

Effect of Mg²⁺ doping on beta - alpha phase transition in tricalcium phosphate (TCP) bioceramics

Matteo Frasnelli¹ and Vincenzo M. Sglavo^{1,2}

¹ Department of Industrial Engineering, University of Trento, via Sommarive 9, 38123 Trento, Italy

² INSTM - National Interuniversity Consortium of Materials Science and Technology, Trento Research Unit, Via G. Giusti 9, Firenze 50121, Italy

ABSTRACT

The beta to alpha transition in tricalcium phosphate (TCP) bioceramics containing different amount of magnesium was studied in the present work. Mg-doped TCP powder was obtained by solid-state reaction starting from pure calcium carbonate, ammonium phosphate dibasic and magnesium oxide powders. The β to α transformation temperature was identified by dilatometric and thermo-differential analyses. Small pellets produced by uniaxial pressing samples were employed to study the influence of Mg²⁺ on the transition kinetic, after sintering at 1550°C and subsequent slow or fast cooling down to room temperature. The evolution of β - and α -TCP crystalline phases during each thermal treatment was determined by X-ray powder diffraction analysis combined with Rietveld method-based software. An annealing treatment, suitable to reconvert metastable α phase to the more clinically suitable β phase, was also investigated. It is shown that the presence of magnesium within the TCP lattice strongly influences the kinetic of the $\beta \rightleftharpoons \alpha$ phase transition, promoting the spontaneous $\alpha \rightarrow \beta$ reversion even upon fast cooling, or slowing down the $\beta \rightarrow \alpha$ transition during heating. Similarly, it allows the $\alpha \rightarrow \beta$ transformation in TCP sintered components by optimized annealing treatment at 850°C.

KEYWORDS: β -TCP, α -TCP, Mg²⁺ doping, annealing

Published version available at:

<https://www.sciencedirect.com/science/article/pii/S1742706116300174>

INTRODUCTION

Calcium phosphate-based ceramics and, above all, hydroxyapatite $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ (HA) and tricalcium phosphate $\text{Ca}_3(\text{PO}_4)_2$ (TCP), are currently employed in several biomedical applications as injectable bone cements [2], osteoconductive coatings on metal prosthesis [3] or bulk components [4] for bone repair [1-5]. Their excellent biocompatibility and osteointegrative properties are due to the chemical affinity related with the mineralized phase of human bone tissue, which consists mainly of nano-sized crystallites of calcium deficient HA [6, 7] [5], partially enriched by a large variety of substitutional ions such as CO_3^{2-} , Mg^{2+} , Sr^{2+} , F^- , Cl^- or HPO_4^{2-} [8] [6].

TCP ceramic exists in three different allotropic polymorphs: β -TCP stable at low-temperature ($< \sim 1150^\circ\text{C}$), α -TCP occurring at high-temperature (~ 1150 - 1460°C) and α' -TCP stable at even higher temperature ($> \sim 1460^\circ\text{C}$) [9, 10] [7]. β -TCP possesses a rhombohedral crystal structure (space group $R\bar{3}c$, $Z=21$), related to whitlockite ($\text{Ca}_{18}\text{Mg}_2\text{H}_2(\text{PO}_4)_{14}$) [11] [8], while α -TCP is monoclinic (space group $P2_1/a$, $Z=24$), related to glaserite ($\text{K}_3\text{Na}(\text{SO}_4)_2$) [12] [9]. There is not a technological interest for α' -TCP polymorph because of its spontaneous and complete reconversion into α -TCP upon cooling. Conversely, both β -TCP and α -TCP have been widely studied for low temperature applications, α -TCP phase being often retained at room temperature in a metastable state [13]. This irreversibility makes the β to α phase transition at $\sim 1150^\circ\text{C}$ the main technological issue encountered during the consolidation/densification of TCP components, especially in high temperature process such as plasma spray coating [14] [10].

The structural difference between the two fundamental considered polymorphs accounts for a different biological response. In particular, α -TCP shows solubility at 25°C [2, 15] [2] larger (2.5 mg/L) than β -TCP (0.5 mg/L) and, therefore, it is considered unsuitable for surgical implants, whereas it is usually employed as component for bone cements. There is a great interest and several works have been carried out in the last decades in order to obtain fully dense monophasic β -TCP components for prosthetic applications or β -/ α -TCP biphasic mixture with tailored bioactivity [16] [12].

β to α phase transition affects the sintering behaviour and the final mechanical properties of TCP components. Due to the cell volume increase, the transition is associated with a volumetric expansion ($\sim 7\%$) [17] [13], which reduces the shrinkage and prevents TCP from further densification [18] [14].

β to α phase transition in pure TCP was studied by Monma et al. [19] [15] in the '80s. It was shown that the transformation follows a first-order kinetic and has a reconstructive character, involving an overall reorganization of the crystal structure with an apparent activation energy of 250 kcal/mol. The reverse transformation α to β was shown to be kinetically inhibited upon cooling and α -TCP remained metastable at room temperature, also during moderate cooling at 10°C/min. On the other hand, other authors [20, 21] [16] have found β -TCP phase after quenching α -TCP from high temperature, it being attributed to partial reconversion upon cooling but making the transition mechanism less clear than expected. In a recent review [22] [17], Carrodeguas *et al.* clarified the reconstructive nature and the irreversibility of the β to α transformation, establishing that the presence of reconverted β -TCP after cooling may indicate that (a) the equilibrium was not reached in the α region upon heating, (b) β -stabilizing impurities increased the transformation temperature more than expected or (c) very slow cooling rate (<10°C/min) was employed.

Monma *et al.* [19] [15] also studied the α to β reconversion kinetic during an isothermal annealing process carried out on pure α -TCP powders. A maximum transformation rate temperature of ~870°C was found, this allowing the complete reconversion in 2 h. It was also shown that α to β transformation can be promoted by the introduction of strains into the starting α -TCP sample by grinding.

In order to postpone the β to α transition upon heating, thus increasing the β phase stability field and the TCP sinterability, the influence of Ca-substitutional ions like K⁺, Na⁺, Mg²⁺ and Zn²⁺ has been reported in previous works [22-29] [18-21]. Mg-doped TCP exhibits the most valuable results in terms of stabilization [30] [22]. Ando [31] [23] and Enderle *et al.* [32] [24] proposed a phase diagram for the Mg₃(PO₄)₂-Ca₃(PO₄)₂ system, where the maximum solubility of magnesium within TCP is equal to 14 mol% (Mg²⁺ substituted Ca²⁺) and at 9.1 mol% Mg concentration, β to α transition temperature occurs a temperature as high as ~1600°C. Recently, the Mg-TCP phase diagram has been revised proving the existence of the (α' + α) and (α + β) biphasic regions [33] [25].

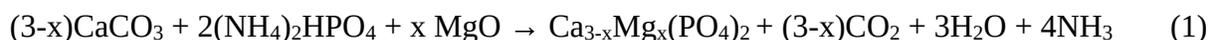
As previously pointed out, magnesium is naturally present in calcified living hard tissues. Ryu *et al.* [34] [27] successfully tested *in vivo* biphasic components made by MgO-doped HA/ β -TCP with ~9.5 mol% Mg²⁺, showing good biodegradability without any cytotoxicity or inflammations. The presence of Mg in TCP has been shown to improve also biocompatibility [35-37] [28-30].

Considering the importance and the potential applications of β -TCP bioceramics, with the aim to clarify the phase evolution better in the presence of Mg, the β to α transformation in the systems Mg-TCP was deeply investigated in the present work as specifically regards dopant

concentration and post-transformation cooling rate; the effect of a secondary heat treatment (annealing) suitable to induce α to β reversion is also analysed.

EXPERIMENTAL PROCEDURE

Magnesium doped-TCP powders were synthesized by solid-state reaction starting from calcium carbonate (CaCO_3 , >99.95 wt%, Sigma-Aldrich), ammonium phosphate dibasic ($(\text{NH}_4)_2\text{HPO}_4$, >99.0 wt%, Fluka) and magnesium oxide (MgO , 98.8 wt%, Farve). The raw materials were weighed in different amounts in order to maintain the TCP stoichiometric ratio $(\text{Ca}+\text{Mg})/\text{P}$ of 1.50 and determine a magnesium content $\text{Mg}/(\text{Ca}+\text{Mg})$ equal to 0, 1.0, 2.0, 4.6, 9.1 mol%. Corresponding samples were respectively labelled as TCP, 1.0Mg, 2.0Mg, 4.6Mg and 9.1Mg (AS series). Raw materials in form of powders were mixed in ethanol and homogenized by using ZrO_2 balls; then they were dried and calcined at 1000°C for 30 h. The expected occurring reaction, according to previous works [38, 39] [30,31], is:



where the Mg-TCP compounds correspond to the formula $\text{Ca}_{3-x}\text{Mg}_x(\text{PO}_4)_2$ and the amount of Mg^{2+} substituting Ca^{2+} can be expressed as $\text{Mg}/(\text{Ca}+\text{Mg}) \cdot 100 = x/0.03$. As previously pointed out, an Mg^{2+} content equal to 9.1 mol% theoretically leads to the maximum structural stability of β -TCP phase due to the saturation of Ca(5) sites by Mg^{2+} ions within the TCP lattice [24].

Considering the strong influence of Ca-substitutional ions on the TCP system, the purity and chemical composition of the synthesized powders were checked by inductivity coupled plasma - optical emission spectroscopy (ICP-EOS, Spectro Ciros Vision CCD, 125-770 nm) using a hydroxyapatite ultrapure standard (>99.995% trace metal basis, Sigma-Aldrich) and a multi-element standard (Merck KGaA, type IV). Standard and samples were dissolved in ultrapure nitric acid (70 vol%) and diluted in pure water produced by reverse osmosis (conductivity $<0.1 \mu\text{S}/\text{cm}$).

β to α transformation temperature was identified by Differential Thermal Analysis - DTA (Netzsch Gerätebau STA409 / DAS 414). The experiments were carried out in static air at 2 / 5 / $10^\circ\text{C}/\text{min}$ up to 1550°C .

A portion of the synthesized Mg-TCP powder was shaped into circular green pellets (thickness ~ 3 mm, diameter ~ 13 mm) by uniaxial pressing in steel mould at ~ 350 MPa. Dilatometric analysis was carry out at $20^\circ\text{C}/\text{min}$ up to 1550°C in a horizontal-loading dilatometer (Lineis L75 Platinum Series) with Al_2O_3 ram and boat. In addition, sintering treatment at 1550°C

(10°C/min, 2 h dwelling) were performed, followed by two different cooling process, (i) controlled cooling down to room temperature at 2°C/min (C series) and (ii) air-quenching down to room temperature (Q series).

In order to analyse the possibility to reconvert the metastable α -TCP phase retained after cooling, annealing processes were carried out under continuous heating condition (2°C/min) within the dilatometer on the previously quenched also pellets (QA series). Some synthesized pure TCP powder (with no Mg doping) was heated at 1300°C for 5 h, air-quenched at room temperature and then isothermally treated at 850°C for 20, 40 and 120 min following the same conditions used by Monma *et al.* [19] [15].

The crystalline phase composition was determined by X-ray powder diffraction (XRD) using a Debye-Scherrer diffractometer (Italstruttura CPS) working with Cu K_{α} radiation (8.08 keV) at 40 kV and 30 mA; the measurement was carried out in the 2θ range of 10-80°, with step of 0.03° and 10 min of acquisition time. The detection limit of the instrument under these conditions can be fixed at 0.5 w% for the considered crystalline phases. The acquired spectra were analysed by the Rietveld method-based software (MAUD 2.55) to quantify the α/β phase relative amount, using #29-0359 α -TCP and #09-0169 β -TCP phase PFD cards as structural models.

RESULTS

Synthesized powders

The ICP-OES analysis confirmed the high purity level of the synthesized Mg-TCP powders, the impurities (substantially, Na, K, Fe, Mn and Sr, only) being always lower than 50 ppm. The Mg/(Ca+Mg) molar ~~ratio~~ ratios, i.e. Mg²⁺ substituted Ca²⁺ amount (Tab. 1), show little differences with respect the nominal ones, probably due to the high MgO hygroscopy or weighing errors. Similarly, (Ca+Mg)/P atomic ratios are slightly larger than the stoichiometric 1.5 value.

<i>Sample</i>	<i>Mg nominal, mol%</i>	<i>Mg/(Ca+Mg), mol%</i>	<i>(Ca+Mg)/P</i>
<i>TCP_AS</i>	0.0	0.00 ± 0.04	1.500 ± 0.001
<i>1.0Mg_AS</i>	1.0	0.79 ± 0.04	1.507 ± 0.001
<i>2.0Mg_AS</i>	2.0	2.03 ± 0.04	1.508 ± 0.001
<i>4.6Mg_AS</i>	4.6	4.12 ± 0.04	1.503 ± 0.001
<i>9.1Mg_AS</i>	9.1	9.10 ± 0.04	1.529 ± 0.001

Tab. 1 Stoichiometric values for Mg-TCP synthesized powders (AS series) by ICP-OES.

From a mineralogical point of view, as shown in Fig. 1, all samples are formed by β polymorph only, with a variable but negligible amount of hydroxyapatite (HA) as secondary phase.

Therefore, referring to the pseudo-binary CaO-P₂O₅-(H₂O) phase diagram [40, 41] [32,33], positive deviations from the stoichiometric TCP conditions and possible humidity can lead to the formation of border phases such as HA, as expected from ICP data. The presence of HA can be very likely accounted for by the incomplete reaction between H₃PO₄ and HA occurring at about 800°C as pointed out by Pan *et al.* [38] [30] in the TCP synthesis. Nevertheless, no free/unreacted MgO or other crystalline phases have been detected and Mg²⁺ ions can be considered completely solubilized within the β -TCP lattice. This is confirmed by the gradual shift of the XRD peaks position and by the linear decrease of the refined cell parameters (Tab. 2) at increasing doping amount, as a consequence of the Mg²⁺ → Ca²⁺ partial replacement. The average crystallite size estimated by the Warren-Averbach method is equal to 706 ± 90 nm for undoped TCP and it gradually decreases along the series down to 223 ± 27 nm (4.6Mg), reaching the final value of 298 ± 19 nm in 9.1Mg.

	<i>TCP</i>	<i>1.0Mg</i>	<i>2.0Mg</i>	<i>4.6Mg</i>	<i>9.1Mg</i>
β -TCP, wt%	98.0 ± 0.0	94.0 ± 0.0	98.0 ± 0.0	91.0 ± 0.0	97.0 ± 0.0
<i>a</i> , Å	10.4357 ± 0.0006	10.4259 ± 0.0006	10.4071 ± 0.0003	10.3786 ± 0.0004	10.3396 ± 0.0003
<i>c</i> , Å	37.389 ± 0.002	37.385 ± 0.002	37.354 ± 0.002	37.274 ± 0.002	37.135 ± 0.001
<i>XS</i> , nm	706 ± 90	515 ± 37	301 ± 24	223 ± 27	298 ± 19
HA, wt%	2.0 ± 0.3	6.0 ± 0.4	2.0 ± 0.3	9.0 ± 0.6	3.0 ± 0.2
<i>R_{wp}</i>	0.1394	0.1422	0.1801	0.1877	0.1408

Tab. 2 Rietveld refinement parameters and crystalline phase quantification for Mg-TCP synthesized powders (AS series). The reported errors and *R_{wp}* correspond to the data fitting.

Fig. 1. XRD spectra of the synthesized Mg-TCP powders (AS series).

Thermal behaviour of Mg-TCP series

Figure 2 shows the DTA plots for the Mg-TCP powders in the range of interest here, between 1000 and 1550°C. For undoped TCP, 1.0Mg and 2.0Mg compositions, the curves are characterized by two main endothermic events: a weak signal ($\beta \rightarrow \alpha$) and a very strong and sharp

peak ($\alpha \rightarrow \alpha'$). Regular drifts to higher temperature, as well as increased normalized intensities, are observable in the DTA peaks by increasing the adopted heating rate.

As expected, the first event is gradually postponed by the Mg^{2+} presence: considering data acquired at $2^\circ C/min$, it reaches the maximum velocity at $1196^\circ C$ (TCP), $1276^\circ C$ (1.0Mg), and $1313^\circ C$ (2.0Mg). Therefore, the signal shift leads to overlap the 4.6Mg peaks ($1454^\circ C$) with the second event. Conversely, for the highest Mg composition (i.e. 9.1Mg), no evidence of $\beta \rightarrow \alpha$ transition can be observed up to $1550^\circ C$. Also the second thermal phenomenon seems to be affected by Mg^{2+} : it takes place at $1471^\circ C$ (TCP), $1425^\circ C$ (1.0Mg), $1429^\circ C$ (2.0Mg), $1467^\circ C$ (4.6Mg), and finally occurs at $1488^\circ C$ (9.1Mg).

Fig. 2. DTA curves for Mg-TCP powders at different heating rate (dotted line: $2^\circ C/min$; dashed line: $5^\circ C/min$; solid line: $10^\circ C/min$) and details of the thermal events (cross: $2^\circ C/min$; circle: $5^\circ C/min$; triangle: $10^\circ C/min$). The temperature values refer to the minimum of the peak.

Preliminary considerations on the sintering behaviour of the Mg-TCP can be done from the dilatometric curves reported in Fig. 3. For all compositions, green pellets start to shrink at $\sim 1000^\circ C$. Then, the densification is stopped by the volumetric expansion associated to the $\beta \rightarrow \alpha$ transition. Therefore, magnesium doping allows to achieve higher final shrinkage than in pure TCP (2.3%), equal to 5.8% for 1.0Mg, 9.0% for 2.0Mg, 12.5% for 4.6Mg, and 35.3% for 9.1Mg.

Fig. 3. Dilatometric plots of Mg-TCP pellets. Circles represent the $\beta \rightarrow \alpha$ transition.

Reversibility of β to α transformation

The results of the quantitative analysis carried out on the collected XRD spectra are summarized in Tab. 3. For pure TCP, only α phase is present regardless the used cooling rate. Conversely, C series data show the concurrent presence of both polymorphs for the 1.0Mg composition ($\beta = 46$ wt%), while 2.0Mg and 4.6Mg are completely constituted by β phase. Although the very slow cooling rate ($2^\circ C/min$) used here can justify the spontaneous $\alpha \rightarrow \beta$ reconstructive reconversion [22] [17], it is clear that Mg^{2+} presence proportionally promotes such phenomenon. Q series data follow a similar trend, accordingly. The amount of retained α phase increases after the quenching process and, in this case, 1.0Mg sample is completely constituted by α -TCP. Unexpectedly, 2.0Mg shows the presence of both polymorphs ($\beta = 64$ wt%), while 4.6Mg

is only constituted by β -TCP. Consequently, for Mg-doped TCP composition, $\beta \rightarrow \alpha$ transition has to be considered partially or totally reversible.

Sample	β phase, wt%	α phase, wt%	R_{wp}
C series – cooled			
TCP_C	< DL	100 \pm 0	0.2439
1.0Mg_C	46 \pm 2	54 \pm 0	0.2889
2.0Mg_C	100 \pm 0	< DL	0.2793
4.6Mg_C	100 \pm 0	< DL	0.2799
9.1Mg_C	100 \pm 0	< DL	0.2897
Q series – quenched			
TCP_Q	< DL	100 \pm 0	0.2036
1.0Mg_Q	< DL	100 \pm 0	0.2285
2.0Mg_Q	64 \pm 2	36 \pm 2	0.2822
4.6Mg_Q	100 \pm 0	< DL	0.2694
9.1Mg_Q	100 \pm 0	< DL	0.2797
QA series – quenched and annealed			
TCP_QA	< DL	100 \pm 0	0.2137
1.0Mg_QA	100 \pm 0	< DL	0.2585
2.0Mg_QA	100 \pm 0	< DL	0.2708

Tab. 3. Quantitative analysis on XRD collected spectra as a function of Mg doping amount and performed treatment. DL (detection limit) = 0.5 wt%.

Annealing treatment

The dilatometric plots of the QA pellets during the annealing process (heating rate = 2°C/min) are reported in Fig. 4. An evident phenomenon takes place at about 770°C and 680°C for 1.0Mg and 2.0Mg, respectively, whereas undoped TCP does not show any effect up to 1000°C. The shrinkage is proportional to the initial amount of α phase within the quenched sample; for this reason, no tests were performed on 4.6Mg and 9.1Mg samples (these being completely constituted by β phase). The quantitative analysis carried out on the XRD spectra of the QA series after annealing (Tab. 03) points out that pure TCP remains as α -TCP, while 1.0Mg and 2.0Mg are completely reconverted into β -TCP.

However, the annealing process carried out isothermally at 850°C on pure TCP powder actually proves the possibility to reconvert metastable α -TCP even in absence of doping. The XRD

quantitative analysis allows to estimate a β -TCP amount equal to 13 wt%, 20 wt% and 42 wt% after 20 min, 40 min and 120 min isothermal treatment, respectively. Such values are considerably smaller than those previously reported [19] [15] at very similar conditions; the only difference can be found in the particle size of the samples (the size being larger in the present work, $\sim 300 \mu\text{m}$, compared to $\sim 100 \mu\text{m}$ measured by Monma *et al.* [19] [15]) or in the purity of the raw materials.

Fig. 4. Dilatometric plot of Mg-TCP sintered pellets during the annealing treatment (QA series).

DISCUSSION

Thermal behaviour of Mg-TCP series

The first endothermic event revealed in the DTA plots can be unequivocally assigned to the $\beta \rightarrow \alpha$ transition, in very good agreement with previous results [32, 33] [24, 25], considering the heating rates employed for the present analysis. Nevertheless, it should be pointed out that the specified temperatures represent specifically the lower boundary of the biphasic region where the two polymorphs coexist, *i.e.*, more precisely, the $\beta \rightarrow (\beta+\alpha)$ transition temperature. Similarly, a second event could be associated with $\alpha \rightarrow (\alpha + \alpha')$ reversible transformation.

However, $\beta \rightarrow \alpha$ transition takes place for every compositions but 9.1Mg, within the 1000-1550°C range; in addition, dilatometric plots show a sudden interruption of shrinkage at equivalent temperatures.

Reversibility of β to α transformation

Pure TCP sample confirms the irreversible behaviour of the $\beta \rightarrow \alpha$ transition in absence of doping, also after a slow cooling at 2°C/min. Conversely, β phase can be found in Mg-doped TCP samples belonging to C or Q series. It has to be recalled here that C and Q series samples were heated up to 1550°C, kept for 2 h at such temperature and then slowly cooled or quenched to room temperature, respectively. According to Fig. 2, during the heat treatment all compositions exceed the $(\beta+\alpha)$ region and, therefore, if the dwell time is considered as sufficient to reach the equilibrium, $\beta \rightarrow \alpha$ transition completely occurs. Only the 9.1Mg composition, remaining within the monophasic β region, shall be excluded from such considerations.

The observed behaviour can be explained considering that magnesium, not only increases the β phase stability, but kinetically promotes the spontaneous α to β reversion upon cooling, even during very rapid quenching in air.. Moreover, the time required by the system to reach the equilibrium shall be accounted for explaining the observed behaviour. However, since pure TCP

and 1.0Mg contain only α phase after quenching, the used dwell time (2 h) is adequate for all compositions; one can eventually consider that magnesium slows down the $\beta \rightarrow \alpha$ transition upon heating, larger doping amount requiring longer time to reach the equilibrium. In any case, Mg^{2+} presence within the TCP lattice clearly influences not only the $\beta \rightleftharpoons \alpha$ ($\beta \rightarrow \alpha$ and $\alpha \rightarrow \beta$) transition thermodynamic but also its kinetics.

Annealing treatment

If the XRD quantitative data for Mg-doped QA samples ($\beta = 100$ wt%) and the initial α phase amount in the quenched samples (Q series) are considered, the shrinkage measured by dilatometer, which simulates the chosen annealing treatments, can be certainly associated with the $\alpha \rightarrow \beta$ reconversion process. This statement is in agreement with the lattice parameters difference between β and α TCP, keeping in mind that $\beta \rightarrow \alpha$ transition is instead associated with an expansion. Therefore, to summarize, an annealing treatment at $2^\circ\text{C}/\text{min}$ up to 1000°C allows the transformation of α phase in Mg-doped TCP sintered pellets; conversely, the transformation can not be activated in pure TCP. In addition, Mg^{2+} presence proportionally decreases the onset temperature of the reconversion in agreement with previous observation regarding the magnesium kinetic contribution on the spontaneous $\alpha \rightarrow \beta$ transformation upon cooling.

On the basis of the obtained results, one can point out a lower efficiency of the isothermal annealing on pure TCP considered in the present work in comparison to previous activities [19] [15]; this can be explained considering that the reconstructive transformation $\beta \rightarrow \alpha$ TCP, based on nucleation and growth processes [31] [22], is strongly affected by the reactive surface area, i.e. by the particles size: as a matter of fact Monma *et al.* [19] [15] performed the analyses on finely ground powders while coarser powders were used here. Correspondingly, upon continuous heating, $\alpha \rightarrow \beta$ reconversion should be much faster in TCP powders than in sintered bulk components. In the latter situation, the transition can anyway take place if it is kinetically promoted by the presence of Mg^{2+} , whereas for undoped TCP it is too slow to occur within a reasonable time. Nevertheless, from a technological point of view, this secondary heat treatment (i.e., annealing) is more useful if applied on bulk components after sintering where the presence of retained α phase is an undesired side effect. On the other hand, for powder-like TCP, it is easier to control the crystalline phase composition, directly avoiding the $\beta \rightarrow \alpha$ transition.

CONCLUSIONS

In the present work, the thermal behaviour of Mg-doped tricalcium phosphate was investigated, with specific attention to the $\beta \rightleftharpoons \alpha$ phase transitions.

Magnesium strongly increases the β polymorph stability, postponing the transformation temperature into α phase. Therefore, during the sintering process of Mg-TCP powders, this allows to reach a higher densification.

In the presence of magnesium, $\beta \rightarrow \alpha$ transition is spontaneously reversible upon cooling. This indicates that Mg^{2+} promotes the kinetic of $\alpha \rightarrow \beta$ reconversion upon cooling or, at least, proportionally slows down the kinetic of the $\beta \rightarrow \alpha$ transition upon heating, increasing the time necessary to reach the equilibrium.

Regarding the possibility to reconvert the possible retained α phase in the TCP sintered components by a secondary heat treatment (i.e. annealing), it has been demonstrated that their limited surface area, much lower in comparison to grinded powders, make the process more difficult and non-functional for undoped TCP. Nevertheless, also in this case magnesium promotes the $\alpha \rightarrow \beta$ reconversion kinetically and thermodynamically, allowing the transition and decreasing the starting process temperature down to 680°C (2 mol% of Mg^{2+}).

REFERENCES

- [1] L.L. Hench, *Bioceramics*, J. Am. Cer. Soc. 81 (1998) 1705-1728.
- [2] S.V. Dorozhkin, *Self-Setting Calcium Orthophosphate Formulations: Cements, Concretes, Pastes and Putties*, Int. J. Mater. And Chem. 1 (2011) 1-48.
- [3] R. Narayanan, S.K. Seshadri, T.Y. Kwon, K.H. Kim, *Calcium Phosphate-Based Coatings on Titanium and its Alloys*, J. Biomed. Mater. Res. Part B: App. Biomat. 85B (2008) 279-299.
- [4] E. Champion, *Sintering of calcium phosphate bioceramics*, Acta Biomater. 9 (2013) 5855-5875.
- [5] M. Piccinini, A. Rebaudi, V.M. Sglavo, F. Bucciotti, P. Robotti, *A New HA/TTCP Material for Bone Augmentation: An In Vivo Histological Pilot Study in Primates Sinus Grafting*, Impl. Dent. 22 (2013) 83-90.
- [6] J. Gomez-Morales, M. Iafisco, J.M. Delgado-Lopez, S. Sarda, C. Drouet, *Progress on the preparation of nanocrystalline apatites and surface characterization: Overview of fundamental and applied aspect*, Progr. Cryst. Growth and Char. Mater. 59 (2013) 1-46.
- [7] D. Zahn, O. Hochrein, *On the composition and atomic arrangement of calcium-deficient hydroxyapatite: An ab-initio analysis*, J. Sol. St. Chem. 181 (2008) 1712-1716.

- [8] M. Supova, Substituted hydroxyapatites for biomedical applications: A review, *Cer. Int.* 41 (2015) 9203-9231.
- [9] N. Rangavittal, A.R. Landa-Canovas, J.M. Gonzales-Calbet, M. Vallet-Regi, Structural study and stability of hydroxyapatite and β -tricalcium phosphate: Two important bioceramics, *J. Biomed. Mater. Res.* 51 (2000) 660-668.
- [10] M. Yashima, A. Sakai, High-temperature neutron powder diffraction study of the structural phase transition between α and α' phases in tricalcium phosphate $\text{Ca}_3(\text{PO}_4)_2$, *Chem. Phys. Lett.* 372 (2003) 779-783.
- [11] M. Yashima, A. Sakai, T. Kamiyama, A. Hoshikawa, Crystal structure analysis of β -tricalcium phosphate $\text{Ca}_3(\text{PO}_4)_2$ by neutron powder diffraction, *J. Sol. St. Chem.* 175 (2003) 272-277.
- [12] M. Mathew, L.W. Schroeder, B. Dickens, W.E. Brown, The Crystal Structure of α - $\text{Ca}_3(\text{PO}_4)_2$, *Acta Cryst.* B33 (1977) 1325-1333.
- [13] N. Döbelin, L. Galea, U. Eggenberger, J.M.F. Ferreira, M. Böhner, Recrystallization of amorphized α -TCP, *Key Eng. Mater.* 493-494 (2012) 219-224.
- [14] R.A. Surmenev, A review of plasma-assisted methods for calcium phosphate-based coatings fabrication, *Surf. & Coat. Tech.* 206 (2012) 2035-2056.
- [15] L. Wang, G.H. Nancollas, Calcium orthophosphates: crystallization and dissolution, *Chem. Rev.* 108 (2008) 4628-4669.
- [16] R. Famery, N. Richard, P. Boch, Preparation of α - and β -Tricalcium Phosphates Ceramics, with and without Magnesium Addition, *Cer. Int.* 20 (1994) 327-336.
- [17] H.S. Ryu, H.J. Youn, K.S. Hong, B.S. Chang, C.K. Lee, S.S. Chung, An improvement in sintering property of β -tricalcium phosphate by addition of calcium pyrophosphate, *Biomater.* 23 (2002) 909-914.
- [18] K. Itatani, T. Nishioka, S. Seike, F.S. Howell, A. Kishioka, M. Kinoshita, Sinterability of β -orthophosphate powder prepared by spray pyrolysis, *J. Am. Cer. Soc.* 77 (1994) 801-805.
- [19] H. Monma, M. Goto, Behaviour of the α - β phase transformation in tricalcium phosphate, *J. Cer. Soc. Jap.* 91 (1983) 473-475.
- [20] E. Fernandez, M.P. Ginebra, M.G. Boltong, F.C.M. Driessens, J. Ginebra, E.A.P. De Maeyer, et al, Kinetic study of the setting reaction of a calcium phosphate bone cement, *J. Biomed. Mater. Res.* 32(1996) 367-374.

- [21] P.M.C. Torres, J.C.C. Abrantes, A. Kaushal, S. Pina, N. Döbelin, M. Bohner, J.M.F. Ferreira, Influence of Mg-doping, calcium pyrophosphate impurities and cooling rate on the allotropic $\alpha \leftrightarrow \beta$ -tricalcium phosphate phase transformations, *J. Eur. Cer. Soc.* 36 (2016) 817-827.
- [22] R.G. Carrodeguas, S. De Aza, α -Tricalcium phosphate: Synthesis, properties and biomedical applications, *Acta Biomater.* 7 (2011) 3536-3546.
- [23] D.M.B. Wolff, E.G. Ramalho, W. Acchar, Phase Transition behaviour of Tricalcium phosphate (TCP) doped with MgO and TiO₂ as additives, *Mat. Sci. Forum* 530-531 (2006) 581-586.
- [24] R.S. Pillai, V.M. Sglavo, Effect of MgO addition on solid state synthesis and thermal behaviour of beta-tricalcium phosphate, *Cer. Int.* 41 (2015) 2512-2518.
- [25] L. Carbajal, A. Caballero, M.A. Sainz, Design and processing of ZnO doped tricalcium phosphate based materials: Influence of β/α polymorph phase assemblage on microstructural evolution, *J. Eur. Cer. Soc.* 32 (2012) 569-577.
- [26] R.G. Carrodeguas, A.H. De Aza, I. Garcia-Paez, S. De Aza, P. Pena, Revisiting the Phase-Equilibrium Diagram of the Ca₃(PO₄)₂-CaMg(SiO₃)₂ System, *J. Am. Cer. Soc.* 93 (2010) 561-569.
- [27] E.R. Kreidler, F.A. Hummel, Phase Equilibria in the System Ca₃(PO₄)₂ - Zn₃(PO₄)₂, *Inorg. Chem.* 3 (1967) 524-528.
- [28] S.J. Kalita, H.A. Bhatt, A. Dhamne, MgO-Na₂O-P₂O₅-Based Sintering Additives for Tricalcium Phosphate Bioceramics, *J. Am. Cer. Soc.* 89 (2006) 875-881.
- [29] S. Kannan, J.M. Ventura, J.M.F. Ferreira, Aqueous precipitation method for the formation of Mg-stabilized β -tricalcium phosphate: An X-ray diffraction study, *Cer. Int.* 33 (2007) 637-641.
- [30] N. Matsumoto, K. Yoshida, K. Hashimoto, Y. Toda, Thermal stability of β -tricalcium phosphate doped with monovalent metal ions, *Mater. Res. Bull.* 44 (2009) 1889-1894.
- [31] J. Ando, Phase diagrams of Ca₃(PO₄)₂-Mg₃(PO₄)₂ and Ca₃(PO₄)₂-CaNaPO₄ systems, *Bull. Chem. Soc. Jap.* 31 (1958) 201-205.
- [32] R. Enderle, F. Götz-Neunhoeffler, M. Göbbels, F.A. Müller, P. Greil, Influence of magnesium doping on the transformation temperature of β -TCP ceramics examined by Rietveld refinement, *Biomater.* 26 (2005) 3379-3384.
- [33] R.G. Carrodeguas, A.H. De Aza, X. Turrillas, P. Pena, S. De Aza, New Approach to the $\beta \rightarrow \alpha$ Polymorphic Transformation in Magnesium-Substituted Tricalcium Phosphate and its Practical Implications, *J. Am. Cer. Soc.* 91 (2008) 1281-1286.

- [34] H.S. Ryu, K.S. Hong, J.K. Lee, D.J. Kim, J.H. Lee, B.S. Chang, D. Lee, C.K. Lee, S.S. Chung, Magnesia-doped HA / β -TCP ceramics and evaluation of their biocompatibility, *Biomater.* 25 (2004) 393-401.
- [35] X. Li, A. Ito, Y. Sogo, X. Wang, R.Z. LeGeros, Solubility of Mg-containing β -tricalcium phosphate at 25°C, *Acta Biomater.* 5 (2009) 508-517.
- [36] S.S. Banerjee, S. Tarafder, N.M. Davies, A. Bandyopadhyay, S. Bose, Understanding the influence of MgO and SrO binary doping on the mechanical and biological properties of beta-TCP ceramics, *Acta Biomater.* 6 (2010) 4167-4174.
- [37] S. Bose, S. Tarafder, S.S. Banerjee, N.M. Davies, A. Bandyopadhyay, Understanding in vivo response and mechanical property variation in MgO, SrO and SiO₂ doped β -TCP, *Bone* 48 (2011) 1282-1290.
- [38] Y. Pan, Preparation of β -TCP with high thermal stability by solid reaction route, *J. Mater. Sci.* 38 (2003) 1049-1056.
- [39] N. Matsumoto, K. Yoshida, K. Hashimoto, Y. Toda, Dissolution mechanisms of β -tricalcium phosphate doped with monovalent metal ions, *J. Cer. Soc. Jap.* 118 (2010) 451-457.
- [40] K.A. Gross, C.C. Berndt, Thermal processing of hydroxyapatite for coating production, *J. Biomed. Mater. Res.* 39 (1998) 580-587.
- [41] S. Serena, L. Carbajal, M.A. Sainz, A. Caballero, Thermodynamic Assessment of the System CaO-P₂O₅: Application of the Ionic Two-Sublattice Model to Glass-Forming Melts, *J. Am. Cer. Soc.* 94 (2011) 3094-3103.

Figure 1

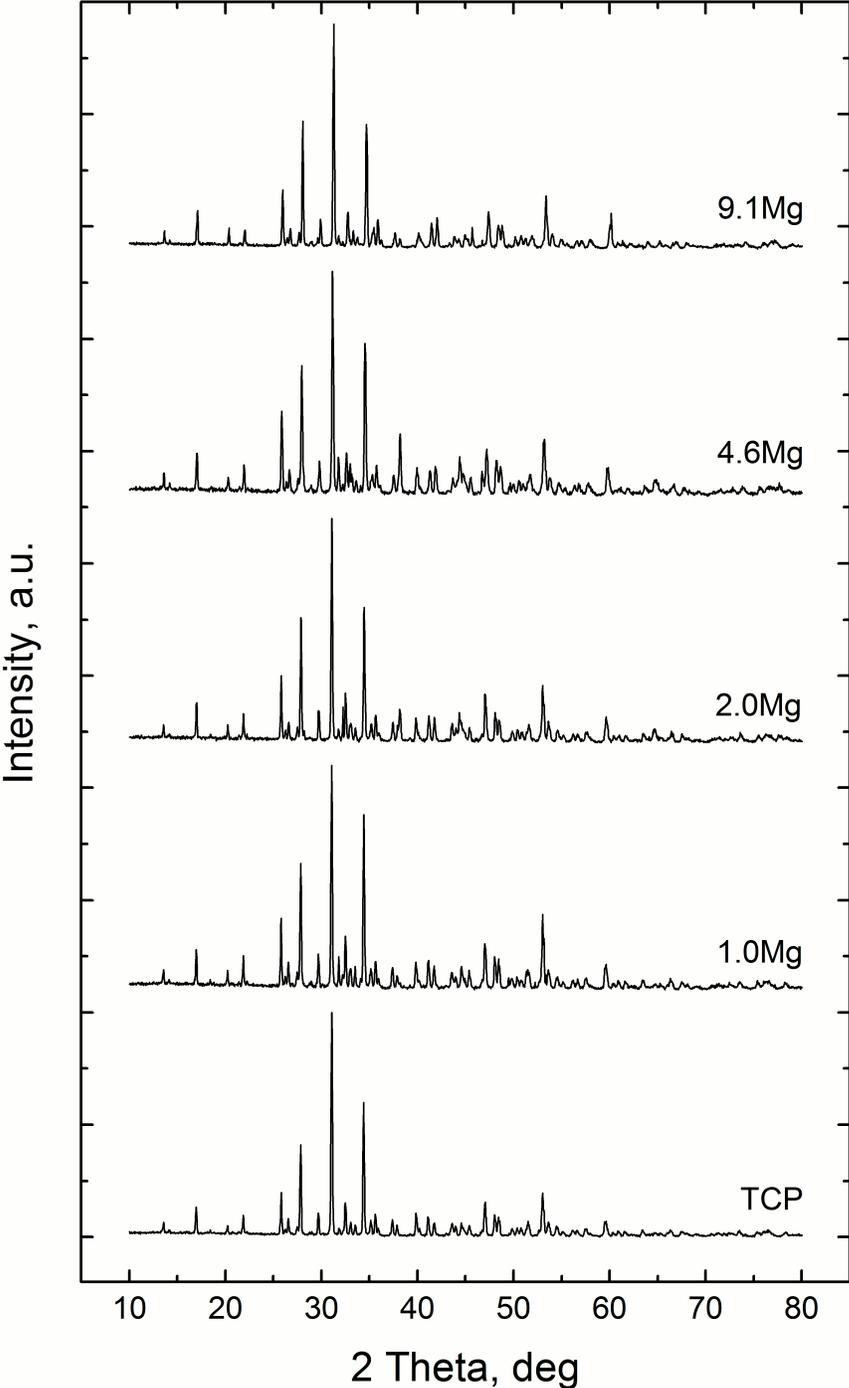
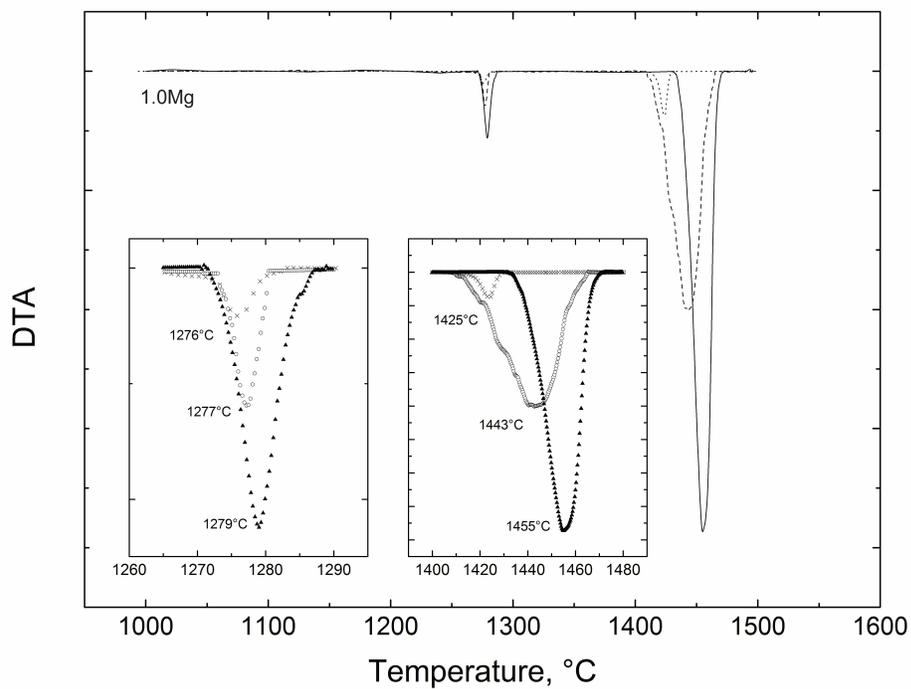
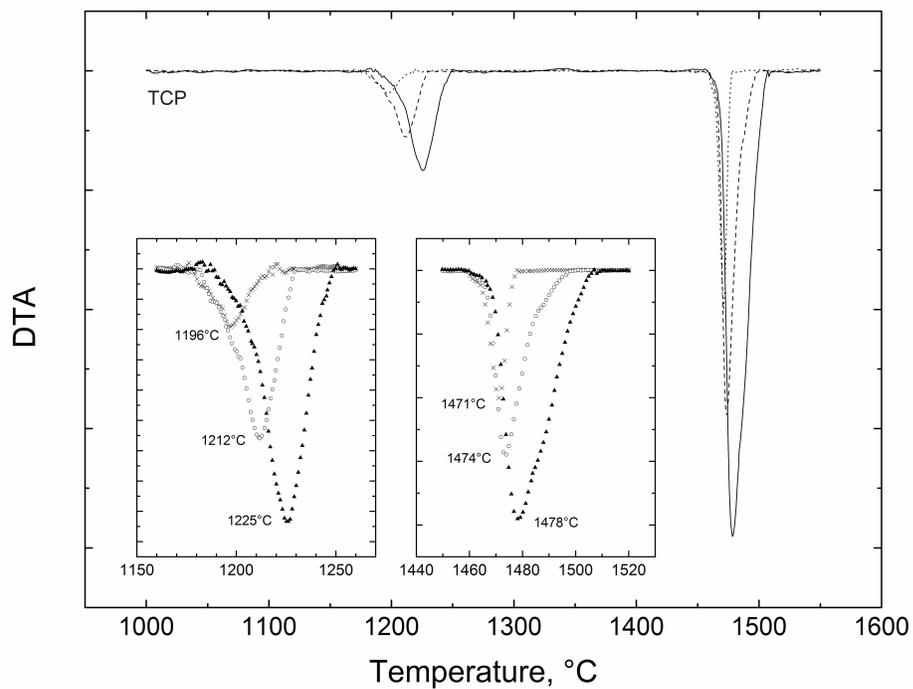
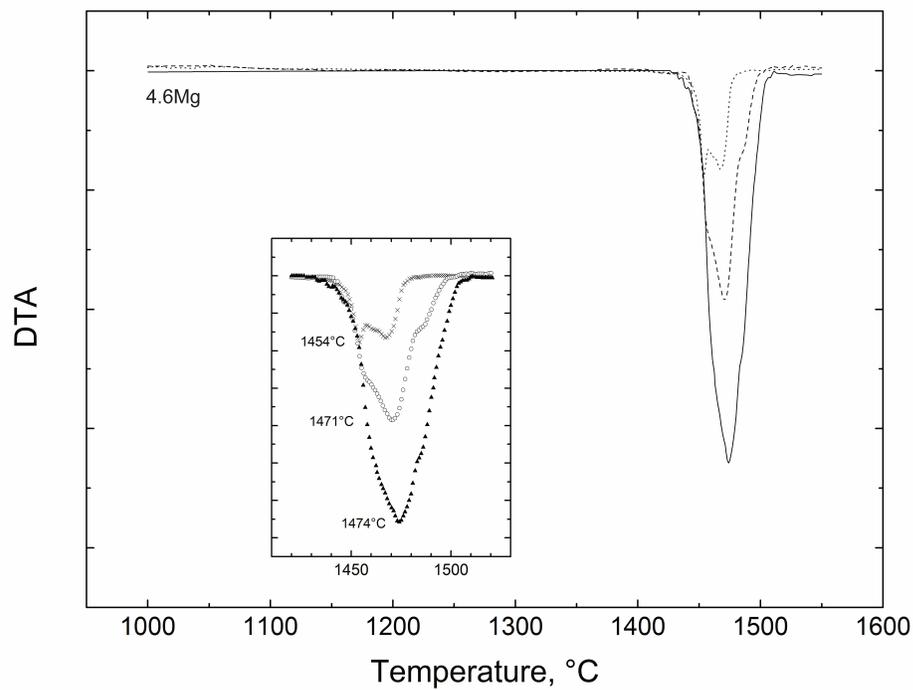
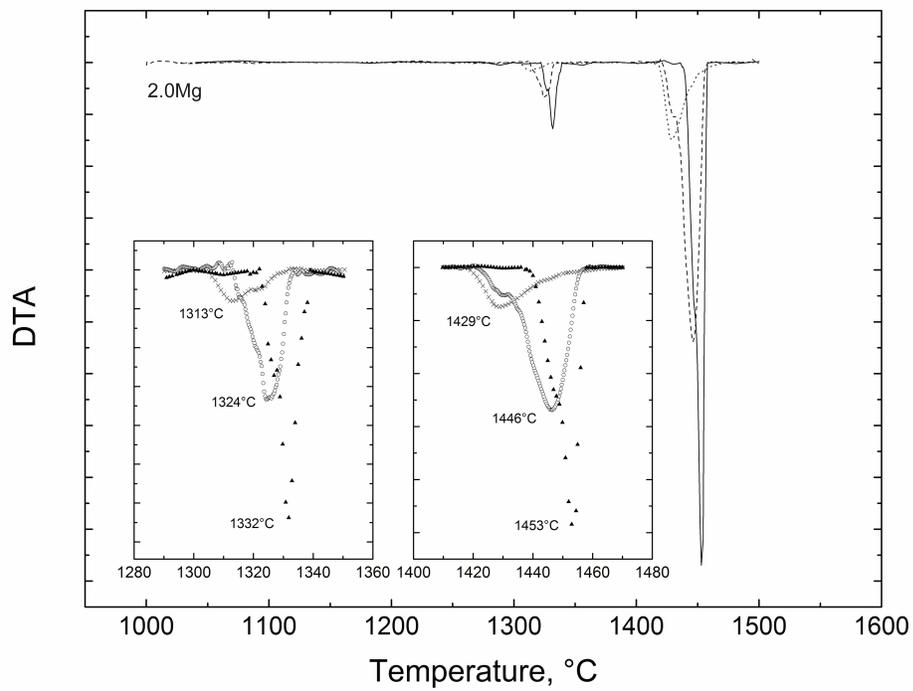


Figure 2





DTA

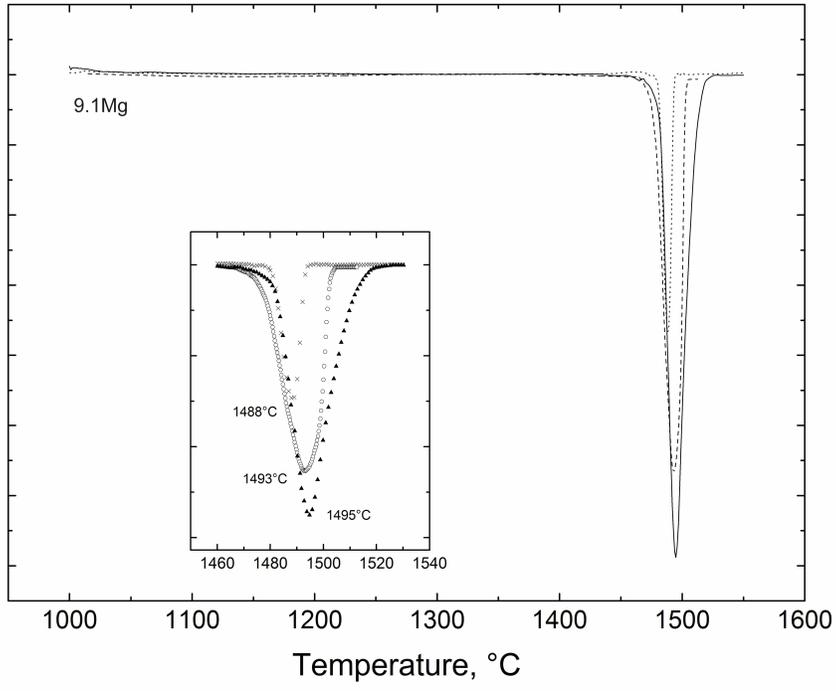


Figure 3

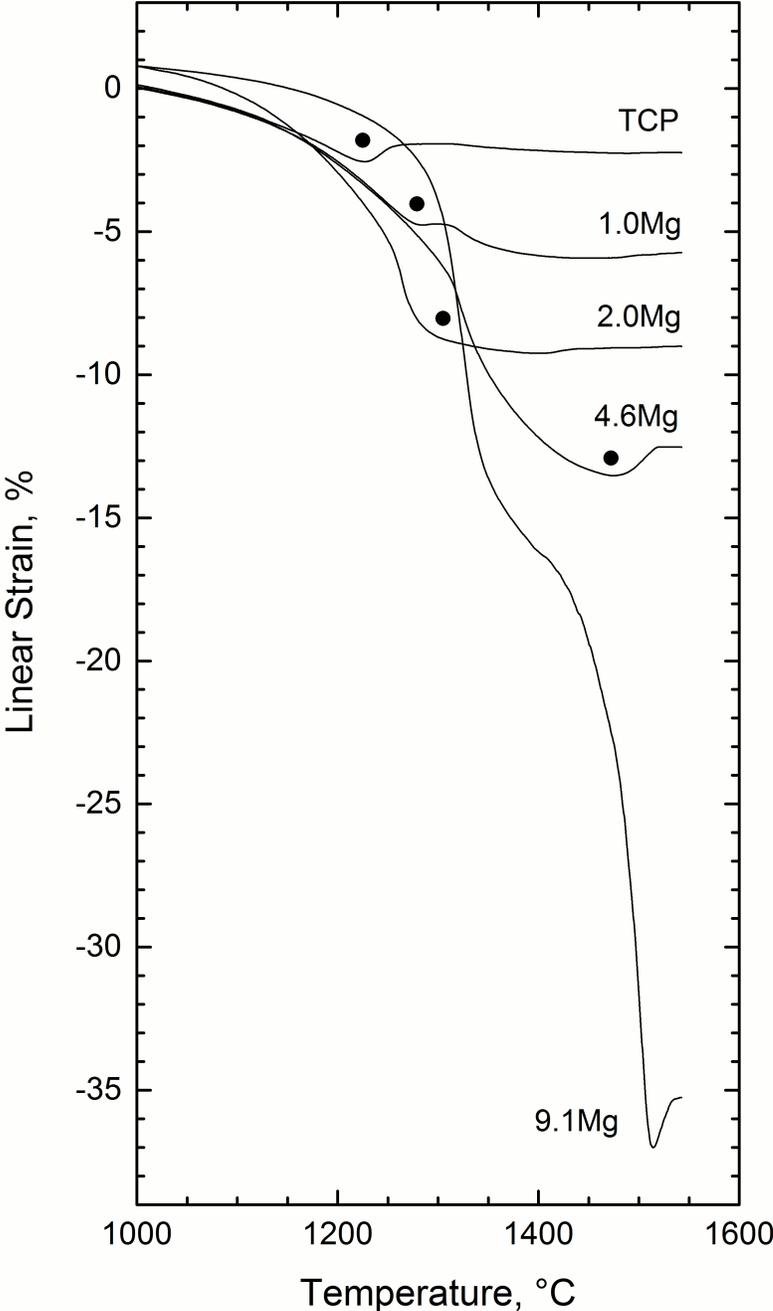


Figure 4

