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Comment on "Self-Hardening Microspheres of Calcium Phosphate Cement with Collagen for Drug Delivery and Tissue Engineering in Bone Repair"

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Recently, Park *et al.*[1] described the addition of calcium phosphate into a stirred olive oil bath to produce microspheres of the same. Although the novelty of this communication is not questionable in using a paste-like mixture of α-TCP powders with collagen-containing Na_2HPO_4 setting solution, the process of obtaining microspheres, has been described previously. The process that involves introducing calcium phosphate, especially in combination with collagen, into a stirred olive oil bath was previously described by Hsu *et al.*[2] at 200, 350, 500, and 650 rpm and described by Sun *et al.*[3] at 400 rpm. It must also be noted that Park *et al.*[1] only reported a constant stirring rate of the oil bath at 380 rpm, which was quite comparable to the stirring rates used in the above-mentioned previous studies.

It is known that the stirring rate of the vegetable oils, into which the calcium phosphates were dropped, strongly influences the average size and size distribution of the microspheres to be obtained.[3] The spheres of the present communication[1] were similar in diameter (Fig. 1(a)) to those reported by Hsu *et al.*[2] and Sun *et al.*[3] The work of Hsu *et al.*[2] tested the hydroxyapatite-collagen microspheres produced in a stirred olive oil bath with osteoblasts in vitro, whereas the study of Sun *et al.*[3] tested the hydroxyapatite-tricalcium phosphate-collagen microspheres (produced in an olive oil bath) *in vivo* by using a New Zealand rabbit model over a period of 5–15 weeks.

Within minutes following the mixing of α-TCP powders with a setting solution of 3.5%–5% Na_2HPO_4 (having a pH value in the vicinity of 9– 9.2), the powder particles of the formed paste would start undergoing a hydraulic cement reaction and partially transform (within hours) into Ca-deficient apatite.[4] Therefore, even though the starting material used by Park *et al.*[1] was single-phase α-TCP, once the microspheres were obtained they would no longer be pure α-TCP. The α-TCP particles would be covered with apatitic nanocrystals on their surfaces even in dry conditions, and these nanocrystals were helping to improve the cohesive properties and strength of such microspheres. The authors should also have labeled the peaks of the apatite phase visible in the XRD data of Fig. 2(b), specifically in the trace with the legend "before." The phase assemblage of the microspheres in the study by Park *et al.*[1] resemble those prepared by Sun *et al.*[3]

The SBF soaking process apparently benefited from the presence of small amounts of apatite in the microspheres together with α-TCP and that minor phase of apatite could have readily acted as the seed to accelerate the nucleation and growth of those nanocrystals (shown in Fig. 2(a)) in the specific SBF solution used.

It would have been preferable for the journal readers if Park *et al.*[1] had cited the above-mentioned references on using olive oil,[2,3] or vegetable oil[5] to produce calcium phosphate microspheres and then provided a comparative discussion based on their results and those of the others which included *in vitro*[2] and *in vivo*[3] data on such similar microspheres.

References

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