The Sintering Behaviour and Mechanical Properties of Hydroxyapatite - Based Composites for Bone Tissue Regeneration

CAMELIA TECU[1], AURORA ANTONIAC[1], GULTEKIN GOLLER[2], MUSTAFA GUVEN GOK[3], MARIUS MANOLE[4], AUREL MOHAN[5]*, HORATIU MOLDOVAN[6], KAMEL EARAR[7]

[1]University Politehnica of Bucharest, 313 Splaiul Independentei Str., 060042, Bucharest, Romania

[2]Faculty of Chemical and Metallurgical Engineering, Istanbul Technical University, Resitpasa District, ITU Ayazaga Campus, 34467, Istanbul, Turkey

[3] Hakkari University, Karsiyaka District, 433 Str.,30000, Hakkari, Turkey

[4]Iuliu Hatieganu University of Medicine and Pharmacy Cluj Napoca, 8 Babes Str.,400012 Cluj Napoca, Romania

[5]University of Oradea, 1 Universitatii Str., 410087, Oradea, Romania

[6]Titu Maiorescu University, Faculty of Medicine, 22 Dambovnicului Str., 040441, Bucharest, Romania

[7]Dunarea de Jos University of Galati, Medicine and Pharmacy Faculty, 47 Domneasca Str., 800008, Galati, Romania

Bone reconstruction is a complex process which involves an osteoconductive matrix, osteoinductive signaling, osteogenic cells, vascularization and mechanical stability. Lately, to improve the healing of the bone defects and to accelerate the bone fusion and bone augmentation, bioceramic composite materials have been used as bone substitutes in the field of orthopedics and dentistry, as well as in cosmetic surgery. Of all types of bioceramics, the most used is hydroxyapatite, because of its similar properties to those of the human bone and better mechanical properties compared to β-tricalcium phosphate [1]. Currently, the most used raw materials sources for obtaining the hydroxyapatite are: bovine bone, seashells, corals, oyster shell, eggshells and human teeth. There are two common ways to obtain hydroxyapatite: synthetically and naturally. Generally, for the improvement of the mechanical properties and the structural one, hydroxyapatite is subjected to the sintering process. Considering the disadvantages of hydroxyapatite such as poor biodegradation rate, β-TCP has been developed, which has some disadvantages too, such as brittleness. For this reason, the aim of this study is to look into the effect of adding magnesium oxide on the sintering behavior, the structure and the mechanical properties of the hydroxyapatite-tricalcium phosphate composites.

Keywords: hydroxyapatite, composites, tricalcium phosphate, sintering

As a consequence of ageing and of various accidents, bioceramics have gained an increased importance not only in orthopedic treatments, but also in cosmetic surgery and dentistry applications, insofar as they are chemically similar to the bone. Of all types of bioceramics, the most used is hydroxyapatite, with the chemical formula of $Ca_{10}(PO_4)_6(OH)_2$ and Ca/P ratio of 1.67. Hydroxyapatite is considered a biodegradable and bioactive material because of its close resemblance to the bones. There is a variety of raw material sources for hydroxyapatite, including bovine bone, seashells, corals, oyster shell, eggshells and human teeth [2-6].

Various studies on hydroxyapatite demonstrate that there are considerable differences between synthetic hydroxyapatite and natural ones and have compared the efficacy of one form of hydroxyapatite over the other. Synthetic hydroxyapatite exhibits good properties as a biomaterial, such as biocompatibility, osteoconductivity and bioactivity; hence, it has been widely used as a bone substitute, coating on metallic implants and scaffold for tissue engineering. The classical way of obtaining synthetic hydroxyapatite is working with expensive reagent chemicals. The synthetic routes involve time-consuming and laborious work (i.e., main production techniques: precipitation or sol-gel) [7-9]. Generally speaking, hydroxyapatite powders can be obtained commercially in different crystal sizes, but the main disadvantage is that such products may contain some impurities. For example, some commercially available hydroxyapatite particle sizes ranged between 10-40μm, averaged 5.32μm with a Ca/P ratio of 1.62 [10], while other sources had values of 160-200μm with a Ca/P ratio range of 1.66 to 1.69 [11].

Currently, the manufacturers produce sintered components which differ chemically from the biological carbonate apatites [12]. The sintering process of hydroxyapatite produces decomposition of the calcium phosphate phases to oxyapatite and possibly tetracalcium phosphate and tricalcium phosphate (TCP). The most important parameter in this decomposition process is the sintering temperature which could adversely affect the strength of composites. Moreover, sintering at high temperatures has the tendency to eliminate the hydroxyl group in the hydroxyapatite matrix and this would result in the decomposition of hydroxyapatite phase to form α-tricalcium phosphate (α-TCP), β-tricalcium phosphate (β-TCP) and tetracalcium phosphate (TTCP).

Although hydroxyapatite is a promising implant material, its use under load bearing applications such as artificial joints has been restricted by the low flexural strength (<140 MPa) of the ceramic body [7] and the low toughness [13-16]. In order to increase the mechanical properties of sintered hydroxyapatite, the properties of the powder precursors have been studied by controlling some important parameters such as particle shape and size, particle distribution and agglomeration.

Thus, bone substitutes must perform combined functions of mechanical support and osteo-regeneration, which involve three important biological properties: osteoinduction, osteoconduction and osteogenesis. Also,

* email: mohanaurel@yahoo.com ; Phone: 0740514636

All authors have participated equally in developing this study.

bone substitutes should be thermally nonconductive, sterilizable, bioresorbable and available at a reasonable cost [17-20].

The aim of the present work was to study the effects of the sintering temperatures and the addition of the magnesium oxide (MgO) on the structure and properties of the experimental hydroxyapatite based composites.

Magnesium oxide (MgO) is an inorganic ceramic material. Oliveira et al. [21] claimed that magnesium oxide has beneficial effects as it improves the early stages of mineralization and contributes to an intimate contact with the living tissue. Magnesium (Mg) is the fourth most abundant cation in the human body and is naturally found in the bones. The use of magnesium oxide is useful from biological point of view, because Mg^{2+} plays a physiological role in positively influencing bone strength. Based on these considerations, we select MgO to be used as filler for the hydroxyapatite based composites [21-22].

Experimental part

Materials and methods

The synthetic hydroxyapatite and β - tricalcium phosphate powders were purchased from the company SIGMA - ALDRICH. Magnesium oxide (MgO) known as magnesia is a material used in numerous fields as catalysis, ceramics, and refractory as well as paint industry which improves the mechanical properties of the other materials. In this study, a commercially produced magnesium oxide was used, manufactured by Merck, KGaA*64271 Darmstadt, Germany, encoded under the name of extra pure magnesium oxide. The molecular weight of the magnesium oxide powder, with the formula MgO, is 40.3 g/mol.

The composite biomaterials which were developed contain in different proportions the following materials: (1) synthetic hydroxyapatite (HA); (2) β - tricalcium phosphate (β-TCP) and (3) magnesium oxide additions (10, 15, 20 % wt). The experimental compositions are showed in table 1. Hydroxyapatite powder was used as matrix while tricalcium phosphate and magnesium oxide were used as reinforcement materials.

The experimental hydroxyapatite based composite samples was obtained by mixing hydroxyapatite with the fillers, respectively β - tricalcium phosphate and magnesium oxide powders. After homogenization of the mixed powders, these were subjected to pressing by cold isostatic pressing (CIP) and sintering. The sintering was carried out at different temperatures, namely 1000, 1100 and 1200°C using a sintering furnace Nabertherm.

The experimental materials were structurally characterized using a FT-IR spectrometer (JASCO 6200 FT-IR with the MK II Golden Gate ATR system) with a spectral range of 4.000 to 600 cm^{-1}. The identification of the crystalline phases precipitated within the heat-treated ceramic samples, of the phase composition and of the index of the diffraction peaks was carried out by means of X-ray diffraction analysis using an X-ray diffractometer (Rigaku MiniFlex diffractometer, 30 kV, 15 mA). Scanning electron microscopy (JEOL 7000F) was used to examine the microstructural, morphological and textural features of the experimental composites.

Regarding the mechanical properties, the following were investigated: the Vickers microhardness and the compressive strength. Vickers hardness testing along the cross sections of samples was conducted using a microhardness tester under a load of 9.8N (VHMOT, Leica Corp.) and the average values were calculated after 20 indentations. Compressive strength was measured using a high-capacity universal mechanical testing machine (Instron 1195). The test was carried out with the specimen dimension of 25x10x10 mm^3 at 2 mm/s cross-head speed.

Results and discussions

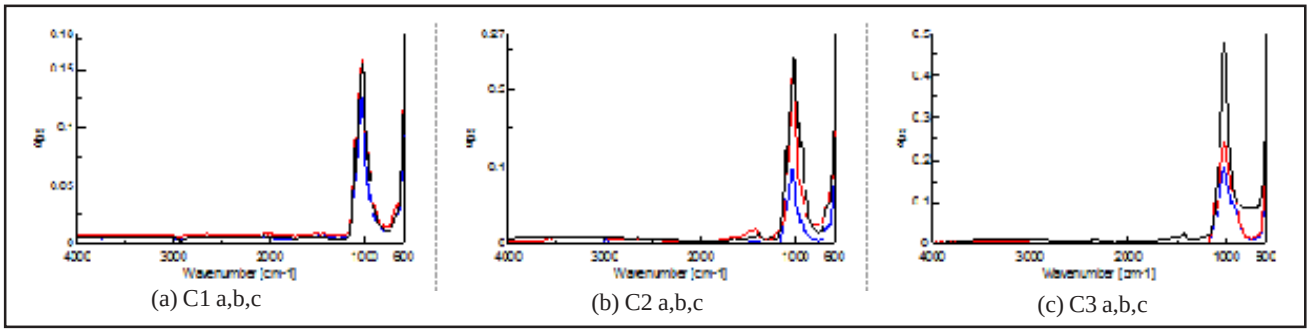
Fourier-Transform Infrared Spectroscopy Results

Fourier-Transform Infrared Spectroscopy (FTIR) it was used in order to monitoring the variations in structural groups and vibration bands, providing information on the structure of the experimental samples. The spectra recorded on the sintered hydroxyapatite based composites at various temperatures (1000, 1100 and 1200°C) are shown in the figure 1.

Encoding of the composites / Materials		*Synthetic hydroxyapatite (% wt)*	*β-Tricalcium Phosphate (% wt)*	*Magnesium oxide (% wt)*
C1 a,b,c	**HA+β-TCP+MgO**	70	10	20
C2 a,b,c		70	15	15
C3 a,b,c		70	20	10

Table 1
THE EXPERIMENTAL COMPOSITIONS OF MATERIALS USED TO OBTAIN BIOCOMPOSITES

where a, b, c - composites obtained at different sintering temperatures (a-1000 °C, b-1100 °C, c-1200 °C)



(a) C1 a,b,c (b) C2 a,b,c (c) C3 a,b,c

Fig. 1. FTIR spectra of the hydroxyapatite based composites sintered at all of the three sintering temperature (a-1000°C, b-1100°C, c-1200°C)

C1, C2, C3_1000;
C1, C2, C3_1100;
C1, C2, C3_1200;

The spectra recorded on the hydroxyapatite based composites indicate the presence of phosphate $(PO4)^{3-}$ and hydroxyl groups OH^-. The absorption bands positioned at low wavelengths are due to the deformation vibration of the phosphate group (600-610 cm^{-1}) and the structural OH group (~630 cm^{-1}). The absorption bands at ~ 960 cm^{-1} are due to the symmetrical stretching vibration of the P-O bond in the phosphate group, while the bands in the range of 1000-1200 cm^{-1} are due to the asymmetric stretching vibration of the P-O bond in the phosphate group. During the sintering process, hydroxyapatite undergoes the following processes: dehydration, dehydroxylation and hydroxyapatite decomposition with the formation of new phases. Such behavior is consistent with XRD assays, which indicated dehydration of hydroxyapatite leading to hydroxyapatite decomposition. This aspect is also observed in FTIR spectra by disappearing bands in the range of 2500 – 3700 cm^{-1}.

X-ray diffraction results

The diffraction spectra for all experimental hydroxyapatite based composites are shown in figure 2.

The X-ray diffraction spectra of the hydroxyapatite powder indicate only the crystalline phase of hydroxyapatite structure, demonstrating that the experimental composites contain hydroxyapatite. In order to identify the phases resulting from the sintering process at different temperatures, the position of the peaks was compared to those from the International Center for Diffraction Data (ICDD) lists.

The intensity of hydroxyapatite peaks decreases as the sintering temperature increases, due to the decomposition of hydroxyapatite at high temperatures. Regarding the evolution of the crystalline phases it can be noticed that with the increase of the sintering temperature, new phases have been identified up to 1200°C. XRD peaks of the α-TCP phase become apparent at the time of sintering at 1200°C.

SEM results

The experimental results obtained after the surface investigation of the experimental composites by scanning electron microscopy are shown in figure 3. It has been

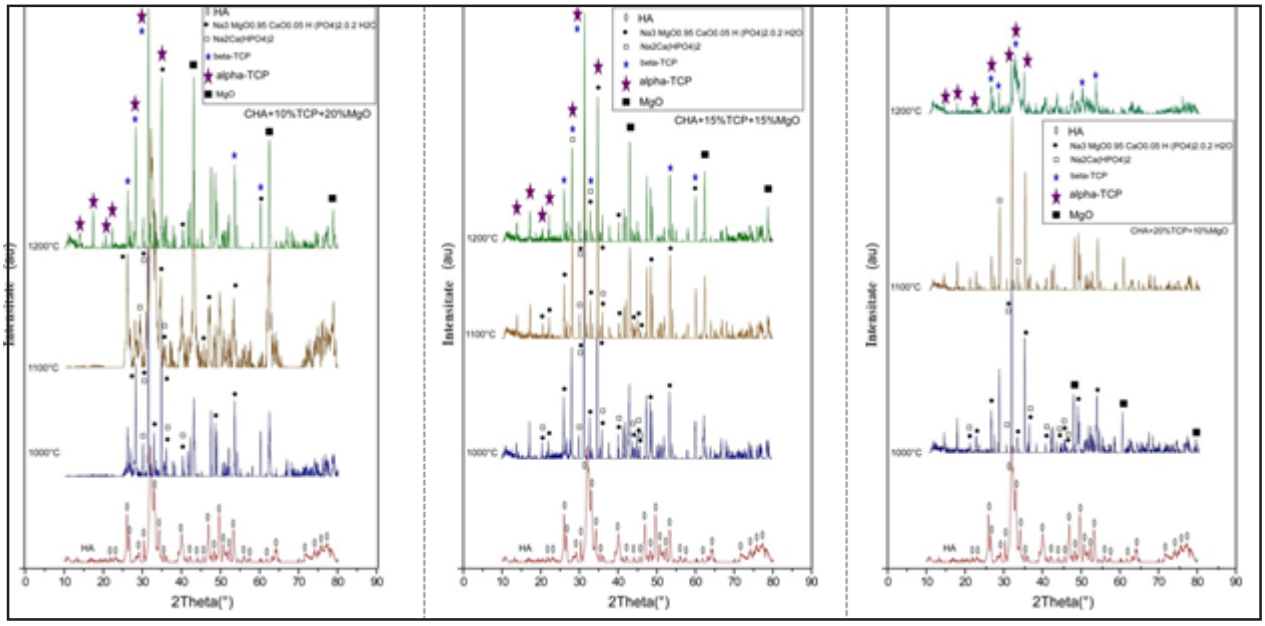


Fig. 2. The diffraction spectra of the experimental hydroxyapatite based composites

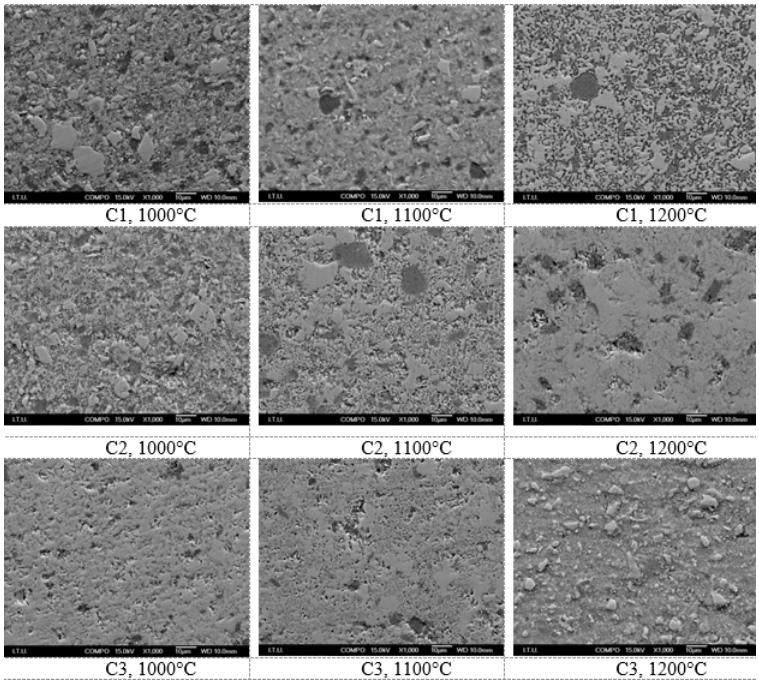


Fig. 3. SEM micrographs of the hydroxyapatite based composites

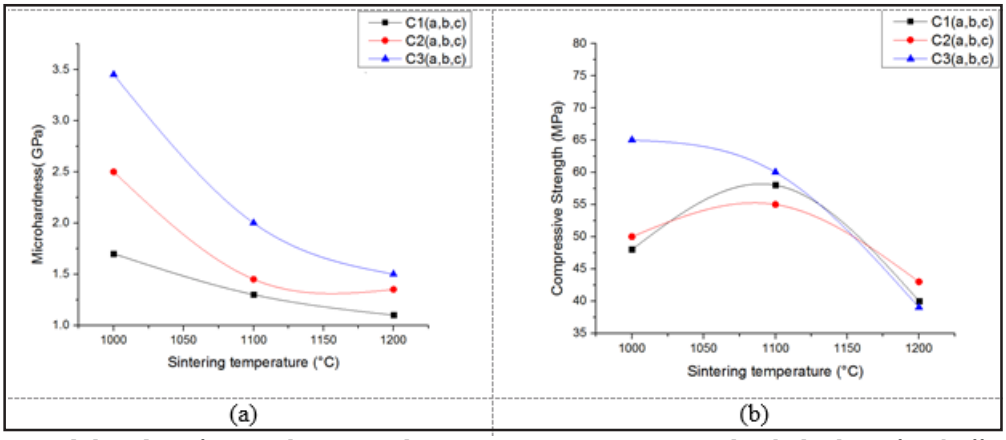


Fig. 4. The variation of the (a) Vickers microhardness and (b) compressive strenght depending on the sintering temperature

noticed that densification begins with sintering at 1000°C and continues to increase with temperature up to 1200°C, except for the composite C3. It is noted that for the C3 composite which contains the smaller amount of MgO, increasing the sintering temperature did not improve the densification, in the microstructure of the composite material appear some inhomogeneities.

Vickers microhardness and compressive strength results

For each properties and each type of experimental material three determinations were made. The compressive strength of the composite materials was obtained by their compression using a load applied gradually while the maximum value of the compressive load supported by the material before fracturing is recorded.

The variation of Vickers microhardness and compressive strength depending on the sintering temperature are shown in figure 4.

In case of Vickers microhardness the maximum value was recorded at 1000°C, demonstrating thereby that at high sintering temperatures the new phases formed negatively influence the obtained values. Regarding the compressive strength results, it can be said that the optimal sintering temperature is 1000°C, at higher sintering temperatures, significant changes are not observed. The addition of an increasing amount of MgO as the secondary phase does not show promising effect on the mechanical properties of the sintered composites. It is noteworthy that both Vickers microhardness and compression resistance record the best experimental results for C1 composite sintered at 1000°C.

Conclusions

Our experimental study on obtaining new ceramic-ceramic composite biomaterials (the hydroxyapatite matrix was reinforced with a variable mixture of β-tricalcium phosphate and magnesium oxide) usable as bone substitutes revealed some important aspects. The experimental results regarding the use of hydroxyapatite as a matrix of the experimental composites revealed that the final properties of the samples are different depending on the sintered temperatures and the composition of the samples. According to our experimental data presented in this paper the experimental composites showed a higher degree of homogeneity due to the formation of new structural phases following the sintering process.

From the obtained results we can say that the addition of an increasing amount of MgO does not bring improvements in terms of mechanical properties. In order to check the beneficial effects on the human body of the magnesium oxide, future studies on biocompatibility and degradation will be made.

References

1. EBRAHIMI M., BOTELHO M.G., DOROZHKIN S.V., Materials Science and Engineering C, **71**, 2017, p.1293–1312.
2. ANTONIAC I., NEGRUSOIU M., MARDARE M., et al., Medicine. **96(19):**e6687, 2017.
3. GRECU D., ANTONIAC I., TRANTE O., et al., Mat. Plast., **53,** no.4**,** 2016, p.776-780.
4. ANDREI B., NICULESCU M., POPESCU GH., International Orthopaedics, **40(2)**, 2016, p.393-397.
5. CAVALU S., EARAR,K., LASLO V., et al., Rev. Chim (Bucharest), **68,** no.12, 2017, p.2963
6. ANTONIAC I., BURCEA M., IONESCU R.D., BALTA F., Mat. Plast., **52,**no.1, 2015, p.109
7. FILLINGHAM Y., JACOBS J., Bone Joint J., **98**, 2016, p.6–9.
8. FLORENCIO-SILVA R., RODRIGUES DA SILVA SASSO G., SASSO-CERRI E., SIMOES M.J., CERRI P.S., Biomed Res Int., **2015**, 2015; p.1-17.
9. GOLLER G., OKTAR F.N., OZYEGIN L.S., KAYALI E.S., DEMIRKESEN E., Mater Lett. **58**, 2004, p.2599-2604.
10. HSU F.Y., CHUEH S.C., WANG J.Y., Biomaterials, **20,** 1999, p.1931-1936.
11. SCABBIA A., TROMBELLI L., J Clin Periodontol, **31**, 2004, p.348-355.
12. OKAZAKI M., OHMAE H., TAKAHASHI J., KIMURA H., SAKUDA M., Biomaterials, **11**, 1990, p.568-572.
13. KHAN S.N., CAMMISA F.P., SANDHU H.S., DIWAN A.D., GIRARDI F.P., LANE J.M., J. Am Acad Orthop Surg., **13**, 2005, p.77-86.
14. MICULESCU F., STAN G.E., CIOCAN L. T., MICULESCU M., BERBECARU A., ANTONIAC I., Digest Journal of Nanomaterials & Biostructures, **7**, 2012, p.1667-1677.
15. ANTONIAC I., Handbook of Bioceramics and Biocomposites. Springer Ed., 2016, p.301-324.
16. PRYOR L.S., GAGE E., LANGEVIN C.J., HERRERA F., et al., Craniomaxillofac Trauma Reconstr., **2(3)**, 2009, p.151–60.
17. BUCHOLZ R.W., CARLTON A., HOLMES R.E., Orthop Clin North Am., **18**, 1987; p.323-334.
18. EGGLI P.S., MULLER W., SCHENK R.K., Clin Orthop Relat Res., **232**, 1988, p.127-138.
19. JENSEN S.S., BROGGINI N., HJORTING-HANSEN E., SCHENK R., BUSER D., Clin Oral Implants Res., **17**, 2006, p.237-243.
20. RAPA M., MATEI E., GHIOCA P.N., CINCU C., NICULESCU M., J Adhes Sci Technol., **30(16)**, 2016, p.1727-1740.
21. OLIVEIRA J.M., CORREIA R.N., FERNANDES M.H., ROCHA J., J. Non-Cryst. Solids, **265**, 2000, p.221-229.
22. MIRANDA P., PAJARES A., SAIZ E., TOMSIA A.P., GUIBERTEAU F., J Biomed Mater Res., **85**, 2008, p.218-227.

Manuscript received: 12.10.2017