Research Article

Samah S. Eldera, Nourah Alsenany, Sarah Aldawsari, Gehen T. El-Bassyouni, and Esmat M. A. Hamzawy*

Characterization, biocompatibility and in vivo of nominal MnO₂-containing wollastonite glass-ceramic

https://doi.org/10.1515/ntrev-2022-0477
received January 24, 2022; accepted August 1, 2022

Abstract: The present work pointed out the effect of adding different concentrations of MnO₂ (0.25, 0.50, 1.00 and 2.00 wt%) on the structure and crystallization performance of wollastonite glass. Nominal MnO₂-containing wollastonite glass was prepared with the addition of 10% Na₂O to decrease the melting temperature through melt quenching technique. The thermal history of glasses indicated that the crystallization temperature was between 864 and 895°C. The heat treating of glasses at ~900 and 1,100°C gave combeite (Na₃Ca₆Si₆O₁₈), rankinite (Ca₃Si₃O₉), pseudowollastonite (Ca₃SiO₇), bustamite (CaMn₂Si₄O₁₁) and cristobalite. The later sample densities increased with the incorporation of MnO₂ from 1.88 to 2.24 g/cm³ concomitant with decrease of porosities from 32.59 to 20.83%. The microstructure showed nano-size crystals in rounded, angular or irregular micro-size clusters, whereas after soaking in simulated body fluid for 1 month showed submicron crystals of carbonated calcium phosphate phase. Both fourier transform infrared spectroscopy and scanning electron microscopy/energy dispersive X-ray delineated the samples’ biocompatibility. Also, the negative zeta potential results enabled bone cell activity. Moreover, the bone healing with complete mineralization was remarked in case of the in vivo implantation of the G0.50 group. These results can be of a great significance in the application of MnO₂-containing combeite, rankinite phases for bone treatment and biomedical applications.

Keywords: glass-ceramic, biocompatibility, in vitro, in vivo

1 Introduction

Wollastonite (Ca–Si-based bioceramic, CaSiO₃) is an attractive candidate for bioengineering owing to the release of the Si⁴⁺ and Ca²⁺ ions upon degradation, such ions play a significant role in osteogenesis and angiogenesis. Wollastonite doped with bioactive elements is believed to be a good candidate for bone tissue engineering due to their amendable biodegradation and bioinductivity [1,2]. Doping of wollastonite with manganese (Mn²⁺) can fortify the capacity of the calcium silicate [3,4]. CaSiO₃ has been premeditated as a bioactive material due to its excellent bioactivity and degradability [5]. Silicon and calcium act as a potential network modifier for the improvement of the bone substitutions by therapeutic inorganic ions during the early stages of bone development, mineralization and growth [6]. Their good biological properties are accredited to their capacity for alkalinizing activity and the release of calcium which is ideal for the calcium phosphate (Ca-P) nucleation [7]. Calcium silicate is an osteoinductive non-cytotoxic material [8,9].

Manganese dioxide (MnO₂), is a non-stoichiometric inorganic material which added an important consideration in the material science field due to its distinctive physicochemical properties [10]. Among metal oxides, MnO₂ has received a considerable attention because of its cost-effective, great activity, high stability, low toxicity, large specific surface area, flexible structure and strong oxidizing properties [11]. The dimensions, crystallographic phases, morphology and particle size are the unique physicochemical properties of the MnO₂. Manganese can improve several functional materials as it fulfils the strict biomedical necessities [12]. Researchers, revealed
that doping of MnO₂ can improve the dielectric properties of ceramics [13,14]. The influence of MnO₂ mostly impacts the microstructure and the energy storage properties of the calcium silicate. In 2017, Xiu et al. concluded that the addition of a small amount of MnO₂ can improve the homogenization and densification of the ceramic material and subsequently improve its microstructure [15]. In 2016, Danewalia and Singh indicated that the existence of MnO₂ increases the leakage of the Na⁺ ions from the glasses and likewise attracts the Ca²⁺ cations from the simulated body fluid (SBF) [16]. They similarly mentioned that the incidence of MnO₂ may improve the glass surface activity to form an apatite layer. In 2015, Kolmas et al. noted that Mn-doping could increase the compressive strength and density of the scaffolds [17].

In the current research, nominal wollastonite glass-ceramic with various concentrations of MnO₂ was prepared through the melt quench method. The produced manganese/wollastonite glasses were characterized in terms of morphology and composition via in vitro and in vivo bioactivity. Characterization of the glasses was obtained using differential thermal analysis (DTA), X-ray diffraction (XRD) and scanning electron microscope (SEM) coupled with energy dispersive X-ray microanalysis (EDX). For in vitro biocompatibility, glass powder was pressed into discs before immersion in SBF for 1 month. For the in vivo investigation, the base nominal wollastonite glass (G0), and those combined with 0.25 M and 0.50 M of MnO₂ samples were implanted in the femur bone defects of hamster rats for 45–90 days to identify the new bone formation.

2 Experimentation

Wollastonite (CaSiO₃) was prepared through the melt quench route. The influence of MnO₂ (BDH) on the characterization and biocompatibility of the glass was investigated. The content of MnO₂ in glass samples was 0.0, 0.25, 0.50, 1.00 and 2.00 wt%. To reduce the melting temperatures of the glass batches, 10% Na₂O was added over the 100% glass oxide composition (Table 1). The glass batch constituents were pure limestone (LS contains CaO: 55.7, Al₂O₃: 0.22, Fe₂O₃: 0.02, MgO: 0.1, Na₂O: 0.1, K₂O: 0.16 and TiO₂: 0.02 wt%) as the source of CaO; whereas, silica sand was used as the source of SiO₂. Over 100% glass batch oxides were MnO₂ (Sigma Aldrich, USA) and sodium carbonate (Na₂CO₃, BDH) as the source of Na₂O. The melting temperature of the batches was between 1,350 and 1,400°C for 2 h in a platinum crucible. After adequate homogeneity, glass melt was poured into distilled water (at room temperature) before dryness and pulverization (<0.083 mm). The pulverized glass powder was shaped into discs of diameter 1.00 cm, using 7% poly vinyl alcohol as a binder, via Paul Weber Maschinen- und Apparatebau, Remshalden, Germany at 20 kN for 20 s.

DTA (Perkin Elmer DTA-7, USA) was used to trace the thermal behavior of the glasses, under argon gas condition and a heating rate of 10°C/min up to 1,000°C. Identification of the crystalline phases of glasses at 900 and 1,100°C was performed using XRD analysis (BRUKER, D8 ADVANCED CuO target, Germany) with CuKα radiations (λ = 1.54 Å). XRD patterns were recorded in the range of 2θ = 5–60°. The morphology and microcrystalline structure of samples were verified by SEM equipped with EDX (SEM/EDX, model FEJ Quanta 250 Fei, Holland) at operating voltage of 15 kV. Prior to the SEM measurements, fresh fractured samples were etched with the solution of 1 wt% HNO₃ + 1 wt% HF to clear the outlines of the developed crystalline particles.

Standard in vitro bioactivity tests using SBF at 37°C were carried out upon incubation for 1 month. SBF has ion concentrations, pH and temperature almost identical to that of the human blood plasma [18].

SBF was prepared following Kokubo’s protocol by dissolving appropriate amounts of reagent-grade chemicals NaCl, NaHCO₃, KCl, Na₂HPO₄, MgCl₂·6H₂O, Na₂SO₄,
(CH₂OH)₃CNH₂ and CaCl₂·2H₂O in deionized water [19,20]. To mimic the concentration of human blood plasma, 1 M of HCl and tris-hydroxymethyl amino methane [(CH₂OH)₃CNH₂] was used to maintain the pH of SBF solution at 7.4 [21]. Bioactivity test was performed for sintered glass discs sintered at 1,100°C/2 h. Discs were immersed in sealed sterilized polyethylene boxes enclosing SBF for 1 month, at a constant ratio of sample to SBF volume without refreshing the solution throughout the immersion. At the end of the immersion period, discs were removed from the solution, rinsed with distilled water to stop the reaction, and then dried at room temperature. Discs were successively characterized using SEM/EDX and fourier transform infrared spectroscopy (FT-IR reflection (Jasco, FT/IR-4600, USA) to detect the possible formation of the Ca-P crystals and to assess the microanalysis and the Ca/P ratio on the sample. Also, the Zetasizer ([Malvern Instrument Ltd, UK] fortified with a 633 nm laser) was used to determine the electrical surface charges on the sample powder. A well-dispersed sample in deionized water at temperature 25°C was caught for the measurement of the zeta potential (each measurement being the average of 12 runs).

For in vivo tests, the G0, G0.25M and G0.50M sintered glass-ceramic were implanted in the femur bone defects of hamster rats, besides a positive control (empty bone gap). Normal healing of the soft tissues was identified.

Figure 1: DTA thermograms of the glasses heated up to 1,000°C.
All rats were healthy and did not show any signs of edema in the tissues all through the post-operative period.

After 45 and 90 days’ post-surgery, the animals were lacerated with an overdose of anesthesia, and both femurs were extracted, cleaned of soft tissues and soaked in 10% phosphate-buffered formalin for 7 days. The rat bones were prepared for histological evaluation via normal light microscope (Leica, model: DM 2500).

3 Results and discussion

3.1 Characterization of samples

The thermal behavior of the glasses is elucidated by means of DTA in Figure 1. The glass transition temperature is near 675°C and softening temperature near 685°C. Such small heat absorption may designate the occurrence of molecular relocation earlier than the glass crystallization. Exothermic peaks demonstrating the crystallization reaction are also revealed [22]. The crystallization temperature is between 864 and 872°C. The onset and offset temperatures of all the glasses crystallization are between 830 and 900°C, respectively. It is manifested that the incorporation of MnO₂ in the wollastonite glass does not show noticeable changes in the temperature of the endothermic and exothermic effect.

XRD analysis of the sintered glasses near the crystallization temperature (at 900°C/2 h) is presented in Figure 2. It exhibits main crystalline phases of complex silicates. The crystallization of combiete (Na₄Ca₄Si₆O₁₈) particularly in the G0 (base) [23]; whereas the incorporation of MnO₂ enhances the crystallization of both pseudowollastonite (CaSiO₃) [24] and rankinite (Ca₃Si₂O₇) [25]. At higher concentration of MnO₂ content (i.e., in G2.00M), bustamite (Mn,Ca)₃Si₃O₉ phase is indexed along with the later phases [26]. At higher temperature (1,100°C), the crystallization of rankinite and combiete is noticed as major phases with little cristobalite (SiO₂) in all samples [27] (Figure 3). For the parent (G0) sample, the XRD pattern concurs with those reported in the previous work [28,29].

SEM of G0, G0.50M and G2.00M glasses sintered at 1,100°C/2 h are shown in Figure 4. G0 sample shows massive microstructure with some irregular clusters and very little pores. Subsequently at high magnification, connected rounded clusters appear in the range of the nano-size. Once a small amount of MnO₂ is added, the microstructure of the sintered samples becomes more uniform and denser having a spheroidal morphology and disordered mesoporous structure [15]. The G0.50M and G2.00M samples present mesoporous glass together with a mix of irregular, angular and fine rod-like crystals with pores in between. At higher magnifications, the microstructure of the later crystals exposes nano-size crystals (30–100 nm) as shown in Figure 4. The EDX microanalysis of G0 indicates the integration of Na, Ca, Si and O. However, the EDX of the G0.50M and G2.00M glass samples confirms the incorporation of the manganese into the glassy matrix. Thus, it exhibits an indication
Figure 3: XRD of glasses heated at 1,100°C/2 h.

Figure 4: SEM micrographs of G0, G0.50M and G2.00M glasses sintered at 1,100°C/2 h.
of rankinite crystallization and due to the similarity of ionic radius of calcium and sodium, the possible replacement of Ca (116 pm) by Na (114 pm) may take place (Figure 5 and Table 2).

Figure 5: EDX microanalysis of G0, G0.50M and G2.00M glasses sintered at 1,100°C/2 h.
3.2 Densities, porosities and zeta potential

The densities and porosities of the glass samples sintered at 1,100°C are demonstrated in Figure 6. Upon incorporation of MnO₂, the densities of the samples relatively increase from 1.88 to 2.24 g/cm³ and the porosities relatively decrease from 32.59 to 20.83%. Although the prementioned densities of rankinite (2.844 g/cm³), combeite (2.690 g/cm³) and cristobalite (2.33 g/cm³) are higher than the present results, it must be mentioned that the increase of the porosities initiate decrease in such values. It is notable that all samples create negative zeta potentials as presented in Table 3. Such negative zeta potentials may possibly be a useful property for bone-derived appliance when fixed in bone containing viable cells and deliberated for in vivo tests. From the author's point of view, the most motivating finding was a negative zeta potential to enable the bone cell activity.

3.3 Biocompatibility

3.3.1 In vitro results

To check the biocompatibility of the glasses, in vitro tests by means of the SBF are carried out. SEM micrographs of G0, G0.50M and G2.00M discs sintered at 1,100°C/2 h are soaked in SBF for 4 weeks as shown in Figure 8. G0 sample displays a mix of irregular angular, rod-like crystals with pores in between; whereas, at high magnification rounded, sub-rounded and rod clusters in the nano-size range are scattered all over the sample. On the other hand, G0.50M and G2.00M samples expose fine plate-like crystals mounting on the surface of the immersed samples. As shown in Figure 8, the later plate-like crystals are associated with tiny crystals with little pores in between and at high magnification the later crystals

| Sample/Notation | Zeta potential (mV) | Conductivity (mS/cm) | Std. Dev. |
|-----------------|---------------------|----------------------|-----------|
| G0              | −40.3               | 0.0402               | 4.64      |
| G0.50M          | −25.1               | 0.0574               | 4.61      |
| G2.00M          | −27.0               | 0.0888               | 3.78      |

Table 3: The zeta potential measurements

Table 2: EDX microanalysis of G0, G0.50M and G2.00M samples

| Chemical constituents weight% | Na | Ca | Si | Mn | O |
|-------------------------------|----|----|----|----|---|
| Nominal rankinite             | —  | 41.69 | 19.48 | —  | 38.83 |
| G0                            | 2.66 | 57.68 | 15.73 | —  | 23.93 |
| G0.50M                        | 2.52 | 42.5 | 17.65 | 1.71 | 35.62 |
| G2.00M                        | 4.19 | 30.73 | 19.2 | 0.83 | 45.04 |

Figure 6: Densities and porosities of the samples sintered at 1,100°C/2 h.
display nano-size crystals between 100 and 200 nm. On high magnification, the microstructure of the G2.00M sample is modified by means of interlocked ribbon containing nano-tiny crystals on its edges. Furthermore, the development of agglomerates is as a consequence of the van der Waals interaction forces between the particles [33]. EDX microanalysis demonstrates a growth in the intensity of the P and Ca peaks together with carbon and decline in the intensity of the Si peaks of all samples, which reflect the deposition of carbonated calcium phosphates (c-CaPs) (Figure 9). Also, the Ca/P ratios were 2.17, 2.30 and 2.97 for G0, G0.50M and G2.00M, respectively. Coating of the material surfaces by Ca-P can be used to increase the biological responses and decrease the toxicity [34]. Ca-P may happen in crystalline and amorphous phases with variable stoichiometry [35]. The in vitro results improve the osteoblast adhesion on the Ca-Ps with elevation in Ca/P ratio (up to 2.9) [36]. In classical condition, as the pH value of SBF was kept constant at 7.40 (i.e., over the isoelectric point of the particles), the surface charge of the particles is of negative charge when immersed in SBF, which managed to adsorb the $\text{Ca}^{2+}$ ions from the SBF solution and ultimately form a crystalline layer of calcium-enriched apatite. In Figure 8, the EDX microanalysis of G2.00M sample shows a minute release of Mn ions, which recommends using such sample as a vehicle for providing therapeutic manganese ions [37].

Danewalia and Singh [16] mentioned that the incidence of $\text{MnO}_2$ proliferates the disordering, thus improving the glass surface activity to form an apatite layer. Such findings approve their fittingness for being applicable in bone tissue engineering. However, in the present work, the
increase of the c-CaP ratio monitors the successive incorporation of the MnO₂ into the glass network [16].

The in vitro bioactivity studies in SBF designate that samples could prompt the Ca-P layer and propose the opportunity of relating the Mn-modified sample for bone regeneration as comprehended in Figure 9. Earlier, it was informed that the induction of Ca-P layer on surfaces of the bioactive materials was extremely important for the incorporation of materials with normal bone tissue [38]. The steps of the Ca-P layer formation stages on samples surface in SBF may possibly be summarized in the next six steps [36]:

1) Exchange of Ca²⁺ from the material surface with H⁺ or H₂O⁺ in the SBF.
2) Release of soluble silica in the form of silicic acid [Si (OH)₄] into the SBF and the formation of several silanol (Si–OH) groups onto the immersed surface.
3) Development of hydrated silica rich layer on account of re-polymerization and condensation of the Si–OH groups.
4) Precipitation of the Ca²⁺ ions and the PO₄³⁻ groups aboard of the silica rich layer; consequently, an amorphous layer of Ca-P was established on the surface.
5) Evolution of the amorphous Ca-P (ACP) rich layer by enhancing more Ca²⁺ and PO₄³⁻ groups from the SBF.
6) The crystallization of ACP rich layer by insertion of OH⁻ and CO₃²⁻ anions from SBF and finally the yield of the hydroxyl carbonate Ca-P layer [39].

3.3.2 FT-IR reflection

FT-IR spectra in Figure 10 elucidate the characteristic vibrational bands of the hydroxyapatite (HA) in the G0 and G2.00M glass discs sintered at 1,100°C/2 h and soaked in SBF for a month. Bands at 941 and 561 cm⁻¹ are related to the P–O bending mode of vibration of the HA. At higher Mn content, the 561 band is shifted to 546 cm⁻¹ [40]. Other bands at 1,597 and 845 cm⁻¹ match the carbonate groups of the HA [41]. Likewise, a hump present at the 681 cm⁻¹ is

Figure 8: SEM micrographs of the G0, G0.50M and G2.00M glasses sintered at 1,100°C/2 h and soaked in SBF for a month.
Figure 9: EDX microanalysis of G0, G0.50M and G2.00M glasses sintered at 1,100°C/2 h and soaked in SBF for a month.
related to the hydroxyl group of the HA. The band at 501 cm\(^{-1}\) is credited to the Si–O–Si symmetric bending mode in the silicate network \[42\]. The band at 845 cm\(^{-1}\) corresponds to the C–O stretching mode of vibration.

Thus it can be concluded that the characteristics of FT-IR reflection spectra in Figure 10 correspond to the development of the carbonated hydroxyapatite (c-HA) layer on the sintered glass-ceramic discs. Consequently, the major combeite, rankinite/MnO\(_2\) lead to the development of c-CaP on their surface after immersion in SBF, which is similarly confirmed by the SEM/EDX. Miola et al. concluded that the Mn-leaching test in SBF delineated inconsistent trends probably due to a re-precipitation of the manganese compounds during the process of bioactivity \[37\]. The study of the in vitro bioactivity designates that all samples are capable to form Ca-P layer above their surfaces as specified by the FT-IR reflection and the SEM/EDX analysis.

### 3.3.3 In vivo tests

The in vivo results are verified on G0, G0.25M and G0.50M sintered at 1,100°C/2 h, and the positive group (empty bone gap) is the reference for the pre-mentioned

![Figure 10: FTIR reflection spectra of G0 and G2.00M glass discs sintered 1,100°C/2 h and soaked in SBF for a month.](image)

![Figure 11: Microscopic examination of (a) normal bone, (b) positive control and sample containing sintered (c) G0, (d) G0.25M and (e) G0.50M samples. Both G0.25M and G0.50M samples show nearly normal bone after 45 days of implantation. NFB: new formed bone, NT: necrosed tissue and PO: proliferating osteoblasts.](image)
sintered samples. Samples are implanted in the femur bone defects of hamster rats, and the results are examined after 45 and 90 days.

Light microscopic examination after 45 days of bone tissues for the control group (Figure 11) reveals normal histology of compact and trabecular bone without any detectible alterations and the positive control group shows an area of bone necrosis with the existence of some newly formed bone tissue that showed an irregular calcification pattern. On the other hand, the bone defect in the (G0) group displays delayed healing with the existence of necrotic tissue filling the bone gap. However, the edges of the defect demonstrate proliferating osteoblasts (PO). The area of bone defect in both G0.25M and G0.50M groups is filled by necrosed tissue debris along with the applied formula as shown in Figure 11.

After 90 days of implantation, both the control and positive groups illustrate PO filling the defect area (Figure 12). In the same period, the G0 indicates new formed osteoid tissue filling the defect area with defective mineralization. Moreover, as shown in Figure 12, the G0.25M group elucidates an apparently normal bone tissue at the defect area and perfect bone healing with complete mineralization is noticed in the G0.50 group.

In general, no inflammation or endothelial swelling or granulation tissue or fibrotic tissue or any rejection in both tested samples is detected. The results show that although the treatment and formation of new bone tissues are slow in the G0 sample, it is fast in case of incorporation of the MnO$_2$ in G0.25M and G0.50M sintered samples. The presence of the major combeite ($Na_4Ca_4Si_6O_{18}$) and rankinite ($Ca_3Si_2O_7$) with/without MnO$_2$, as the major phases, not only stimulates the bioactivity but also triggers the activation of the osteoblast cell.

4 Conclusion

Nominal wollastonite with the successive four additions of MnO$_2$ (0.25, 0.50, 1.00 and 2.00 mol%) contents are synthesized through melt quenching route. The incorporation of MnO$_2$ does not show much changes in the temperature of endothermic and exothermic effect. XRD analysis of the sintered glasses near the crystallization temperature (at 900°C/2 h) showed the crystallization of combeite, pseudowollastonite, rankinite, bustamite and cristobalite. At higher temperature (1,100°C) the crystallization of the major rankinite and combeite was noticed as major phases with little cristobalite. In the later samples, with incorporation of MnO$_2$, the densities were increased from 1.88 to 2.24 g/cm$^3$ and the porosities decreased from 32.59 to 20.83%. The negative zeta potential of the present samples could be a useful property enhancing attachment and proliferation of bone cells when fixed in bone containing viable cells. The SEM of samples shows a mix of irregular angular and rod-like crystals with very fine pores in between. At higher magnifications, the microstructure of the later crystals shows nano-size crystals (between 30 and 100 nm). Post-immersion in SBF for 1 month the surface of the samples was studied via SEM/EDX and FT-IR reflection. However, the EDX microanalysis reflected the possible formation of c-HA on the surfaces upon immersion. The \textit{in vivo} results show that although the formation of new bone tissues was slow in the case of the G0 sample, it was fast in case of G0.25M and G0.50M samples (i.e., the incorporation of MnO$_2$ improved the new bone formation). Such outcomes are important in the application of MnO$_2$-containing wollastonite glass for bone treatment and biomedical applications.

**Figure 12:** Light microscopic examination of (a) G0, (b) G0.25M and (c) G0.50M demonstrates nearly normal bone after 90 days of implantation. NFO: new formed osteoid.
**Acknowledgments**: The authors extend their appreciation to the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia for funding this research work through project number (IFPHI-054-247-2020)” and King Abdulaziz University, DSR, Jeddah, Saudi Arabia.

**Funding information**: Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia through project number (IFPHI-054-247-2020)” and King Abdulaziz University, DSR, Jeddah, Saudi Arabia.

**Author contributions**: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

**Conflict of interest**: The authors state no conflict of interest.

**Ethical statement**: The in vivo research protocol was reviewed and approved by the Animal Care Committee of the National Research Centre (NRC), Egypt, which follows the guidelines of the National Institutes of Health Guide for Care and Use of Laboratory Animals (approval registration No. 16-254).

**References**

[1] Du Z, Leng H, Guo L, Huang Y, Zheng T, Zhao Z, et al. Calcium silicate scaffolds promoting bone regeneration via the doping of Mg²⁺ or Mn²⁺ ions. Compos Part B Eng. 2020;190:107937. doi: 10.1016/j.compositesb.2020.107937.

[2] Beherei HH, Mohamed KR, El-Bassyouni GT. Mechanical and microstructure of reinforced bioactive calcium/calcium silicate nano-composites materials. Mater Des. 2013;44:461-8. doi: 10.1016/j.matdes.2012.08.020.

[3] Abdel-Fattah WI, Jiang T, El-Bassyouni GT, Laurencin CT. Synthesis, characterization of chitosan and fabrication of sintered chitosan microsphere matrices for bone tissue engineering. Acta Biomater. 2007;3(4):503–14. doi:10.1016/j.actbio.2006.12.004.

[4] Gritsch L, Perrin E, Chenal J-M, Fredholm Y, Maçon ALB, Chevalier J, et al. Combining bioresorbable polyesters and bioactive glasses: orthopedic applications of composite implants and bone tissue engineering scaffolds. Appl Mater Today. 2021;22:100923. doi: 10.1016/j.apmt.2020.100923.

[5] Mahdy MA, Kenawy SH, El Zawawi IK, Hamzawy EMA, El-Bassyouni GT. Optical and magnetic properties of wollastonite and its nanocomposite crystalline structure with hematite. Ceram Int. 2020;46(5):6581–93. doi: 10.1016/j.ceramint.2019.11.144.

[6] Hoppe A, Mournino V, Boccaccini AR. Therapeutic inorganic ions in bioactive glasses to enhance bone formation and beyond. Biomater Sci. 2013;1(3):254–6. doi:10.1039/C2BM00116K.

[7] Prati C, Gandolfi MG. Calcium silicate bioactive cements: biological perspectives and clinical applications. Dent Mater. 2015;31(4):351–70. doi: 10.1016/j.dental.2015.01.004.

[8] Almeida MS, Fernandes GVO, Oliveira AM, Granjeiro JM. Calcium silicate as a graft material for bone fractures: a systematic review. J Int Med Res. 2018;46(7):2357–48. doi: 10.1177/0300060518770940.

[9] Mabrouk M, Taha SK, Abdel Hamid MA, Kenawy SW, Hassan EA, El-Bassyouni GT. Radiological evaluations of low cost wollastonite nano-ceramics graft doped with iron oxide in the treatment of induced defects in canine mandible. J Biomed Mater Res. 2021;109:1029–44. doi: 10.1002/jbm.b.34767.

[10] Husnain SM, Asim U, Yaqub A, Shahzad F, Abbas N. Recent trends of MnO2-derived adsorbents for water treatment: a review. N J Chem. 2020;44(16):6096–120. doi: 10.1039/C9NJ06392G.

[11] Zhou L, Huang Y, Qiu W, Sun Z, Liu Z, Song Z. Adsorption properties of nano-MnO2-biochar composites for copper in aqueous solution. Molecules. 2017;22(1):173. doi: 10.3390/molecules22010173.

[12] Qian X, Han X, Yu L, Xu T, Chen Y. Manganese-based functional nanoplatforms: nanosynthetic construction, physicochemical properties, and theranostic applicability. Adv Funct Mater. 2020;30:1907066. doi: 10.1002/adfm.201907066.

[13] Wang CC, Ni W, Zhang D, Sun X, Zhang N. Dielectric properties of pure and Mn-doped CaCuTi2O6 ceramics over a wide temperature range. J Electroceram. 2016;36(1–4):46–57. doi: 10.1007/s10832-016-0024-3.

[14] Yao Y, Zhang Y. Fabrication and dielectric properties of LiTaO3 matrix ceramics with added manganese dioxide. J Ceram Soc Technol. 2020;11(1):27–35. doi: m10.4416/JCST2019-00053.

[15] Xiu S, Shen B, Zhai J. The effects of MnO2 addition on the structure and dielectric properties of the strontium barium niobate glass-ceramics. Mater Res Bull. 2017;95:349–53. doi: 10.1016/j.materresbull.2017.08.008.

[16] Danewalia SS, Singh K. Magnetic and bioactive properties of MnO2/Fe2O3 modified Na2O–CaO–P2O5–SiO2 glasses and nanocrystalline glass-ceramics. Ceram Int. 2016;42:11858–68. doi:10.1016/j.ceramint.2016.04.108.

[17] Kolmas J, Groszyk E, Piotrowska U. Nanocrystalline hydroxyapatite enriched in selenite and manganese ions: physico-chemical and antibacterial properties. Nanoscale Res Lett. 2015;10(1):278–87. doi: 10.1186/s11671-015-0989-x.

[18] Kokubo T, Kushitani H, Sakka S, Kitsugi T, Yamamura T. Solutions able to reproduce in vivo surface structure changes in bioactive. J Biomed Mater Res. 1990;24(6):721–34. doi: 10.1002/jbm.820240607.

[19] Kokubo T, Takadama H. How useful is SBF in predicting in vivo bone bioactivity? Biomaterials. 2006;27(15):2907–15. doi: 10.1016/j.biomaterials.2006.01.017.

[20] Dridi A, Riahi KZ, Somrani S. Mechanism of apatite formation on a poorly crystallized calcium phosphate in a simulated body fluid (SBF) at 37°C. J Phys Chem Solids. 2021;156:110122. doi:10.1016/j.jpcs.2021.110122.

[21] Jalota S, Bhaduri SB, Tas AC. Effect of carbonate content and buffer type on calcium phosphate formation in SBF solutions. J Mater Sci Mater Med. 2006;17(8):697–707. doi: 10.1007/s10856-006-9680-1.
Characterization and biocompatibility of MnO2-containing wollastonite glass-ceramic

[22] Khatar GA. The use of Saudi slag for the production of glass-ceramic materials. Ceram Int. 2002;28(3):59–67. doi: 10.1016/S0272-8842(01)00058-X.

[23] Fischer RX, Tillmanns E. Die Kristallstrukturen von natürlichen Na2Ca2Si3O9 vom Mt. Shaheru (Zaire) und aus dem Mayener Feld (Eifel): Not: this is the high-temperature form of combleite. Neues Jahrb. für Mineral. Monatshefte. 1983;2:49–59.

[24] Yang H, Premitt CT. On the crystal structure of pseudowollastonite (CaSiO3). Am Miner. 1999;84(5–6):929–32. doi: 10.2138/am-1999-5-629.

[25] Kusachi I, Hemmi C, Kawahara A, Hemmi K. The structure of rankinite. Miner J. 1975;8:38–47. doi: 10.2138/miner.j.1975.08.02.

[26] Ohashi Y, Finger LW. The role of octahedral cations in pyroxenoid crystal chemistry; I, bastunite, wollastonite, and the pectolite-schizolite-serandite series. Am Miner. 1978;63(3–4):274–88.

[27] Dove MT, Craig MS, Keen DA, Marshall WC, Redfern SAT, Trachenko KO, et al. Crystal structure of the high-pressure monoclinic phase-II of cristobalite, SiO2. Locality: synthetic note: P = 3.5 GPa, refinement by unconstrained Rietveld analysis. Miner Magaz. 2000;64(3):569–76.

[28] Hamzawy EMA, Kenawy SH, Abd El Aty AA, El-Bassyouni GT. Characterization of wollastonite-copper nanoparticles synthesized by a wet method. Interceram. 2018;67(3):20–3.

[29] Mahdy MA, Kenawy SH, Hamzawy EMA, El-Bassyouni GT, Zawawi I. Influence of silicon carbide on structural, optical and magnetic properties of wollastonite/Fe2O3 nanocomposites. Ceram Int. 2021;47(9):12047–55. doi: 10.1016/j.ceramint.2021.01.048.

[30] Zhang H, Xu F, Xue J, Chen S, Wang J, Yang Y. Enhanced removal of heavy metal ions from aqueous solution using manganese dioxide-loaded biochar: behavior and mechanism. Sci Rep. 2020;10(1):6067. doi: 10.1038/s41598-020-63000-z.

[31] Zych L, Oszyczka AM, Łacz A, Różycka A, Niemiec W, Rapacz-Knita A, et al. How surface properties of silica nanoparticles influence structural, microstructural and biological properties of polymer nanocomposites. Materials. 2021;14(4):843. doi: 10.3390/ma14040843.

[32] Mabrouk M, Mousa SM, Abd ElGhany WA, Abo-elfadl MT, El-Bassyouni GT. Bioactivity and cell viability of Ag+ and Zr4+-co-doped biphasic calcium phosphate. Appl Phys A. 2021;127(12):948. doi: 10.1007/s00339-021-05051-1.

[33] Nawaz Q, Ur Rehman MA, Burkovski A, Schmidt J, Beltrán AM, Shahid A, et al. Synthesis and characterization of manganese containing mesoporous bioactive glass nanoparticles for biomedical applications. J Mater Sci Mater Med. 2018;29:64. doi: 10.1007/s10856-018-9070-4.

[34] Eliaz N, Metoki N. Calcium phosphate bioceramics: a review of their history, structure, properties, coating technologies and biomedical applications. Mater (Basel). 2017;10(4):334.

[35] Mancardi G. Computational study of the nucleation of calcium phosphate. Thesis submitted for the degree of doctor philosophy. University College London, London Department of Chemistry; 2018.

[36] Liu H, Yazici H, Ergun C, Webster TJ, Bermek H. An in vitro evaluation of the Ca/P ratio for the cytocompatibility of nano-to-micron particulate calcium phosphates for bone regeneration. Acta Biomater. 2008;4(5):1472–9. doi: 10.1016/j.actbio.2008.02.025.

[37] Miola M, Brovarone CV, Maina G, Rossi F, Bergandi L, Ghigo D, et al. In vitro study of manganese-doped bioactive glasses for bone regeneration. Mater Sci Eng C. 2014;38:107–18. doi: 10.1016/j.msec.2014.01.045.

[38] Bairo F. Bioactive glass – when glass science and technology meet regenerative medicine. Ceram Int. 2018;44(13):14953–66. doi: 10.1016/j.ceramint.2018.05.180.

[39] Sayed MK, El-Kady AM, Sallam AM, Talaat MS. In vitro bioactivity evaluation of novel manganese modified calcium silicate ceramics for one regeneration. IJSET – Int J Innovative Sci Eng Technol. 2018;5(10):44–9.

[40] Tripathi H, Hira SK, Kumar AS, Gupta U, Manna PP, Singh SP. Structural characterization and in vitro bioactivity assessment of SiO2–CaO–P2O5–K2O–Al2O3 glass as bioactive ceramic material. Ceram Int. 2015;41:11756–69. doi: 10.1016/j.ceramint.2015.05.143.

[41] Beherel HH, El-Bassyouni GT, Mohamed KR. Modulation, characterization and bioactivity of new biocomposites based onapatite. Ceram Int. 2008;34(8):2091–7. doi: 10.1016/j.ceramint.2007.08.003.

[42] Rometis S, Hoppe A, Eiserman C, Schneider N, Boccaccini AR, Schmidt J, et al. Enhancing in vitro bioactivity of melt derived 45SS bioglass by communication in stirred Media Mill. Am Ceram Soc. 2014;97(1):150–6. doi: 10.1111/jace.12615.