

Preparation and characterization of chitosan-calcium phosphate composite powders: effects of spray drying strategies.

Sylvain LE GRILL^(1,2), Fabien BROUILLET⁽¹⁾, Cédric CHARVILLAT⁽²⁾ Ghislaine BERTRAND⁽²⁾, Christian REY⁽²⁾

CIRIMAT, Université de Toulouse, CNRS, INPT, UPS, ¹ ENSIACET, BP 44362, 31030
²Faculté de Pharmacie, 35 chemin des Maraichers, 31062 Toulouse, France

Bone is a complex multi-scale bio-composite mainly made of organic type I collagen and inorganic poorly crystalized apatite. These compounds are strongly linked at a submicronic scale¹ and this interaction plays a major role in the bio mechanical behavior of the bone. New hybrid materials mimicking the bone composition are therefore the next challenge. Shaping the hybrid material as a powder is interesting as it allows many potential uses such as coating material, cement precursor, bone defects filling material or as drug carriers^{2,3}. Techniques like W/O emulsion or sol-gel process have been currently proposed in literature to prepare this type of micron-sized composite powders. Spray drying is an alternative and direct method which has yet to be truly explored. This versatile process, widely used in the pharmaceutical and biomedical fields has many advantages, for example, a continuous production, a temperature range allowing the use of temperature-sensitive products and the opportunity to work with very dilute or highly concentrated media.

In this study calcium phosphates (CaP) with a Ca/P ratio of 1.67 and Chitosan (CTS), a natural polysaccharide bio-polymer exhibiting an ability to promote recruitment and differentiation of osteo-progenitors⁴, were used. The CTS/CaP bio-composite powders were prepared by spray drying implementing two different strategies:

(i) a suspension of stoichiometric hydroxyapatite (HAp) in an acidic solution of CTS. This approach results in a rather heterogeneous mixture of the two phases, clearly identified by BSE-SEM. According to XRD, HAp was not modified during the drying process. However, due to the acidic medium the outer part of the HAp particles was probably dissolved and may reprecipitate in another phase.

(ii) a solution containing both solubilized CaP precursors and CTS. On SEM observations the CaP particles were not distinguished from the CTS ones. Therefore, an intimate and homogeneous mixture of the organic and inorganic phases could be assumed. During the drying stage the solution precipitates into a CTS/amorphous calcium phosphate (ACP) according to FTIR analysis. This CTS/ACP composite further evolves in an aqueous medium into a CTS/poorly crystalized apatite, which is expected to be bio-mimetic.

Both strategies result in composite powders with grain size ranging from 1 to 10 μm available for further shaping processes. The properties of the spray-dried powders can be tuned from a poor to a high resorbability for long-term application or immediate osteointegration, respectively.

1. Weiner, S. & Wagner, H. D. *Annu. Rev. Mater. Sci.* **28**, 271–298 (1998).
2. Wen, C. Y., Qin, L., Lee, K. M. & Chan, K. M. *J. Biomed. Mater. Res. - Part B Appl. Biomater.* **89**, 466–474 (2009).
3. Cai, Y. & Tang, R. *J. Mater. Chem.* **18**, 3775 (2008).

4. Muzzarelli, R. A. A. *Carbohydr. Polym.* **76**, 167–182 (2009).