Supplementary Materials

Comment [DN]: Correction 2-10-

Comment [DN]: Correction 2-12-
And Correction 2-15-

Simple and economic elaboration of high purity $CaCO_3$ particles for bone graft applications by spray pyrolysis technique

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1. Additional information on spray products

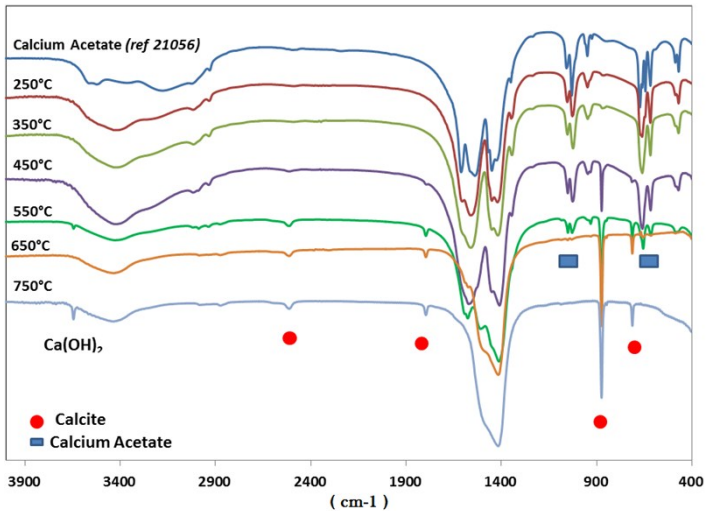

Figure S1- Infrared spectra obtained with calcium acetate and spray products synthetized from 250°C to 750°C.

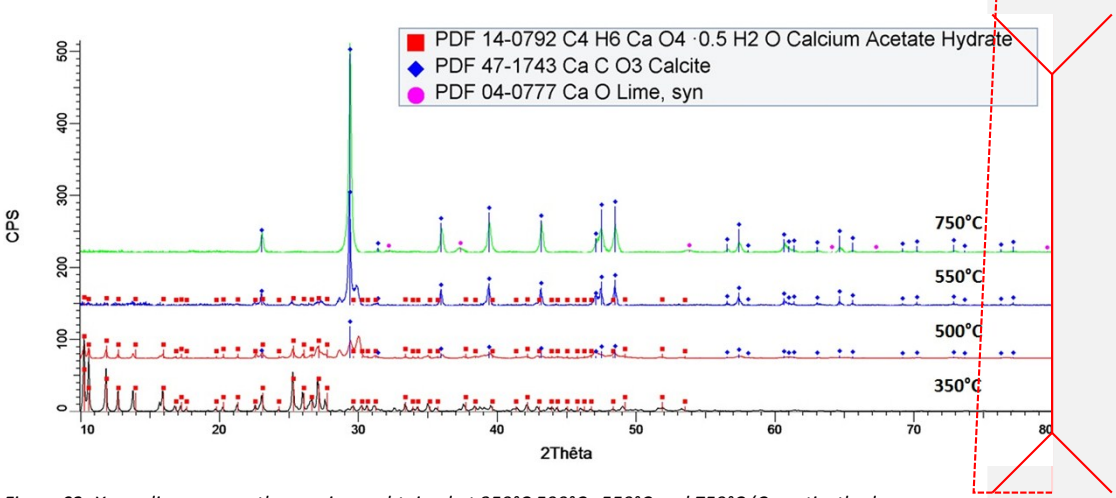

Figure S2- X-ray diagrams on the specimen obtained at 350°C,500°C, 550°C and 750°C (Cu anticathode ($\lambda_{K\alpha}$=1.54Å)).

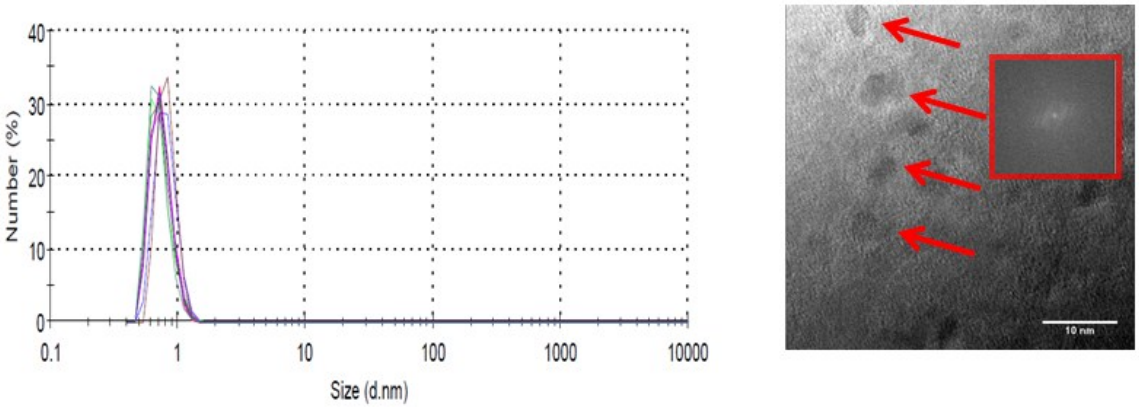

Figure S3 - At left side, DLS results obtained on water dispersed sample obtained after spraying at 350°C (using a Malvern ZetaSizer nano ZS device). At right side, the same sample observed by HRTEM (FEI Sactem Tecnai-F20 Cs at 200 kV), and the FFT corresponding to an observed particle, showing its low internal organization.

Absence or weak X-ray responses related to $CaCO_3$ presence obtained for samples synthetized at lower temperatures (before 500°C) is attributed to low particle size and to their low crystallinity.

Low particles sizes, are illustrated by the DLS results obtained with the 350°C sample in Figure S3. This measurement shows presence of nanometer sized carbonate particles, insoluble in the water suspension, while acetate rests were completely dissolved. The same suspension, deposed on a microscopy grid and dried permit to visualize carbonate particles, and the Fourier transform made on a particle, their low organization.

Results obtained for angles of reposes against synthesis temperature are illustrated in the Figure S4. It is possible to distinguished two steps:

- Between 300°C and 400°C, a little angle increase due to the loss of particles isotropy (sphericity), illustrated with the two SEM images, boxed in blue, for the products formed at 350°C and 400°C.
- The maintaining of angle of repose, on about 20°, observed between 500°C and 650°C, attributable to the permanence of the global morphological parameters of the $CaCO_3$ particles (size and form), due their internal skeleton remaining globally stable. Two SEM images, boxed in red, obtained for samples prepared at 500°C and 650°C illustrate these permanence.

The results obtained for 450°C sample could be considered as an intermediate point, containing rests of acetates, and the 750°C point appears higher due to lime content of the corresponding product.

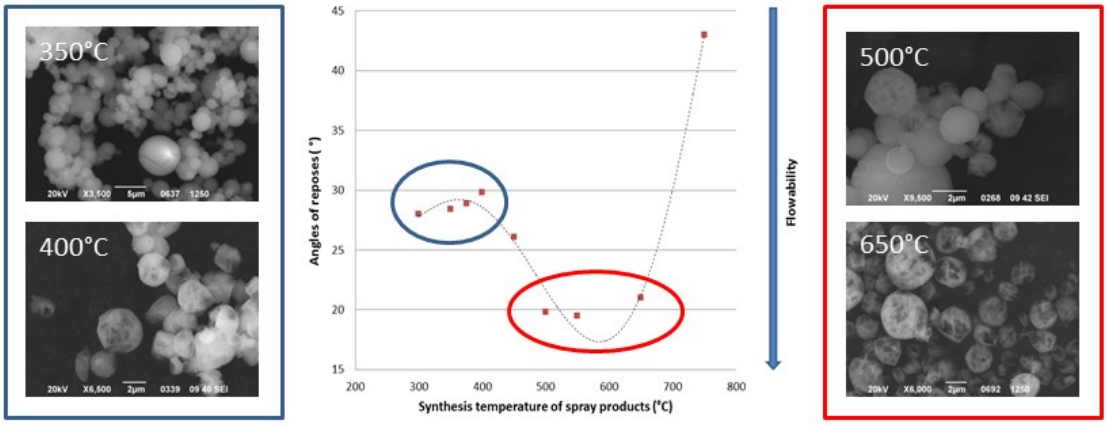

Figure S4 - Means of angles of reposes obtained on more than 5 measurements with each spray products. Results are expressed ± 4°. SEM-SEI images obtained for samples synthetized at 350°C, 400°C, 500°C and 650°C.

2. <u>Additional information on particles after annealing at 500°C</u>

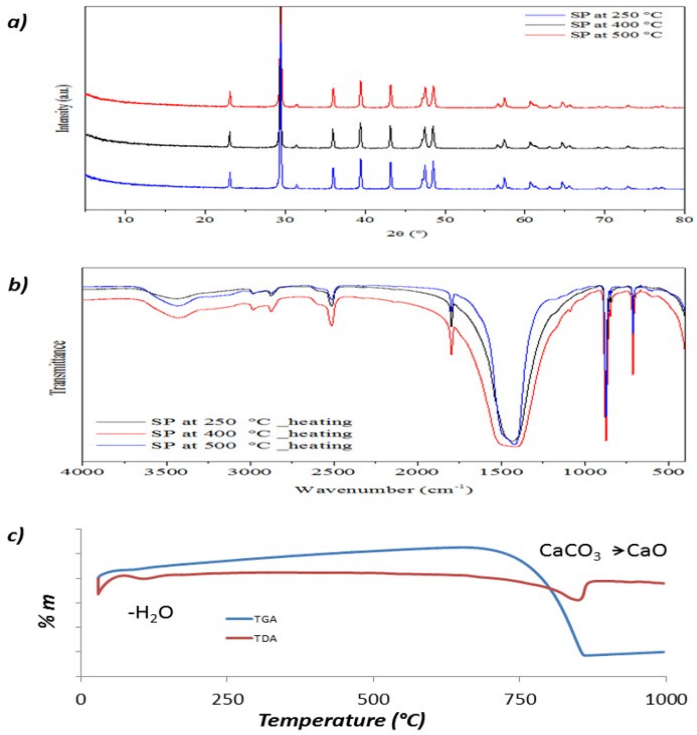

Figure S5 – a) p-XRD diagrams obtained with 250°C, 400°C and 500°C spray samples after annealing at 500°C during 5h. b) IRTF spectra obtained with same products. C) Example of TGA/DTA obtained for sample synthetized at 250°C and annealed at 500°C during 5 h.

XRD diagrams showed well crystalized calcite for all products after annealing (5h at 500°C), and infrared confirmed their high purity. The absence of any detectable signal in ATG and ATD, except those attributable to the water liberation and to the transformation of calcite into lime, confirms the very high purity of the product obtained after annealing.

3. Additional information on obtained pellets formed from spray particles sintering

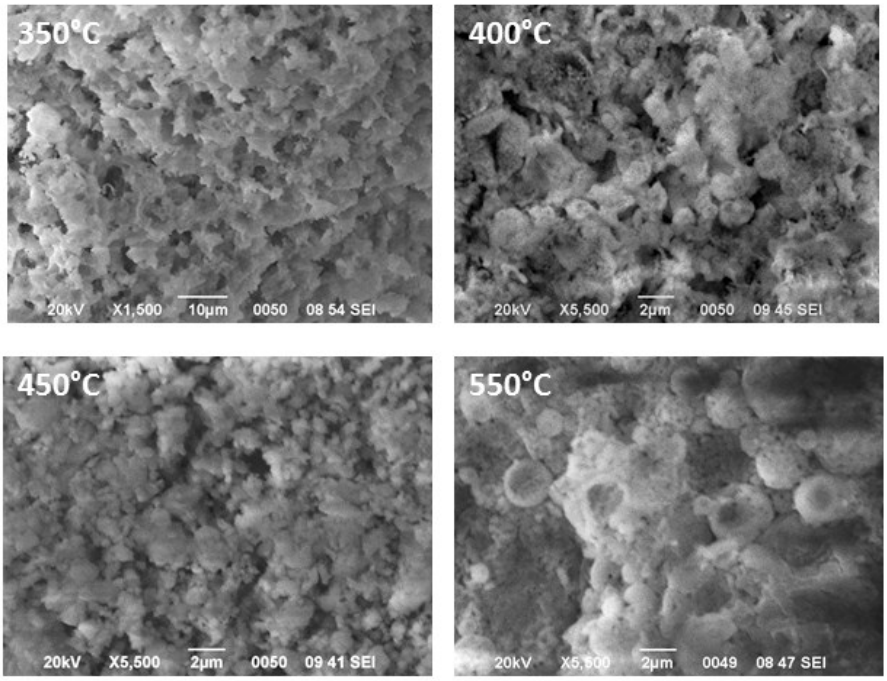

Figure S6 – SEM SEI Photography on tablets formed from spray products obtained for different synthesis temperatures.

Sample obtained from 350°C spray product appears as coral-like 3D arrangement of calcite plates. Then, the presence of spheres in the obtained pellets is more and more blatant whereas the spray temperature increases. At first mixed with plates, the spheres present settle gradually. The pellet obtained from 550°C spray sample appears with a smoothie aspect due to an arrangement of what could appear as spherical crystallites.

4. Principle of anchoring of the particles inside composite matrix

Anchoring of particles inside composite matrix corresponds to the insertion of a part of this matrix inside particles skeleton, in contact with the calcite surfaces. Contrary to smooth particles, for which an applied tensile force leads to the well-known detachment of the matrix from the particles surfaces, this insertion and the better contacting between matrix and particles surfaces would increase the mechanical properties of obtained composites. This principle was illustrated in the following Figure S7.

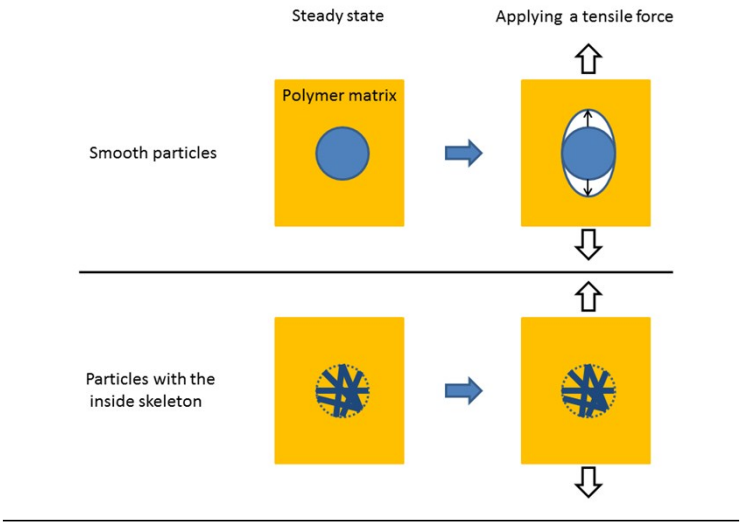

Figure S7 – Principle scheme showing the difference between anchored particles and smooth particles under mechanical stress.

5. Relationship between our properties and bone graft materials.

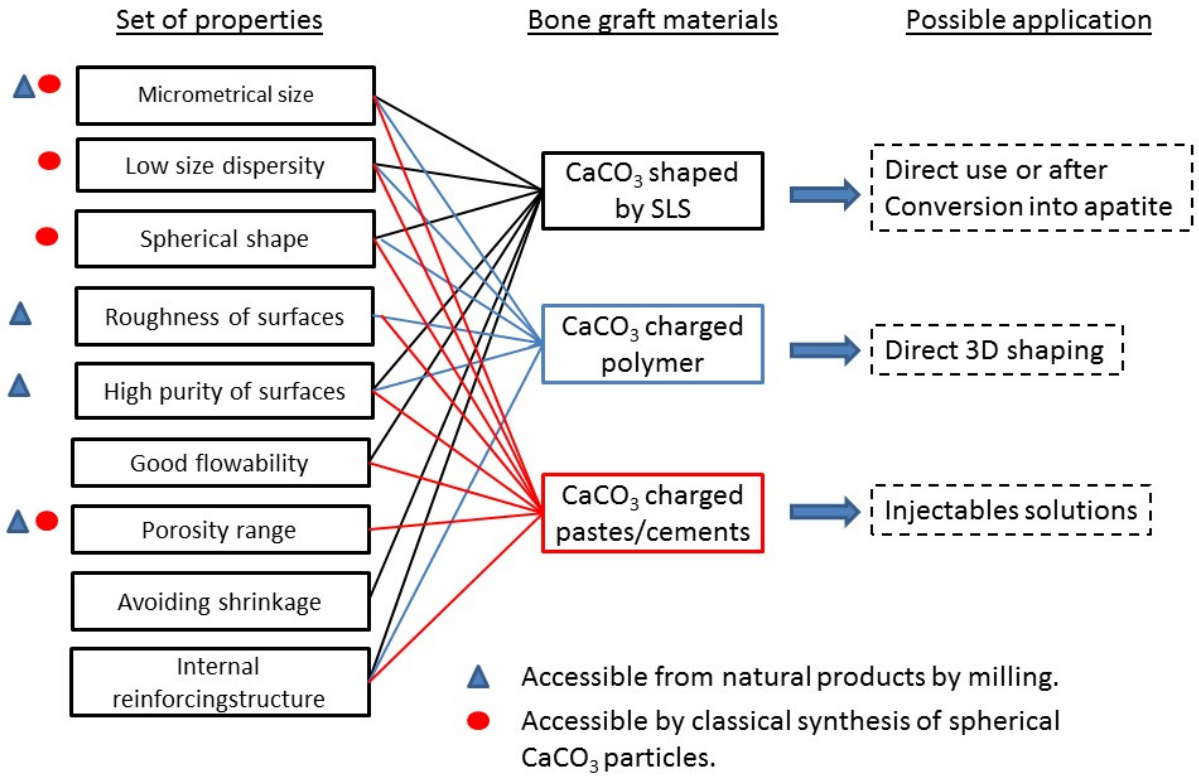

Figure S8 – Principle scheme linking the different important properties of the obtained set with our particles to different bone graft materials. On this scheme were added properties accessible with more classical approaches (of natural and synthetic origin, respectively Blue triangles and red circles).

Classically, commercial calcium carbonate can be of natural origin or synthetized.

In the first cases, this material is generally obtained from limestone, coral or eggshells. Not to mention their necessary purification and the corresponding problematics, powder could be obtained from these natural materials by crushing raw materials. However, such an approach cannot lead to a controlled morphology with a spherical shape and a low dispersity. The needed set of parameters cannot be reached by this way.

In the second case, as described in this article, the preparation of spherical particles, with low dispersity, is possible by precipitation. This way requires the adjunction of a surfactant which remains on the surface of the synthetized particles, even if their purity is high (>99.99%). Besides, these approaches give smooth particles and their anchoring into composite materials is well-known as insufficient (*see Figure S7*). Accordingly, this approach does not lead either to our objectives.

The previous figure S8 shows relationship between properties obtained with our particles and these required or giving a benefit of our products to form many bone graft materials.

We indicate on the same figure the properties accessible with particles obtained from classical ways. It appears clearly that the complete set was not reached by these ways. Consequently, these one cannot lead to a multipurpose material.

To finish, on the same figure we indicate, as a perspective, some possible applications for bone grafting.