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# Análise da influência do tamanho de partícula de β-TCP no processo de desaglomeração

# Analysis of the influence of β-TCP particle size on deagglomeration processes

# Análisis de la influencia del tamaño de partícula β-TCP em los procesos de desaglomeración

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**Resumo**

As cerâmicas de fosfato de cálcio (CFCs) são uma classe de materiais biocompatíveis e bioativos ampla-mente utilizados no reparo do tecido ósseo. A CFC fosfato tricálcico (TCP) ocorre em duas fases: α e β. O β-TCP é mais usado na regeneração óssea do que o α-TCP,

uma vez que é mais biocompatível e estável que o α-TCP. No presente trabalho avaliamos a influência no tamanho de partícula utilizando processos distin-tos na desaglomeração do β-TCP, moagem de alta energia e almofariz, obtido através da reação no estado sólido. Entre todas as rotas utilizadas na pesquisa e na indústria para reduzir o tamanho das partículas de diferentes materiais, a moagem de alta energia, é um método eficaz, devido à alta velocidade de rotação que esse processo alcança. A desagregação em almofariz de ágata é considerada um processo mais econô-mico quando comparado com o moinho de bolas de alta energia. A caracterização dos pós obtidos, desa-glomerados em moinho de bolas de alta energia e almofariz de ágata, foram analisados por meio de micros-copia eletrônica de varredura, para análise da morfologia do pó e granulometria a laser foi utilizada para determinação do tamanho das partículas. Além disso, o pó precursor foi previamente submetido à difração de raios X para confirmar a formação da fase β-TCP. Os resultados obtidos após os processos de desagrega-ção indicaram que a morfologia era predominantemente irregular para ambos os pós. Em relação à granu-lometria, a desaglomeração realizada utilizando almofariz de ágata mostrou produzir partículas com menor tamanho (11,4µm e 0,9µm) e distribuição heterogênea, enquanto o processo de moagem de alta energia produziu partículas com maior tamanho (11,4µm a 1,8µm) e maior homogeneidade.

**Palavras-chave:** β- fosfato tricálcico; tamanho de partícula; moinho de alta energia; almofariz de ágata.

**Abstract**

There are a class of material widely used in bone tissue repair. This material is calcium phosphate ceramics (CPCs)that can be used on two phases: α and β. However, β-TCP is more used in bone regeneration than α–TCP due to the biocompatible and bioactive properties.In the present work evaluate the influence of these two distinct processes to deagglomeration and the consequence in the particle size of the β-TCP obtained through solid-state reaction. Among all of the routes used in research and industry to reduce the particles size of different materials, the high energy ball milling is one of the most effective, due to the high rotation speed that this process achieves. The deagglomeration through agate mortar is considered a cheaper process when compared with the high energy ball milling. The characterization of both powders, deagglomerated in high energy ball milling and agate mortar, was realized through scanning electron microscopy, to analyze the powder morphology, and laser granulometry, to determine the size of the particles. Also, the forerunner powder was previously submitted to x-ray diffraction to confirm the formation of the β-TCP phase. The

analysis through x-ray diffraction confirmed that the phase formed during the calcination process corresponded to the β-TCP. The results obtained after the deagglomeration processes indicated that the morphology was predominantly irregular for both powders. In relation to the granulometry, the deagglomeration performed through agate mortar showed to produce particles with smaller size (11,4μm e 0,9μm) and heterogeneous distribution, while the high energy ball milling process produced particles with larger size (11,4μm a 1,8μm) and higher homogeneity.

**Keywords:** β-tricalcium phosphate; particle size; high energy ball milling; agate mortar.

**Resumen**

Hay una clase de material ampliamente utilizado en la reparación del tejido óseo. Este material es la cerámica de fosfato de calcio (CPC) que se puede usar en dos fases: α y β. Sin embargo, β-TCP se usa más en la regeneración ósea que α-TCP debido a las propiedades biocompatibles y bioactivas.En el presente trabajo, evalúe la influencia de estos dos procesos distintos para la desaglomeración y la consecuencia en el tamaño de partícula del β-TCP obtenido a través de la reacción en estado sólido. Entre todas las rutas utilizadas en la investigación y la industria para reducir el tamaño de partículas de diferentes materiales, el molino de bolas de alta energía es uno de los más efectivos, debido a la alta velocidad de rotación que logra este proceso. La desaglomeración a través del mortero de ágata se considera un proceso más barato en comparación con el molino de bolas de alta energía. La caracterización de ambos polvos, desaglomerados en molienda de bolas de alta energía y mortero de ágata, se realizó mediante microscopía electrónica de barrido, para analizar la morfología del polvo y la granulometría láser, para determinar el tamaño de las partículas. Además, el polvo precursor se sometió previamente a difracción de rayos X para confirmar la formación de la fase β-TCP. El análisis por difracción de rayos X confirmó que la fase formada durante el proceso de calcinación correspondía al β-TCP. Los resultados obtenidos después de los procesos de desaglomeración indicaron que la morfología era predominantemente irregular para ambos polvos. En relación con la granulometría, la desaglomeración realizada a través de mortero de ágata demostró producir partículas de menor tamaño (11,4μm e 0,9μm) y distribución heterogénea, mientras que el proceso de molienda de bolas de alta energía produjo partículas de mayor tamaño (11, 4μm a 1,8μm) y mayor homogeneidad.

**Palabras clave:** fosfato β-tricálcico; tamaño de partícula; molienda de bolas de alta energia; mortero de ágata.

## 1. Introdução

Calcium phosphate ceramics (CPCs) are a class of bioactive materials that are widely used for bone tissue repair [1, 2]. In fact, of all the biomaterials used in the clinic for bone implants, calcium phosphate ceramics have real potential to become a bone substitute biomaterial because of its similarity to bone mineral composition, as well as its biocompatibility, osteoconductivity and osteoinductivity [3-5].

In last decades, there has been an increasing demand associated with the use of CPCs for bone repair due to the aging of the world population and the occurrence of bone fractures associated with accidents. The most commonly used CPCs are hydroxyapatite (HAP), amorphous calcium phosphate (ACP), biphasic calcium phosphate (BCP) and tricalcium phosphate (TCP). TCP occurs in two different phases, α and β. However, β-TCP is more used in bone regeneration than α-TCP (6,7). In fact, chemically the vast majority of synthetic CPCs are based on HA and β-TCP that may promote high bone growth rate at physiological conditions [8].

β-TCP can be synthesized by different methods such as solid-state reactions, precipitation chemistry, sol-gel methods and hydrothermal treatment [9-12] that allow different morphologies with chemical compositions similar to bone tissue to be expanded, increasing the possibilities of use. Each of these methods provides specific characteristics to the TCP, such as particle size, mechanical properties, morphology and crystalline structures [13-18]. In this work, evaluate the influence of these two distinct processes to deagglomeration and the consequence in the particle size of the β-TCP obtained through solid-state reaction.

## 2. Metodologia

The beta tricalcium phosphate (β-TCP) was obtained via solid state reaction through the mixture of the reagents calcium carbonate (CaCO3) and calcium phosphate (CaHPO4), according to the stoichiometric reaction:

$$CaCO3(s) + 2CaHPO4(s) \rightarrow Ca3(PO4)2(s) + H2O(g) + CO2(g)$$

The powders were then inserted in a V-Blender Edibon® 1L mixer during 2 hours,

with a speed of 18 rpm, to homogenize the mixture. After this process, the powders were dried during 1 hours over a tempera-ture of 100 ºC. The sintering process was realized following the procedure described for Cardoso et al. (2012). The powder was inserted in a EDG Equipmentos and Controls Ltda® EDG 3P-S oven during 6 hours over a temperature of 1050ºC with a heating rate of 10ºC/min. The powder was cooled inside of the oven.

For the deagglomeration of the sintered β-TCP powder, were used a high energy ball mill Noah Nuoya® 0.2 L and an agate mortar, with the intention to determine which process was considered more effective. For the milling process, the parameter used were: 150 rpm of milling speed, 1 hours of milling time, mass/sphere relation of 1:10 and milling vases of zirconia. For the agate mortar process, the powder was manually macerated during 3 times: 10, 20 and 30 minutes.

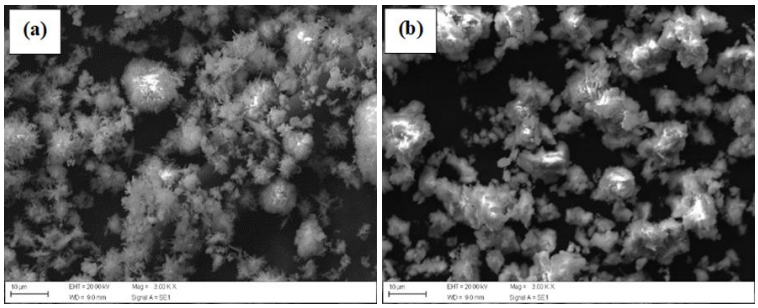
To confirm the obtainment of the β-TCP phase after the synthesis process, x-ray diffraction test was performed in a Panalitycal® X Pert PRO x-ray diffractometer with copper tube ($\lambda$ = 1,5418 Å) and scanning of 0.02º/s and $2\theta$ = 10º a 90º. To evaluate the powders granulometry and morphology after the deagglomeration processes, was used in a Carl Zeiss® Evo MA 15 scanning electron microscope in the secondary electron (SE) and energy dispersive x-ray (EDX) modes. The evaluation of the powders granu-lometry was made in a Microtrac® Turbotrac SDC laser granulometer.

## 3. Results and discussion

The Figure 1 shows with magnification of 3000 x the photomicrographs of the reagents used in the produc-tion of the β-TCP powder. In the Figure 1a, it is possible to observe that the calcium carbonate presents particles size with homogeneous distribution and presence of agglomerates less than 10 microns.

The Figure 1b shows that for calcium phosphate was observed particles size. Differently from Figure 1a, the Figure 1b shows particles with morphology predominantly irregular with variation of 10 to 2 microns. In both photomicrographs, were observed clusters, even after the application of deagglomeration methods.

**Figure 1**: Photomicrographs of the reagents used in the production of the β-TCP (a) Calcium carbonate (b) Calcium phosphate



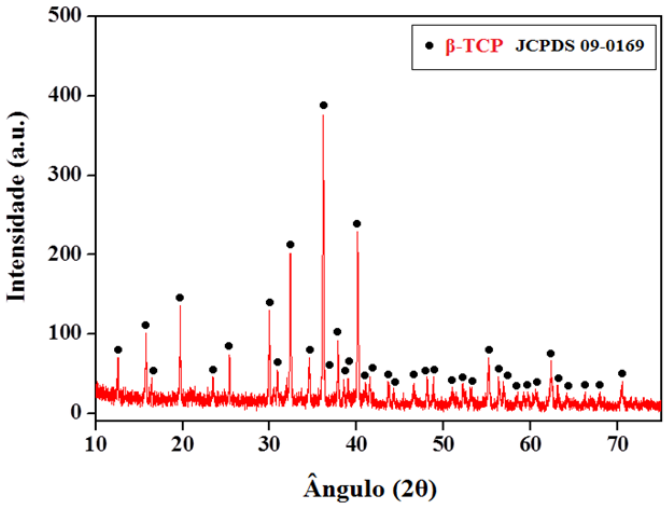

The Table 1 shows the results of particles size versus its volume for each reagent used to produce the β-TCP powder. As it can be seen, the calcium carbonate and the calcium phosphate presented its higher volume of particles in a range of 11.6 – 9.8 μm. Although the calcium carbonate presented particles with different size from the calcium phosphate, both presented practically 80% in volume of particles size locat-ed in the same range (11.6 – 9.8 μm), which is considered very important to obtain a final β-TCP powder with a homogeneous granulometry after sintering.

**Table 1**: Particles size versus percentage of the reagents used to produce the β-TCP

| **Reagent** | **Particle size (μm)** | | | |
|---|---|---|---|---|
| | **29.1** | **11.6 – 9.8** | **3.2 – 1.6** | **0.4** |
| Calcium carbonate | – | 78.8 % | 16.4 % | 4.8 % |
| Calcium phosphate | 21.1 % | 72.6 % | 6.3 % | – |

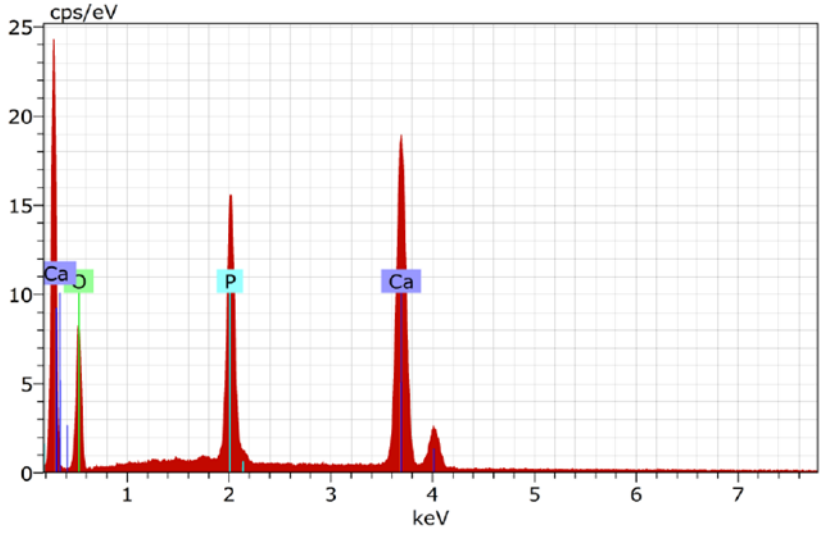
The Figure 2 shows the x-ray analysis of the β-TCP powder after its synthesis. It is possible to observe that, all of the piks were indexed as the β-TCP phase (JCPDS 09-0169). With this, is possible to confirm that after the sintering process, the calcium carbonate and calcium phosphate reagents have originated the desired phase, corresponding only to β-TCP phase.

**Figure 2:** Diffratogram of the β-TCP powder



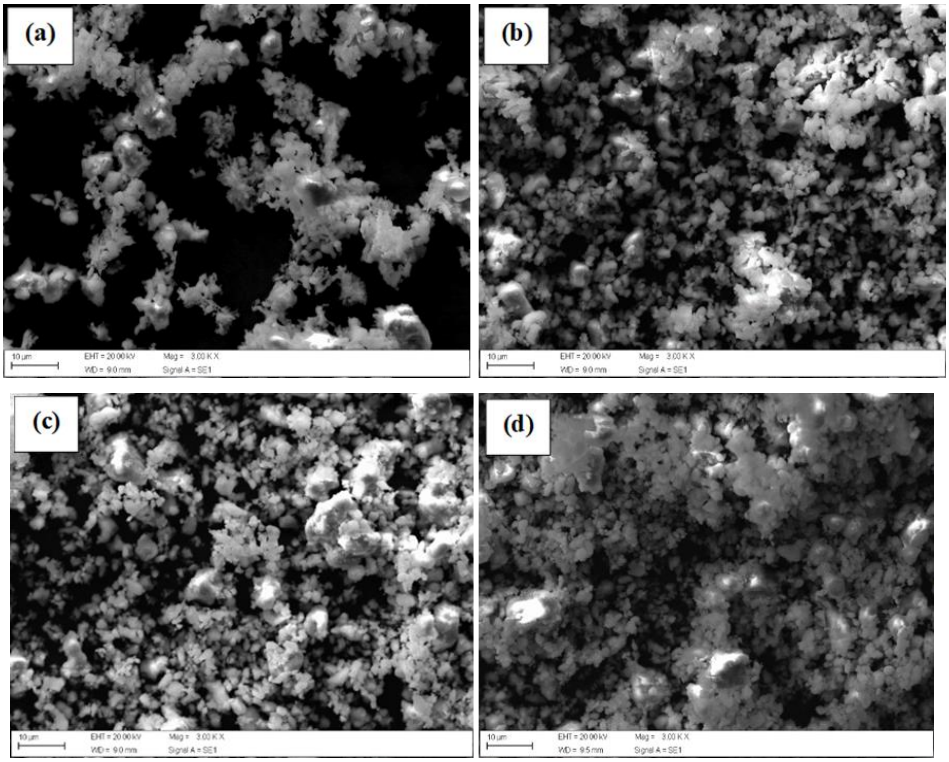

It is also proved through the Figure 3 that the powder analyzed originated the β-TCP phase. With the weight percent (wt.%) values obtained in the test (1.28 for Ca and 0.80 for P) it was possible to obtain a Ca P ratio of 1.60. This value is above 1.5 which is the ideal Ca/P ratio for Ca/P solubility for β-TCP. According to Wang et al. (2003)[19], the lower the values of this ratio, the greater the solubility and biodegradation of the biomaterial in physiological medium. This increase may affect the uptake of β-TCP in vivo, however, it does not compromise the mechanical and physical properties of β-TCP. It is observed in the EDX through pontual analysis the presence of the chemical elements Ca, P and O. These elements are present in the β-TCP phase. After confirming that the β-TCP phase was formed after the synthesis process, the analysis of the best deagglomeration method was performed. The Figure 4 shows with magnification of 3000 x the photomicrographs of the β-TCP powders deagglometared through high energy ball milling and agate mortar in different times.

**Figure 3:** EDS analysis via SEM of the β-TCP powder




As it can be seen in Figure 4a, the high energy ball milling process originated powders with particles size that vary in a range of 11,4□m – 1,8□m . In the Figures 4b, 4c e 4d it is observed that the process of deagglomeration in agate mortar through 10, 20 and 30 minutes it was possible to observe a decrease in particle size. For all of the deagglomeration methods observed in the Figure 4, the powders formed clusters. For the high energy ball milling process (Figure 4a), the presence of clusters was more pro-nounced than the deagglomeration in agate mortar. However, the time of 30 minutes (Figure 4d) demonstrated a higher presence of cluster than the times of 20 (Figure 4b) and 10 minutes (Figure 4a). Also, can be noted through the Figure 4, that the morphology of the particles was maintained as irregu-lar for all of the methods

**Figure 4:** Photomicrographs of the β-TCP powder milled through the process of (a) High energy ball milling (b) Agate mortar 10 min (c) Agate mortar 20 min (d) Agate mortar 30 min




The granulometry test confirms the size of the particles after the deagglomeration processes. As it can be seen in Table 2, the high energy ball milling was the process that produced particles with higher volume in a range of 10.3 – 11.4 μm. Although this is not considered the best result in terms of particles size among all of the methods described in this work, it presented better homogeneity, with almost 90% of particles with the same granulometry. Depending on the application of the β-TCP powder, it can be considered the best material, due this great homogeneity in the particles size. Analyzing the agate mortar methods, it is possible to verify that starting the process with 10 minutes and increasing to 20 and 30 minutes, the partices showed gradual reduction for the range of 10.3 – 11.4 μm to the range of 1.8 – 2.2 μm, being also noted the presence of nanoparticles (0.9 μm) starting from 30 minutes. Comparing with the Table 1, it is observed that the particles followed the size of the forerunner materials used to produce the β-TCP powder (calcium carbonate and calcium phosphate reagents).

**Table 2**: Particles size versus percentage of the β-TCP powders milled through different methods

| Method | Particle size (µm) | | |
|---|---|---|---|
| | **10.3 – 11.4** | **1.8 – 2.2** | **0.9** |
| High energy ball milling | 87.7 % | 12.3 % | – |
| Agate mortar 10 min | 62% | 38% | – |
| Agate mortar 20 min | 57.1 % | 42.9 % | – |
| Agate mortar 30 min | 45.2 % | 29.9 % | % |

## 4. Conclusions

The synthesis of the beta tricalcium phosphate (β-TCP) via solid state reaction, starting from its reagents calcium carbonate and calcium phosphate, was successful through the methods proposed and described in this work. The results obtained after the deagglomeration processes indicated that the morphology was predominantly irregular for both powders. The granulometry shows the deagglomeration performed through agate mortar showed to produce particles with smaller size and heterogeneous distribution, while the high energy ball milling process produced particles with larger size and higher homogeneity. Also, even though the high energy ball milling presented a better homogeneity in its particle size, it was the method that pre-sented the higher particles size. The agate mortar in all of its times was shown as more effective method to deagglomerate the β-TCP powder synthetized, being also the cheapest method.

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**Referências**

Bohner M. (2000). Calcium orthophosphates in medicine: from ceramics to calcium phosphate cements. Injury; 31, S-D37-S-D47.

Cardoso H. A. I.; Motisuke M.; Zavaglia C. A. C. (2012). Análise da influência de dois processos distintos de moagem nas propriedades do pó precursor e do cimento de beta-TCP. Cerâmica; 58, 225-228.

Dorozhkin S. V.; Epple M. (2002). Biological and medical significance of calcium phosphates. Angewandte Chemie International Edition; 41, 3130–3146.

Duncan J.; Macdonald J. F.; Hanna J. V. et al. (2014). The role of the chemical composi-tion of monetite on the synthesis and properties of -tricalcium phosphate. Mater. Sci. Eng. C: Mater. Biol. Appl.; 34, 123–129.

Farzadi A.; Solati-Hashjin M.; Bakshshi F. (2011). Synthesis and characterization of hydroxyapatite/-tricalcium phosphate nanocomposites using microwave irradiation. Ceram. Int.; 37, 65–71.

Hench L. L.; Polak J. M. (2002). Third-generation biomedical materials. Science, 29, 1014–7.
Hong Y.; Fan H.; Li B. et al. (2010). Fabrication, biological effects, and medical applica-tions of calcium phosphate nanoceramics. Mater Sci Eng R Rep;70, 225–42.

Lazar D. R. R. ; Cunha S. M. ; Ussui V. et al. (2006). Effect of calcination conditions on phase formation of calcium phosphates ceramics synthesized by homogeneous precipita-tion. Mater. Sci. Forum; 530–531, p.612-617.

Li X.; GUO B.; Xiao Y. et al. (2016). Influences of the steam sterilization on the proper-ties of calcium phosphate porous bioceramics. J Mater Sci Mater Med; 27, 5–14.

Nasiri- Tabrizi B.; Fahami A. (2013). Mechanochemical synthesis and structural characterization of nano-sized amorphous tricalcium phosphate. Ceram. Int.; 39, 8657–8666.

Parent M.; Baradari H.; Champion E. et al. (2017). Design of calcium phosphate ceramics for drug delivery applications in bone diseases: a review of the parameters affecting the loading and release of the therapeutic substance. Journal of Controlled Release; 252, 1–17.

Ruiz- Aguilar C.; Olivares- Pinto U.; Aguilar- Reyes E. et al. (2018). Characterization of - tricalcium phosphate powders synthesized by sol–gel and mechanosynthesis. Boletín de la Sociedad Española de Cerámica y Vidrio.

Sanosh K. P.; Chu M.; Balakrishnan A. et al. (2010). Sol–gel synthesis of pure nano sized - tricalcium phosphate crystalline powders. Curr. Appl. Phys.; 10, 68–71.

Tang Z.; Li X.; Tan Y. et al. (2018). The material and biological characteristics of oste-oinductive calcium phosphate ceramics. Regen Biomater.;5(1):43-59, Feb.

Thumer M. B.; Diehl C. E.; Dos Santos L. A. L. (2016). Calcium phosphate cements based on alpha-tricalcium phosphate obtained by wet method: synthesis and milling effects. Ceram. Int.; 42, 18094–18099.

Vallet- Regi M.; Gonzalez- Calbet J. M. (2004). Calcium phosphates as substitution of bone tissues. Prog. Solid State Chem.; 32, 1-3.

Wagoner-Johnson A. J.; Herschler B.A. (2011). A review of the mechanical behavior of CaPs and CaP/polymer composites for applications in bone repair and replacement. Acta Biomaterialia; 7:16–30.

Wang H.; Lee J. K.; Moursi A. et al. (2003). Ca/P ratio effects on the degradation of hy-droxyapatite in vitro. Journal of Biomedical Materials Research; 67 (A),. 599–608.

Wang J.; Chen Y.; Zhu X. et al. (2014). Effect of phase composition on protein adsorption and osteoinduction of porous calcium phosphate ceramics in mice. J Biomed Mater Res A; 102:4234–43.

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