



## INTRODUCTION

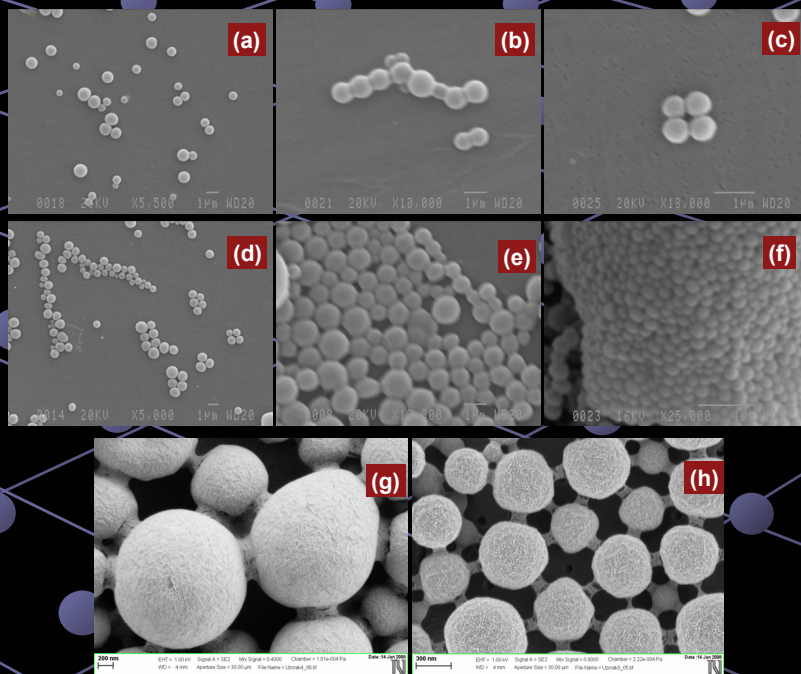
"Self-assembly" has been paid much attention as the next generation micro-/ nano- fabrication process.[1] From a tissue engineering standpoint, self-assembly could be used to engineer different types of surface topography on the nano- and micro-scale. They can influence cell adhesion, migration, function, and tissue integration. It can establish a controlled local microenvironment (protein and other macromolecular patterning) via surface functionalization of biomaterials to generate micro- and nanoscale mechanical stresses affecting cell-biomaterials interactions, and to position cells precisely on scaffold surface in order to control cell interactions.[2] Self-assembly can be used to produce a variety of structures, such as films, bilayer, membranes, nanoparticles, fibers, micelles, capsule, tubes, coils, mesophases, or unilamellar and multilamellar vesicles [3]. These structures can further self-organize into superstructures, such as lamellar, hexagonal, and cubic structures. However, these structures are not very stable, due to noncovalent interactions, such as hydrogen bonds, ionic bonds, hydrophobic interactions, and van der Waals interactions among the assembled molecules.[4]

The aim of this work was to give an explanation for the formation of stable planar spatial organization of PLGA/HAp biocomposite spheres, to analyze their stability and to show influence of poly(vinyl-pyrrolidone) with different average molecular mass on its shape and size.

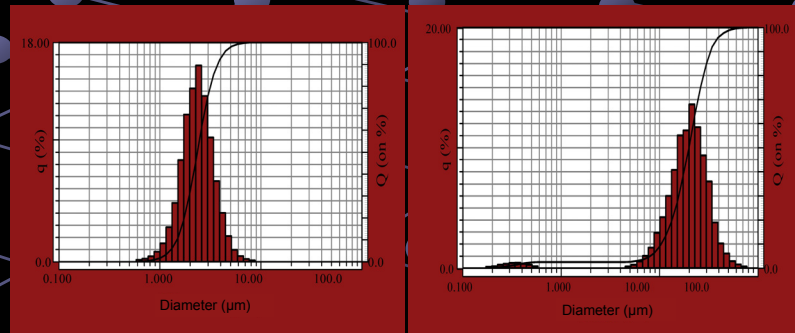
## RESULTS and DISCUSSION

During the process of self-assembly of particles, several stages in their organization, very important for the formation of the final morphology of the material can be observed. The formation of PLGA/HAp composite material in the field of ultrasound is marked by self-assembly of its sphere-like particles which make the final morphology of this material. Figure 1 represents various stages of organization of PLGA/HAp spheres obtained after the ultrasonic processing. The presence of individual particles, linear, tetragonal, pentagonal structures and germs of the final plate-like arrangement of PLGA/HAp sphere-like particles in Figs. 1a, 1b, 1c and 1d, respectively, enables us to grasp the mechanism of the formation of the final plate-like spatial organization of spheres represented in Fig. 1e. It is well-known that ultrasonic field induces collision of solid particles driven by shock wave formed after the bubble collapse in the cavitation process.[8] In the moment of the impact of these sphere-like particles induced by ultrasonic field they remain connected due to the increase in the plasticity of the surface, polymeric part, of the PLGA/HAp spheres.

Figs. 1e and 1f represent planar spatial organization of PLGA/HAp sphere-like particles stabilized with PVP with (e) higher (650 kDa) and (f) lower (25 kDa) average molecular masses. Having in mind that particles stabilized with PVP with lower average molecular mass are smaller and more uniform in size, planar spatial organization represented in Fig. 1f is more regular than those stabilized with PVP with higher average molecular mass represented in Fig. 1e. Physical nature of connections between sphere-like particles can be clearly observed in Figs. 1g and 1h. Figure 2 represents particle size distributions of samples stabilized by PVP with (a) higher and (b) lower average molecular mass. These distributions show significantly larger particle sizes than those measured according to SEM micrographs. These larger sizes correspond to connected sphere-like particles, which indicate the stability of their connections within self assembly planar spatial organization.



**Figure 1:** PLGA/HAp sphere-like particles: (a) individual, (b) linear, (c) tetragonal (d) pentagonal and part of the planar spatial arrangement of spheres. Morphology of composite spheres stabilized by PVP with (e) higher (650 kDa) and (f) lower (25 kDa) average molecular mass. Physical connections between sphere-like particles in PLGA/HAp composite with polymeric-to-ceramic part 75:25 (g) and 90:10 (h) stabilized by PVP with lower average molecular mass.



**FIGURE 2:** Particle size distributions of PLGA/HAp composite stabilized by PVP with: (a) higher (650 kDa) and (b) lower (25 kDa) average molecular mass.

**TABLE 1:** Statistical values of particles size distribution of PLGA/HAp composite stabilized by PVP with different average molecular mass

Sample	PLGA/HAp ( $M_w$ (PVP)=650 kDa)	PLGA/HAp ( $M_w$ (PVP)=25 kDa)
Median diameter on:		
10 %	1.4738	10.3653
20 %	1.7448	13.3742
30 %	1.9522	15.6323
40 %	2.1523	17.6715
60 %	2.5630	21.9334
70 %	2.8246	24.5414
80 %	3.1705	27.9361
90 %	3.7424	33.0428
Mean diameter	2.5090	20.9552

## MATERIALS and METHODS

The formation of poly(d,l-lactide-co-glycolide)/hydroxyapatite (PLGA/HAp) composite material was performed in the following way: HAp was synthesized by homogeneous precipitation method with urea as homogeneous precipitation agent [5], [6]; the obtained apatite crystals were deagglomerated by high-intensity ultrasonic field in a small volume of ethanol as inert medium and coated with PLGA by the use of ultrasonic field [7]. The as-obtained dispersion was stabilized by water solution of poly(vinyl-pyrrolidone) (PVP) with different molecular masses (25 and 650 kDa). After the stabilization, some parts of dispersions were separated and filtered on polycarbonate membranes for SEM and granulometric analyses.

## CONCLUSIONS

In this work, the formation of plate-like spatial organization of sphere-like PLGA/HAp particles was analyzed. Results indicated the formation of linear, tetragonal and pentagonal interparticle connections as lower levels of organization important for the final self-assembly planar plate-like morphology. These organized structures obtained in the field of ultrasound were more regular when PLGA/HAp composite was stabilized with PVP with lower average molecular mass due to smaller and more uniform sphere-like particles. Particles were physically connected and it was the main reason of their stability.

## REFERENCES

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