartilage, or a connectable blood supply. Other researchers, at the Istec bioceramics laboratory in Italy, have produced a nearly-identical substitute for human bone out of rattan wood.

***Corresponding Author:** Balveer Singh, **E-mail:** siinghveer007@gmail.com

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The substitute bone has a porous structure permitting blood vessels and other accessory tissues to penetrate it, allowing seamless integration into the host bone. The process has been tested on sheep, who showed no signs of rejection after several months. Bone takes a long time to grow and repair, so treating serious damage or carrying out reconstructive procedures can be a slow and painstaking process. Writing in issue 6 of Advanced Materials, Jake Barralet of the Faculty of Dentistry, at McGill University, (Montréal, Québec) and Uwe Gbureck, Department for Functional Materials in Medicine and Dentistry, University of Würzburg, (Bavaria) and their team describe a method for "printing" artificial bone from the same chemical components as living bone and including biomolecules that trigger blood vessel growth to bring the bone to life after it is implanted in the body. The process could be much more effective and less risky than removing sections of bone from elsewhere in the body for grafting on to an injured site.[2]

Tissue growth, explain the researchers, is guided by a whole range of cellular signaling molecules that ebb and flow over time, switching on and off yet more molecules that trigger growth, and crucially, growth of blood vessels into a tissue. By incorporating the blood vessel growth factors into their artificial bone implants, Barralet and colleagues hope that their approach will allow acceleration of integration of such implants into a graft site. "This low-temperature direct approach offers several practical advantages and may find application in bone grafting," the researchers say. The team has so far tested blood vessel growth into the implant materials made with and without VEGF. They found that blood vessels can grow only one or two millimetres into the pores of VEGF-free artificial bone. In contrast, the artificial bone made with added VEGF promotes blood vessels growth throughout its network of pores. Such a demonstration bodes well for the further development of bespoke printable bone grafts.[3]

Advantages:

1. Compared with other bone scaffold materials currently available in the market, IBN's scaffold has better mechanical properties, and microstructural and chemical match to natural bone. It also appears more osteoinductive than existing scaffolds.
2. Control of the material's pore size and porosity can be easily achieved by controlling relevant parameters of the freezedrying process, such as the freezing rate and water content of the sample.
3. As IBN is able to produce the raw materials cheaply in large quantities in-house, it will be possible to sell this scaffold at a lower price than existing scaffolds. [3]

Applications:

- This scaffold material can be applied commercially as an osteoinductive load-bearing hard tissue implant.
- It can also be used for other tissue engineering applications. [3]

Structure of Bone

The majority of bone is made of the bone matrix. It has inorganic and organic parts. Bone is formed by the hardening of this matrix entrapping the cells. When these cells become entrapped from osteoblasts they become osteocytes. [4]

1 Inorganic

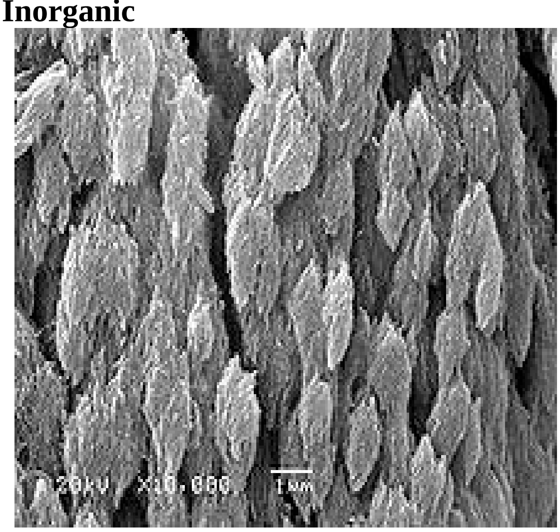

Fig 1: Electronic micrography 10000 magnification of Bone mineral.

2. Organic

The organic part of matrix is mainly composed of Type I collagen. This is synthesised intracellularly as tropocollagen and then exorted, forming fibrils. The organic part is also composed of various growth factors, the functions of which are not fully known. Factors present include glycosaminoglycans, osteocalcin, osteonectin, bone sialo protein,

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osteopontin and Cell Attachment Factor. One of the main things that distinguishes the matrix of a bone from that of another cell is that the matrix in bone is hard. [5,6]

HISTORY [8-20]

1 Hips

Due to the crippling nature of arthritis, surgeons have been trying for well over a century to successfully treat this debilitating disease. It was clear that many people required surgery to relieve the terrible pain and keep their joints mobile. Initial attempts to treat arthritic hips included arthrodesis (fusion), osteotomy, nerve division, and joint debridements

In 1925, a surgeon in Boston, Massachusetts, M.N. Smith-Petersen, M.D., molded a piece of glass into the shape of a hollow hemisphere which could fit over the ball of the hip joint and provide a new smooth surface for movement.

As early as 1938, Dr. Jean Judet and his brother, Dr. Robert Judet, of Paris, attempted to use an acrylic material to replace arthritic hip surfaces. This acrylic provided a smooth surface, but unfortunately tended to come loose. The idea did lead Dr. Edwarc J. Haboush from the Hospital for Joint Diseases in New York City to utilize a "fast setting dental acrylic" to actually glue the prothesis to the bone. A new era in fixation techniques had begun. In England, a very innovative surgeon, John Charnley, was also attempting to solve these ongoing problems. Some of his ideas were so bold and creative that he was seriously questioned by many of his colleagues. He was relegated or banished to an isolated tuberculosis sanatorium that had been converted to a makeshift hospital.

By 1961, Charnley was performing the surgery regularly with good results. He further improved the techniques and component designs. Thousands of people were successfully relieved of their hip pain and the long term results became very predictable. The Queen of England knighted him for his immense contributions.

2. Knees

A parallel line of development occurred with total knees that was occurring with total hips. The first attempt at total knee arthroplasty was a prosthesis which was really a hinge fixed to the bones with stems into the medullary canals (the hollow marrow cavity).

MATERIAL USED FOR ARTIFICIAL BONE [9]

1 Design

The performance of the artificial bone depends on its composition and end use application. Careful selection of the right material with suitable properties is thus important.

2 Raw material preparation

1 The ceramic powder is manufactured elsewhere from mined or processed raw materials. Additional crushing and grinding steps may be necessary to achieve the desired particle size. The ceramic powder plus additives are carefully weighed in the appropriate amounts and then mixed in some type of mixing machine equipped with blades or revolving rolls. [10]

3 Forming

After mixing, the ceramic material is of plastic consistency and now ready for forming into the desired shape. A variety of methods can be used, including injection molding, extrusion, or pressing. In injection molding, the mix is loaded into a heated cylinder, where it softens.[11]

4 Drying and firing

After forming, the ceramic bone must undergo several thermal treatments. The first dries the material to remove moisture using a drying oven or chamber.

5 Finishing

After firing, one or more finishing processes may be required depending on application. To achieve the desired dimensional and surface finish specifications, grinding and/or polishing is conducted. Grinding and polishing of the harder materials usually requires diamond tooling or abrasives. Drilling may be needed to form holes of various shapes. If the application requires joining of two or more components, a brazing or cementing method is used. [12, 13]

6 Byproducts/Waste

Since careful control of the manufacturing process is so important, waste is minimal. Since contamination must be avoided, any waste produced can only be recycled if the properties match the starting material.[14]

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7 Porous Gelcast Ceramics For Bone Repair Implants

Two different carbon powders are added as pore-forming agents: activated carbon and graphite, in varying weight percentages up to 10% of the total mass of added powder, which are burned out when the sample is sintered. [15]

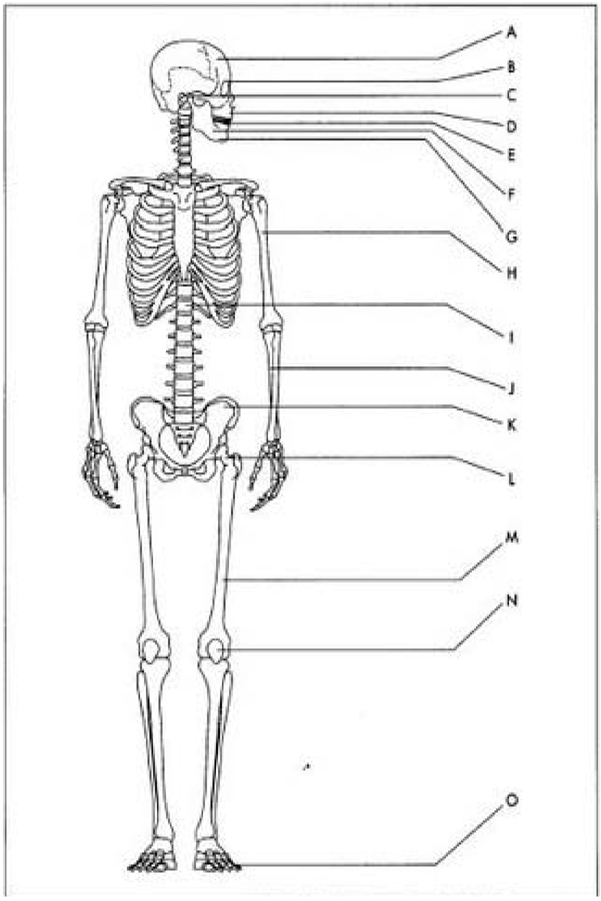

Fig 2: The bioceramic applications. A. Cranial repair. B. Eye lens. C. Ear implants. D. Facial reconstruction. E. Dental implants. F. Jaw augmentation. G. Periodontal pockets. H. Percutaneous devices. 1. Spinal surgery. J. Iliac crest repair. K. Space fillers. L Orthopedic support purposes. M. Orthopedic fillers N. Artificial tendons. O. Joints. [13]

Gelcasting Recipe

Component Name	Percent (%) Weight	Percent (%) Volume
Monomer 15% HMAM solution	19.43	45.31
Dispersant Darvan C as received	2.34	5.93
Polymerizing Agent 10% AZIP solution	1.73	3.93
Powder	76.50	44.83

The alumina that has been used in the experiments is ERC-DBM, with d50 = 0.462 µm obtained from Baikowski Malakoff, Inc. A relatively small particle size has been chosen to try to increase the packing density of the alumina and thus reduce the size and frequency of pores caused solely by the processing of alumina. Eliminating these pores allows for a better interpretation of the results obtained by the addition of the impurity particles. [16]

8 Nacre/polylactide acid

The compound of nano-scale nacre powder and poly-D, L-lactide acid (PDLLA) was used to prepare the cylindrical hollow artificial bone, whose properties including raw material powder scale, pore size, porosity and biomechanical characteristics were compared with another artificial bone made of micron-scale nacre powder and PDLLA. [17]

9 Calcium phosphate

Glass ceramic for use as a biomaterial comprising CaO 34.6 to 54.6%, SiO_2 24.2 to 44.8 %, P_2O_5 0 to 8.0%, CaF_2 0.1 to 1.0% and Mgo 1.0 to 10.0% by weight and characterized by a primary wollastonite crystalline phase (CaO, SiO_2) and a secondary apatite crystalline phase, and the process for the preparation thereof are disclosed. [18]

PROCESS [19-20]

For producing an artificial bone model

The alumina and carbon powders are mixed prior to their addition to the monomer solution in order to achieve a more uniform mpurity powder distribution and to reduce agglomerations. Two different powder mixing methods were tested, by hand and using a double-blade mixer, in an effort to characterize the effects of mixing on the resulting microstructures. After mixing, small quantities of powder are added to the monomer/dispersant solution at a time with approximately 10 minutes of stirring in between powder addition steps. After the addition of all of the powder, the polymerizing agent AZIP is added while the slurry is continuously stirred.

1.A novel - and natural - way of creating new bones for humans could be just a few years away.

Scientists in Italy have developed a way of turning rattan wood into bone that is almost identical to the human tissue. At the Istec laboratory of bioceramics in Faenza near Bologna, a herd of sheep have already been implanted with the bones. The process starts by cutting the long tubular rattan wood up into manageable pieces.

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2 Injectable artificial bone developed

Fig 4: Quirk, a pharmacist and co-founder of RegenTec – the University of Nottingham, In England, and spin-off company commercialising the technology

3 Stimulate tissue repair

Quirk told Cosmos Online that the next generation of technologies based on this method will focus more on the therapeutic drugs and growth factors that can be delivered alongside the injectable bone to stimulate tissue repair.

4 Production of bone stone

Granulation of the basic substance 150 g of the crystals are gradually mixed with approximately 60 g of a 3% gelatin solution (at approximately 40-50°C) to form a moldable mass. This substance is then passed through a sieve with a mesh size of 0.8 mm, and is pre-dried for 3 hours at 30-40°C. The granules that have been formed by this procedure are passed through the sieve again and dried over a period of 24 hours at 30-40°C.

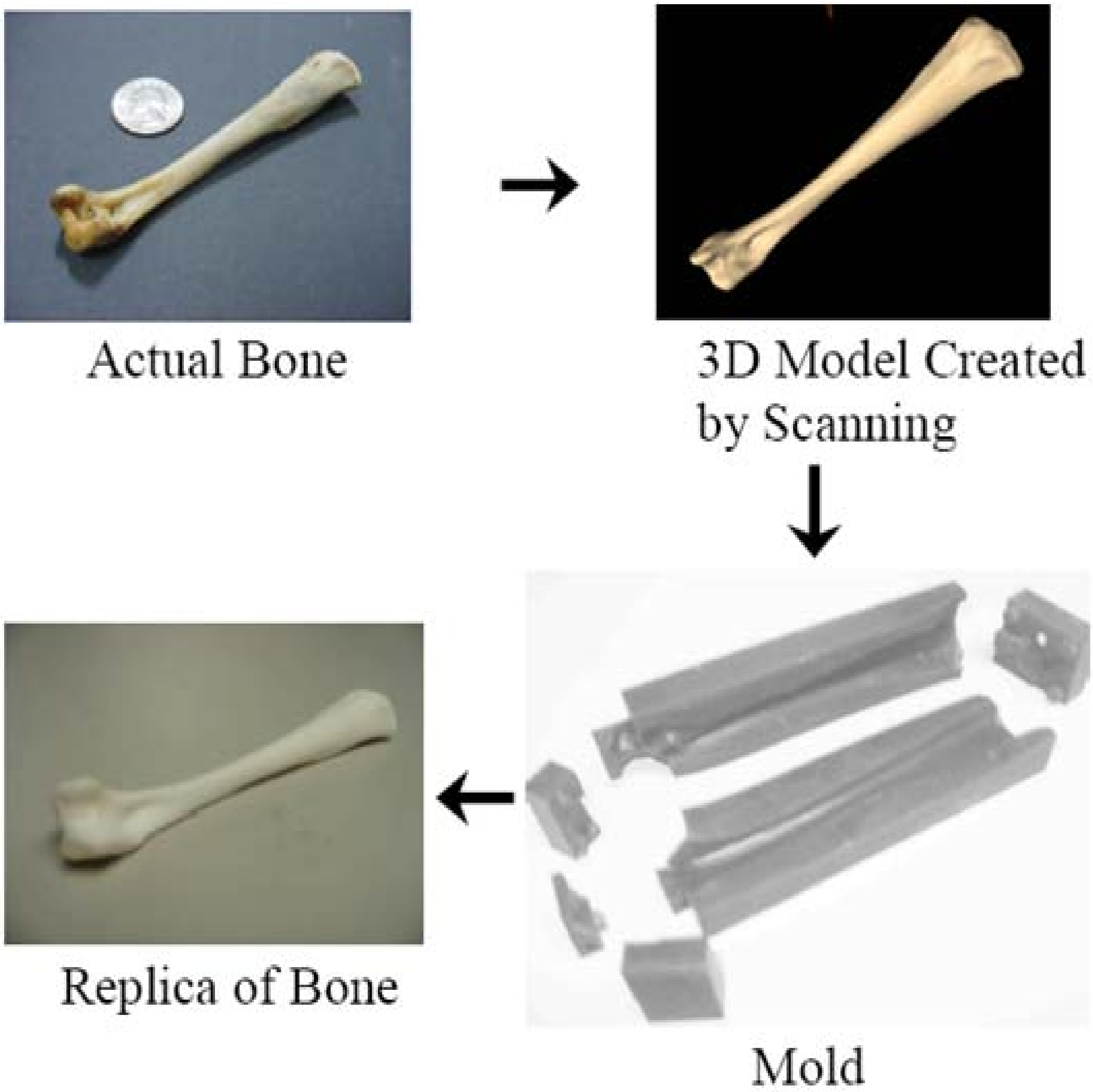

Figure 03- Bone generation process

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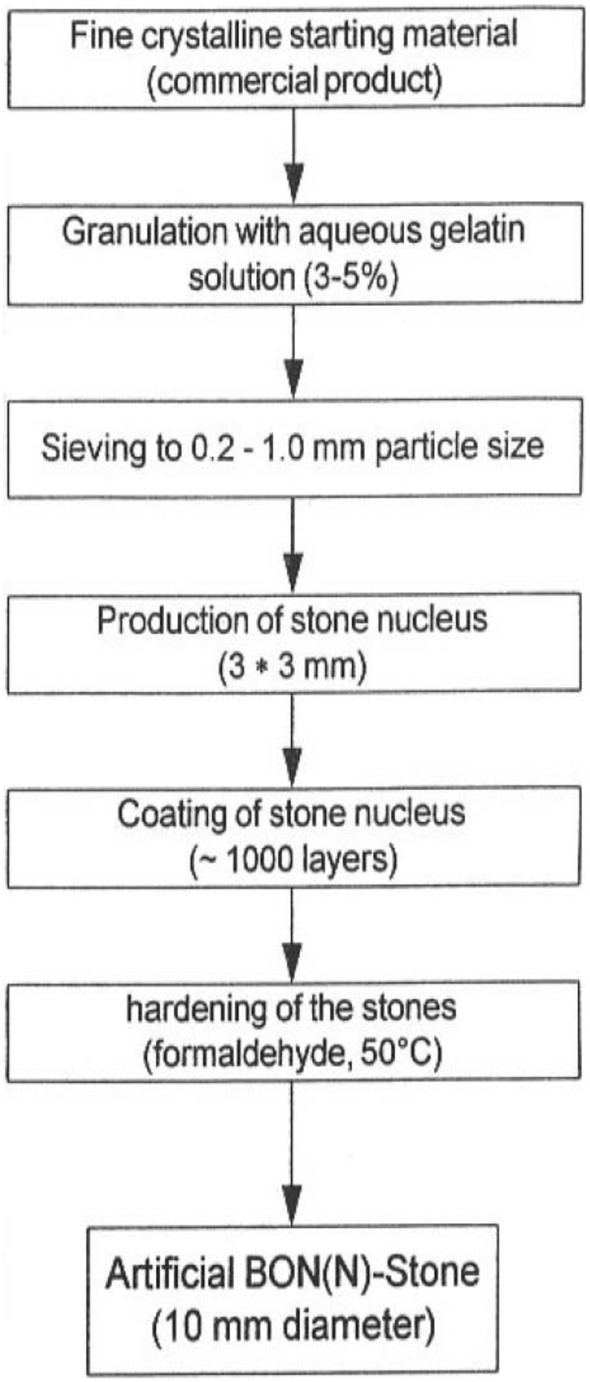

5. CONDITION OF ARTIFICIAL BONE APPLICATION WITH TECHNIQUES

1 Inkjet Technology Applications

Inkjet-produced bones and rapid prototyping are part of a wider effort to use these technologies to make precise, custom-designed implants for medical use.

2 Collagen-Hydroxylapatite

In this study artificial bone was made of collagen-hydroxylapatite (CHA) and its osteogenetic effects in different locations of the rabbit's skeleton were evaluated. Collagen solution extracted from the adult rabbit's skin was mixed with the chemically synthesized hydroxylapatite. 62 rabbits were divided into four groups.

Biological mechanism

Properties of various types of bone graft sources.[12]

	Osteoconductive	Osteoinductive	Osteogenic
Alloplast	+	–	–
Xenograft	+	–	–
Allograft	+	+/–	–
Autograft	+	+	+

Bone grafting is possible because bone tissue, unlike most other tissues, has the ability to regenerate completely if provided the space into which to grow. As native bone grows, it will generally replace the graft material completely, resulting in a fully integrated region of new bone. The biologic mechanisms that provide a rationale for bone grafting are osteoconduction, osteoinduction and osteogenesis.[20]

CONCLUSION

Clearly, in anticipation of the petaop machines, mapping of applications on millions of processing elements will require next generation algorithms and efficient mapping models. In particular, we believe that the models of mapping such as graph partitioning or even the most advanced ones such as hypergraph partitioning, will need to be extended or modified so that the particular underlying architecture is seriously taken into consideration.

REFERENCES

1. Grimm M. E., Francis L. F., Lewis J. L., Oegema T. R., Jr., Connective Tissue Research submitted, (2001).
2. Fedewa M. M., Oegema Jr. T. R., Schwartz M. H., A. MacLeod, J. L. Lewis, Journal of Orthopedics Research 16, 227 (1998).
3. T. Kokubo, H. Kushitani, C. Ohtsuki, S. Sakka, T. Yamamuro, J. Mater. Sci.: Materials in Medicine 1, 233 (1990).
4. Rodriguez-Lorenzo, L.M. and Ferreira, J.M.F., Development of porous ceramic bodies for applications in tissue engineering and drug delivery systems, Materials Research Bulletin, vol. 39, pp. 83-91, 2004.
5. Maca, K., *et al.*, Fabrication of graded porous ceramics using alumina-carbon powder mixtures, Ceramics

International,vol. 27, pp. 577-584, 2001.
6. Angier, Natalie (2009-04-28). "Bone, a Masterpiece of Elastic Strength". The New YorkTimes.http:// www.nytimes.com/2009/04/28/science/28angi.html?_r=1. Retrieved 2010-04-25.
7. "Orthopaedic Trauma Association/ Committee for Coding and Classification:Fracture and Dislocation Compendium". Orthopaedic Trauma Association. .retrieved 2007-11-28.
8. Granz B, Köhler G (1992) what makes a shock wave efficient in lithotripsy? J Stone Dis 4: 123-128.
9. Heimbach D, Jacobs D, Winter P, Süverkrüp R, Hesse A (1996) Production of artificial urinary stones from natural materials and their physical properties - First results. Scand J Urol Nephrol 31: 9-13.
10. Hesse A, Sanders G (1988) Atlas of Infrared Spectra for the Analysis of Urinary Concrements. Thieme Verlag Stuttgart, New York.
11. Hesse A, Heimbach D, Jacobs D, Süverkrüp R (1995) Verfahren zum Herstellen von synthetischen Harnsteinen. (Procedure for the Production of Synthetic Urinary Stones). Deutsches Patent Nr 19: 505 591.
12. B.D. Ratner, A.S. Hoffman, Biomaterials Science: An Introduction to Materials in Medicine, Elsevier Science & Technology, 2004.
13. W. Frieb, J. Warner, in: F. Schuth, K.S.W. Sing, J. Weitkamp (Eds.), Handbook of Porous Solids, Wiley-VCH, Weinheim, 2002, pp 29-23.
14. A. Bigi, E. Boanini, K. Rubini, J. Solid State Chem. 177 (2004) 30-92.
15. L.L. Hench, J. Wilson, An Introduction to Bioceramics, World Scientific, Singapore, 1993.
16. J.C. Le Huec, T. Schaeverbeke, D. Clement, J. Faber, A. Le Rebeller, Biomaterials 16 (1995) 113.
17. Y. Shinto, A. Uchida, F. Korkusuz, N. Araki, K. Ono, J. Bone Joint Surg. 74 (1992) 600.
18. Ramay, H. and Zhang, M., Preparation of porous hydroxyapatite scaffolds by combination of the gel-casting and polymer sponge methods, Biomaterials, vol. 24, pp. 3293-3302, 2003.
19. James, William; Berger, Timothy; Elston, Dirk (2005). Andrews' Diseases of the Skin: Clinical Dermatology. (10th ed.). Saunders. Page 517.
20. Rauch F, Glorieux FH (2004). "Osteogenesis imperfecta". Lancet 363 (9418): 1377–85.
21. Glorieux FH, Bishop NJ, Plotkin H, Chabot G, Lanoue G, Travers R (1998). "Cyclic administration of pamidronate in children with severe osteogenesis imperfecta". N. Engl. J. Med. 339 (14): 947–52.
22. O. Gauthier, J. Bouler, E. Aguado, P. Pilet, G. Daculsi, Biomaterials (1998) 133
23. Chevrel G, Schott AM, Fontanges E, *et al*. (2006). "Effects of oral alendronate on BMD in adult patients with osteogenesis imperfecta: a 3-year randomized placebo-controlled trial". J. Bone Miner. Res. 21 (2): 300–6.
24. Viljoen D, Beighton P (1987). "Osteogenesis imperfecta type III: an ancient mutation in Africa?". Am. J. Med. Genet. 27 (4): 907–12.
25. DiMeglio LA, Peacock M (2006). "Two-year clinical trial of oral alendronate versus intravenous pamidronate in children with osteogenesis imperfecta". J. Bone Miner. Res. 21 (1): 132–40.