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Editorial

Current trends on porous inorganic materials for biomedical applications

This special issue, devoted to recent progress in porous inorganic materials for medical applications, has been made possible thanks to the interest and efforts of many people involved. In particular, I would like to express my gratitude to Elsevier, to the Editorial Board of Chemical Engineering Journal, and to our co-editor, Prof. J. Santamaria, for his constant support in this task.

Nowadays, the research on porous inorganic materials for medical applications is mainly focused in two large subjects: design and fabrication of scaffolds within the field of biomaterials, and development of substrate materials eligible for loading and releasing drugs or biologically active molecules in a controlled manner, within the pharmacology field. Both fields interact deeply in many situations, which points out to the interdisciplinary research necessary in this area. However, even if these are not the only research lines currently in use for this kind of materials with biomedical applications, their relevance is very remarkable.

In order to explain the interest in developing these materials, let me first introduce some statistical data. Life expectancy reached values between 75 and 81 years by the end of the 20th century in the European Union. This is a spectacular figure if compared to those corresponding to early 20th century, around 40 years, while in Imperial Rome the life expectancy was only 22 years of age. Therefore, 19 centuries passed before the expected lifespan doubled and then, in just one century, the 20th century, it doubled again. This outstanding rise is still ongoing, increasing the demand and the need for biomaterials to replace damaged parts of the body. We could define biomaterials as “implantable materials that must be in contact with living tissues”, with the final aim of achieving a correct biological interaction between the material and the host. We know that the reactivity of solids begins on their surface. This general statement is of particular importance in the field of biomaterials, since they will be in contact with a wet medium and in presence of cells and proteins. Depending on the function to perform, biomaterials can be manufactured from very different materials.

Nowadays, it is possible to manufacture implants to replace any part of our body, except the brain. Obviously, different types of materials are in use depending on the tissue to be replaced. Regarding the materials to be used, it is critical to bear in mind that a group of biomaterials will be applied in body reconstruction functions, hence they must perform their duty for an undefined period of time, i.e. for the rest of the patient’s life. Besides, another group of biomaterials will be used in temporary body support functions. This “permanent” or “temporary” feature allows for a larger and better choice of materials for implant manufacture.

At this point, it becomes clear that the field of biomaterials requires the input of knowledge from very different areas so that the implanted material in a living body performs adequately. The biomaterials discipline is founded in the knowledge of Materials Science and Biological Clinical Science. In this sense, biomaterials are an excellent example of a pluridisciplinar field where the material, developed by material scientists and engineers, has to be validated and must perform its task inside the human body, under the expertise of physicians and biologists; the final outcome must be analyzed and coordinated by all the intervening scientists. This fact is also evident in this special issue, with contributions from specialists on all these disciplines, with the common aim to solve biomedical issues.

The process itself is very long because it starts when a specific need is identified, then the idea of a potential implant is developed, and it is concluded with the final insertion of the implant in a patient. Several stages have to be verified: material synthesis, design and manufacture of the prosthesis, combined with multiple material tests. Besides, it must also fulfill all regulatory requirements before its application to patients.

We may begin by reviewing the present solutions for bone repairing, those which are being applied today. Not very long ago, the most popular solutions involved the use of natural materials, using bone from the patient himself, or from a bone donor bank, or even from animals. But there are some disadvantages when using natural materials: in the first case, the patient has to endure two surgical interventions instead of one, and there are general risks of infection (HIV, Creuzfeld-Jacob ...) in all the others. This is why artificial materials are gradually being considered with more interest.

When searching for ceramic bone substitutes, the chronology has been as follows: It all started in the 1950s, when the first attempt was to use inert materials which had no reaction with living tissues. Later on, in the 1980s, the trend changed towards exactly the opposite; the idea was to implant ceramics able to

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react with the environment and produce newly formed bone. And then, in this 21st century, we are searching for new porous ceramics that act as scaffolds for cells while hosting certain molecules, able to drive self regeneration of tissues.

Let us now analyze this situation: The first generation is formed by inert ceramics. From the chemical point of view, two well known examples are zirconia and alumina. But these ceramics, in a similar way to what happens with metallic and polymeric biomaterials, provoke foreign body reactions. Therefore, and although they are biocompatible, the body will react against them due to their foreign nature; the implant will be then surrounded by an acellular collagen capsule which isolates it from the body. In this way, the material will never transform itself into bone, and its artificial nature prevails.

The search for bioactive ceramics yields promising results in the 1980s. These ceramics can react with the physiological fluids forming biological-type apatite as a by-product of said reaction; in the presence of living cells, this apatite can form new bone. Among these ceramics we can mention calcium phosphates, and several compositions of glasses and glass ceramics. For medical applications, these materials are provided in the following forms: powder, porous pieces, dense pieces, injectable mixtures and cements, and coatings. They have excellent features in terms of biocompatibility and bioactivity, but their mechanical properties are very poor.

The bioactive glasses, when in contact with a simulated acellular physiological fluid, react to form an apatite that closely resembles the biological apatite found in bones. But if we perform the same process under *in vivo* conditions, hence in presence of living cells, what is actually obtained is newly formed bone. Although their bioactivity is excellent, the great problem of glasses is that their mechanical properties are very poor, rendering it impossible to use them in the repair of large osseous defects. However, these glasses have an excellent field of application in the filling of small defects, where the rate of regeneration is the main concern, and where mechanical properties are just a secondary issue.

But the glasses can also be used as precursors in the production of glass ceramics. In fact, a certain thermal treatment to a glass yields a glass ceramic, which exhibits better mechanical properties, among other advantages. Therefore, it is possible to obtain bioactive glass ceramics with mechanical properties much closer to those of the natural bone.

Another field of discussion is the possibility to obtain hybrid materials with adequate mechanical properties for bone replacement applications, while resembling the bioactivity of glasses. And in fact, it is possible to synthesise this type of hybrids with mechanical features similar to those of natural bone. It is feasible to obtain bioactive monoliths with moulded shapes and sizes. Therefore, still from the point of view of second generation bioceramics, it has been shown that it is possible to improve their mechanic properties.

We have been dealing so far with dense materials. In fact, we have met the challenge of the 1980s which was to achieve mechanical properties similar to those of natural bone. But the needs have evolved; it is necessary to induce in these materials porosity in the range of microns so that they can fulfil physiological requirements in their use as scaffolds for tissue engineering. In this sense, we need conformation methods that allow to obtain porous scaffolds keeping the small particle size of the ceramics.

At this point, perhaps we should consider briefly what implies the balance between mechanical properties and bioactivity. In second generation ceramics, the aim was primarily to improve their bioactivity, while trying to reach mechanical properties similar to those of natural bone. And following this route, it is possible to obtain bioactive ceramics with improved mechanical properties. It is also known that more dense materials exhibit better mechanical properties, although the transformation into bone becomes less complete. And as a consequence, it was necessary to consider the option of porous materials. On the other hand, driven by biological requirements, it became obvious that the ceramics have to be porous; and such porosity has to exhibit a hierarchical structure.

We may recall here the concept of porosity and its range of order. Those materials with mesoporosity between 2 and 50 nm are of interest for applications where drugs or biologically active molecules are loaded, and later released to help in the bone regeneration process. Macroporous materials, where the pore sizes are in the order of microns, are adequate as scaffolds for tissue engineering. The fabrication of scaffolds for tissue engineering requires choosing a conformation method that yields pieces with interconnected porosity and pores in the 2–400 μm range.

This is in short the path followed to reach third generation bioceramics. The main purpose now is to obtain porous ceramics that act as scaffolds for cells and inducting molecules, able to drive self regeneration of tissues. With these requirements, it would be possible to keep using second generation bioceramics with added porosity. But next generation ceramics could also be devised, with porosity values in agreement with biological requirements. As starting materials nanometric apatites could be used, shaped in the form of pieces with interconnected and hierarchical porosity, within the micron range.

At present, the aim is to find bioceramics which induce the regeneration of hard tissues stimulating the response of the cells involved. The requirements for these ceramics are to act as a scaffold and also to be porous so that the cells can do their job. This porosity implies a certain sacrifice of their mechanical properties. Some sort of ‘smart’ behaviour is also required, so that they can modify their properties in response to certain stimuli. And also, in some cases, to allow the loading of biologically active molecules onto such ceramics.

Therefore, the first step would be to find methods of conformation that yield pieces with interconnected porosity, with porosity in the range of microns. And this must be possible with all the bioceramics previously discussed. Nowadays, there are several conformation methods which allow to obtain pieces at room temperature. Besides, working at room temperature allows to include biomolecules of interest in many cases to treat different diseases, or to improve the treatment of various bone pathologies.

An important challenge is to design materials that can help the human body to improve its regeneration features, not only recovering the structure of the damaged tissue, but also its function.

This special issue contains 18 manuscripts which deal with different trends and techniques aimed at obtaining porous inorganic materials for biomedical applications. Said manuscripts have been subjected to a peer-reviewed process followed by the pertinent revisions by the authors. I would like to express my gratitude to the contributing authors, and to all reviewers involved in the refereeing process. Finally, I hope that the special issue presented will be of value for the scientific and technical community and will stimulate further research, design and application.

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