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(54) Title: METHOD FOR THE PREPARATION OF MICROMETRIC OR NANOMETRIC HOLLOW PARTICLES

(57) Abstract: A method for the preparation of hollow polymeric micrometric or nanometric particles comprising, in sequence, a solubilization step, where a gas or a vapor is solubilized as the blowing agent in thermoplastic polymer bulk particles and a foaming step in order to produce one or more bubbles in said particles. The method comprises an embedding step, at least before the foaming step, where said bulk particles are embedded in a single and continuous barrier film made of a water-soluble polymer and, after the foaming step, a solubilization step where said barrier film polymer is washed out.



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METHOD FOR THE PREPARATION OF MICROMETRIC OR NANOMETRIC HOLLOW PARTICLES

5 FIELD OF THE INVENTION

The present invention relates to a method for the preparation of micrometric or nanometric hollow particles.

BACKGROUND OF THE INVENTION

10 Hollow particles of micrometric or nanometric dimension have attracted industrial attention in recent years for their numerous applications. In effect, these particles can be used as carriers for encapsulation of drugs, enzymes, proteins and genes, as contrast agents in diagnostics, as
15 reactors in chemistry and chemical engineering, as transducers and dielectrics in electronics and as absorbent systems of sound ultrasound and microwaves.

The methods known from the prior art for the preparation of hollow polymeric micro- and nano-particles include:
20 emulsion polymerization, suspension polymerization, core-shell precursors, self-assembly, spraying, electro-spraying and template-directed synthesis. Each of these methods is rather complex, mainly in the fine chemical synthesis, and is limited in terms of particle dimensions and nature of
25 utilizable materials, not being sufficiently versatile to cover all of the different, very specific, application needs. Furthermore, notably, current methods do not easily achieve non-spherical particles, which has been reported to be a critical need, for instance in drug delivery, to
30 enhance the specificity of delivery and in chemistry, to enhance the specificity of catalysis. In effect, each of these methods is able to produce particles in a narrow range of dimensions, with a limited nature of materials and

with spherical shape.

There is, hence, an increased need for a simple method that allows the production of hollow particles from a wide range of particle dimensions, from a wide range of polymers and
5 characterized by non-spherical shapes.

DISCLOSURE OF INVENTION

Therefore, it is an object of the present invention to provide a method for the preparation of hollow micrometric
10 or nanometric particles of a large variety of materials, dimensions, shapes and hollow attributes, as described in CLAIM 1 and in the preferred and/or auxiliary CLAIMS 2 to 9.

Further objects of the present invention are the
15 micrometric or nanometric hollow particles obtained with the method of the present invention.

In the following, examples on how to produce those particles are reported, provided that these are not restrictive as to the generality of the approach.

20

BRIEF DESCRIPTION OF THE DRAWINGS

In Figure 1 four SEM images at variable magnification of hollow particles with diameters of 50 μm , 5 μm , 500 nm and 200 nm produced by the method of the present invention are
25 reported.

In Figure 2, low-magnification SEM images of hollow particles of different dimensions and high-magnification SEM images of hollow particles characterized by both "open" and "closed" hollow are reported.

30 In Figure 3, a high-magnification SEM image of ellipsoidal hollow particles obtained by deformation of the barrier film embedding the particles and by foaming is reported.

BEST MODE FOR CARRYING OUT THE INVENTION

EXAMPLES

The method of the present invention was applied to
5 polystyrene (PS) particles of diameters of 50 μm , 5 μm , 500
nm and 200 nm. The procedure reported below was applied,
separately, for the different particles.

0.1% (wt/vol) of PS spherical particles (50-5-0.5-0.2 μm in
diameter) were dispersed in aqueous solutions of 5%
10 (wt/vol) poly(vinyl alcohol) (PVA) and 2% (wt/vol) of
glycerol. The obtained mixtures were carefully poured in
Teflon molds with flat surfaces and left to dry at room
temperature for 72h. As a result of the drying, a solid
single and continuous PVA film embedding the total amount
15 of PS particles is obtained.

The film embedding the particles is then subjected to a
foaming process, as follows. For the production of foamed
samples, a pressure vessel, having a volume of 0.3 L,
(model BC-1, HiP Erie, US-PA) was used. The pressure
20 discharge system consists of a discharge valve, an
electromechanical actuator and an electro-valve.

The samples (barrier film-embedded PS spheres) were loaded
into the vessel, pressurized with a mixture of N_2 and CO_2
as the blowing agent at 14.0 MPa and 100°C for two hours
25 and then pressure quenched at 100 MPa/s (foaming process).
PS Particles were then recovered by dissolving the PVA film
in water at room temperature and washed centrifuging with
water five times.

Particle morphology was observed by SEM, TEM, Dual Beam
30 SEM/FIB and STED, showing that particles foamed when
embedded in the PVA film presented hollows with
morphologies depending on the different experimental
conditions, as reported in Figure 1 and 2. In particular,

particles foamed when embedded in the PVA film have a slightly larger diameter with respect to unfoamed particles, as a consequence of the formation of the hollow. Those of 5, 0.5 and 0.2 μm have open hollows and are
5 characterized by a bowl shape.

Bare polystyrene spheres (without being embedded in the barrier film - poured on lab paper) were also analyzed and subjected to the foaming process for proper comparison. Bare particles did not present any morphological
10 modification after being subjected to the foaming process reported above, not presenting any hollow.

Authors of the present invention verified that, by modifying the blowing agent composition and other foaming process parameters such as pressure and temperature, it is
15 possible to prepare particles with open or closed hollows, that is particles with a cavity that communicates with the external environment or not, respectively. It is possible, furthermore, by tuning the processing conditions, to modulate the hollow dimension, the hollow number within a
20 single particle, and the eccentricity of the hollow with respect to the center of the particle.

Figure 2 reports SEM images of particles characterized by open hollow and particles characterized by closed hollow obtained by means of the present invention.

25 Furthermore, it has been verified that, by modulating the properties of the barrier film material and/or manipulating the barrier film itself, it is possible to modify the shape of the hollow particles.

For instance, Figure 3 shows an SEM image of kayak-shaped
30 hollow nanometric particles, where the elongated shape was obtained by mechanical stretching at elevated temperature of the particles-embedded barrier film, followed by foaming.

In effect, the method of the present invention allows modifying the shape of the particles by inducing a deformation or a stress on the barrier film. This chance is offered by the presence of the barrier film completely embedding the total amount of particles, conferring to the method of the present invention a very large versatility.

Hollow particles can be obtained from any thermoplastic polymer (other than PS, reported in the example) and the barrier film could be made of a material different from PVA, standing it has the capability of allowing particle deformation/expansion and of keeping the blowing agent concentration in the particle sufficiently high (barrier effect) to induce the hollow formation, after the pressure release during the foaming process.

In the example provided, the blowing agent is solubilized into the particles after they have been embedded in the barrier film. Alternatively, it is also possible to embed blowing agent-laden particles in the barrier film (the blowing agent is solubilized in the particles before the particles are embedded in the barrier film). Furthermore, foaming can be conducted not only by releasing the pressure, but also by increasing the temperature of the blowing agent-laden particles at the glassy state. In other words, the foaming process can be conducted with techniques different from the pressure release technique described in the example.

As it may result evident, the key point of the present invention is embedding the total amount of thermoplastic polymer particles in a single, continuous barrier film, which, during expansion, avoids blowing agent escape from the particles and manages to keep the blowing agent concentration within the particles sufficiently high to allow the hollow formation within the particles.

Furthermore, the barrier film has to allow the particle deformation during foaming.

As it has been reported in the provided example, in case no barrier film is used (bare particles), during the foaming process the blowing agent evolution towards the outside of the particles (blowing agent loss) is so fast that there is no chance for the bubble to nucleate and grow to form the hollow.

The method described in the present invention has the great advantage to produce hollow particles without making use of complex techniques like fine chemical synthesis and, at the same time, may be used on particles without dimensional constraints and made of different polymers.

Furthermore, by means of the present invention, it is possible, by modifying the blowing agent composition, the barrier film composition and by manipulating the barrier film itself, to achieve hollow particles of several shapes, with one or more hollows per particle, with hollows of several shapes, of different open/closed feature and eccentricity with respect to the particle center.

CLAIMS

1. A method for the preparation of hollow particles of a thermoplastic polymer, with micrometric or nanometric dimensions, and comprising, one after the other, a solubilization step for the solubilization of a gas or a vapor acting as the blowing agent into thermoplastic polymeric bulk particles with micrometric or nanometric dimensions, and a foaming step for the expansion of the blowing agent in order to produce one or more bubbles inside said particles; said method being characterized by comprising, at least before said foaming step, an embedding step to include said bulk particles in a single and continuous polymeric barrier film and, after the foaming step, a washing step where the polymeric barrier film is washed out in a proper solvent; said embedding step including:
- a mixing operation, in which the thermoplastic polymer bulk particles and a barrier polymer are dispersed in a proper solvent wherein the polymer of said polymeric barrier film is soluble and at a concentration such that the polymer of said polymeric barrier film is at least five times higher than that of the thermoplastic polymer bulk particles, and
 - a drying operation, wherein the solution coming from the mixing operation is dried obtaining a single and continuous polymeric barrier film embedding the total amount of thermoplastic polymer bulk particles;
 - said polymeric barrier film being made of a polymer that allows, during the foaming step, the particles to dilate and the blowing agent concentration within the particles to be kept sufficiently high to induce bubble nucleation and growth; said polymeric barrier film being made of a polymer

which is soluble in solvents wherein the thermoplastic polymer bulk particles are not soluble.

2. A method for the preparation of hollow particles according to claim 1, characterized in that said polymeric
5 barrier film is made of a water-soluble polymer and in that, in said mixing operation, the solvent is water.

3. A method for the preparation of hollow particles according to claim 2, characterized in that said barrier polymer film is made of poly(vinyl alcohol).

10 4. A method for the preparation of hollow particles according to any of the previous claims, characterized in that in said mixing step the barrier film polymer quantity is at least ten times higher than that of the thermoplastic polymer bulk particles.

15 5. A method for the preparation of hollow particles according to any of the previous claims, characterized in that said embedding step precedes said solubilization step, which is conducted via a high-pressure treatment with the blowing agent gas or vapor.

20 6. A method for the preparation of hollow particles according to any of the previous claims, characterized in that said foaming step is performed via a blowing agent pressure release.

25 7. A method for the preparation of hollow particles according to any of the previous claims, characterized in that said blowing agent is nitrogen, carbon dioxide or their mixture.

8. A method for the preparation of hollow particles according to any of the previous claims, characterized in
30 that said thermoplastic polymer bulk particles are made of polystyrene.

9. A method for the preparation of hollow particles according to any of the previous claims, characterized in

that it comprises a deformation and/or stress transfer step of the polymeric barrier film in order to achieve a deformation of said particles to obtain non-spherical particles and/or hollows.

- 5 10. Hollow polymeric micrometric or nanometric particles prepared with the method described according to any of the previous claims.

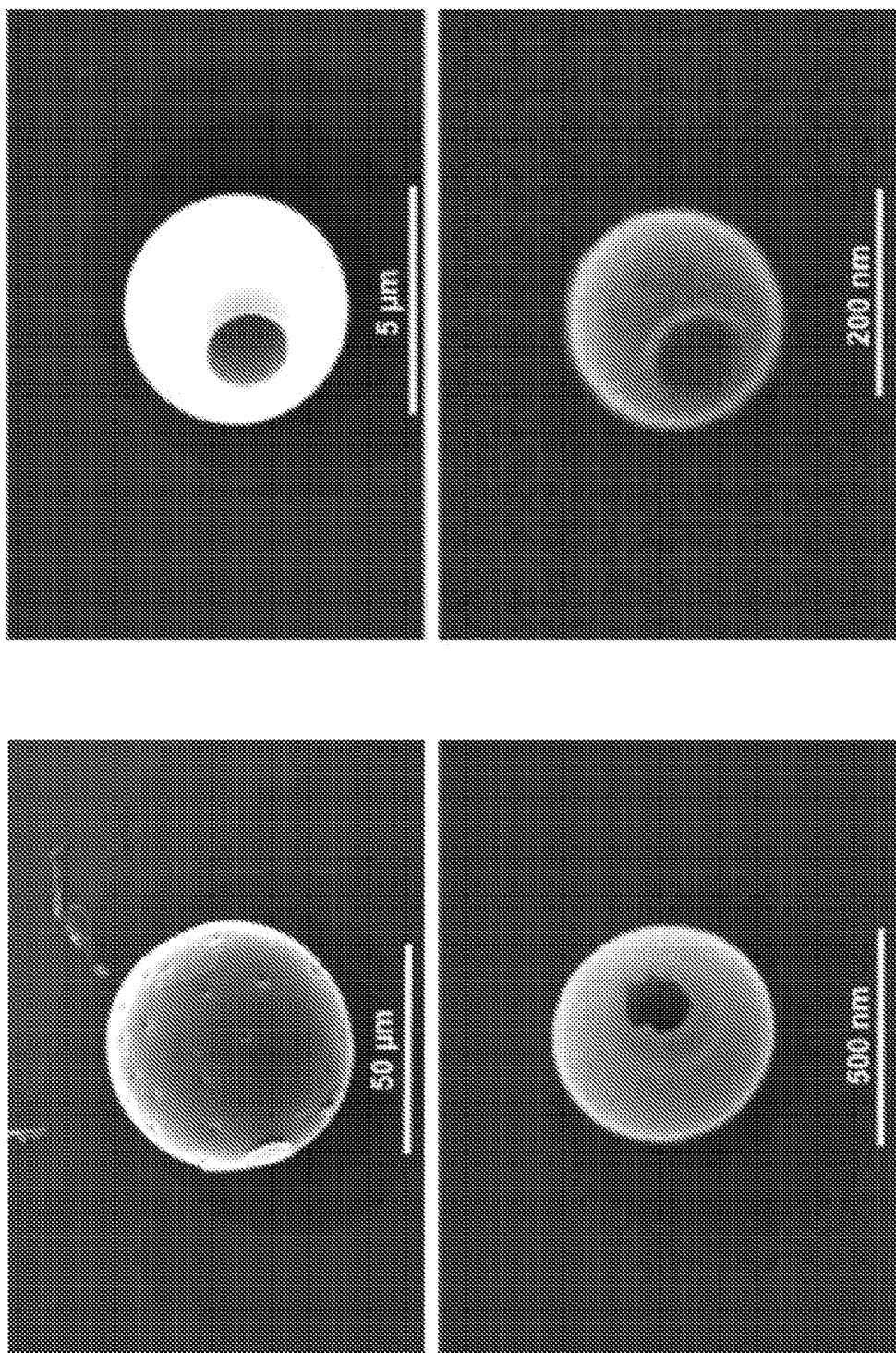


FIG.1

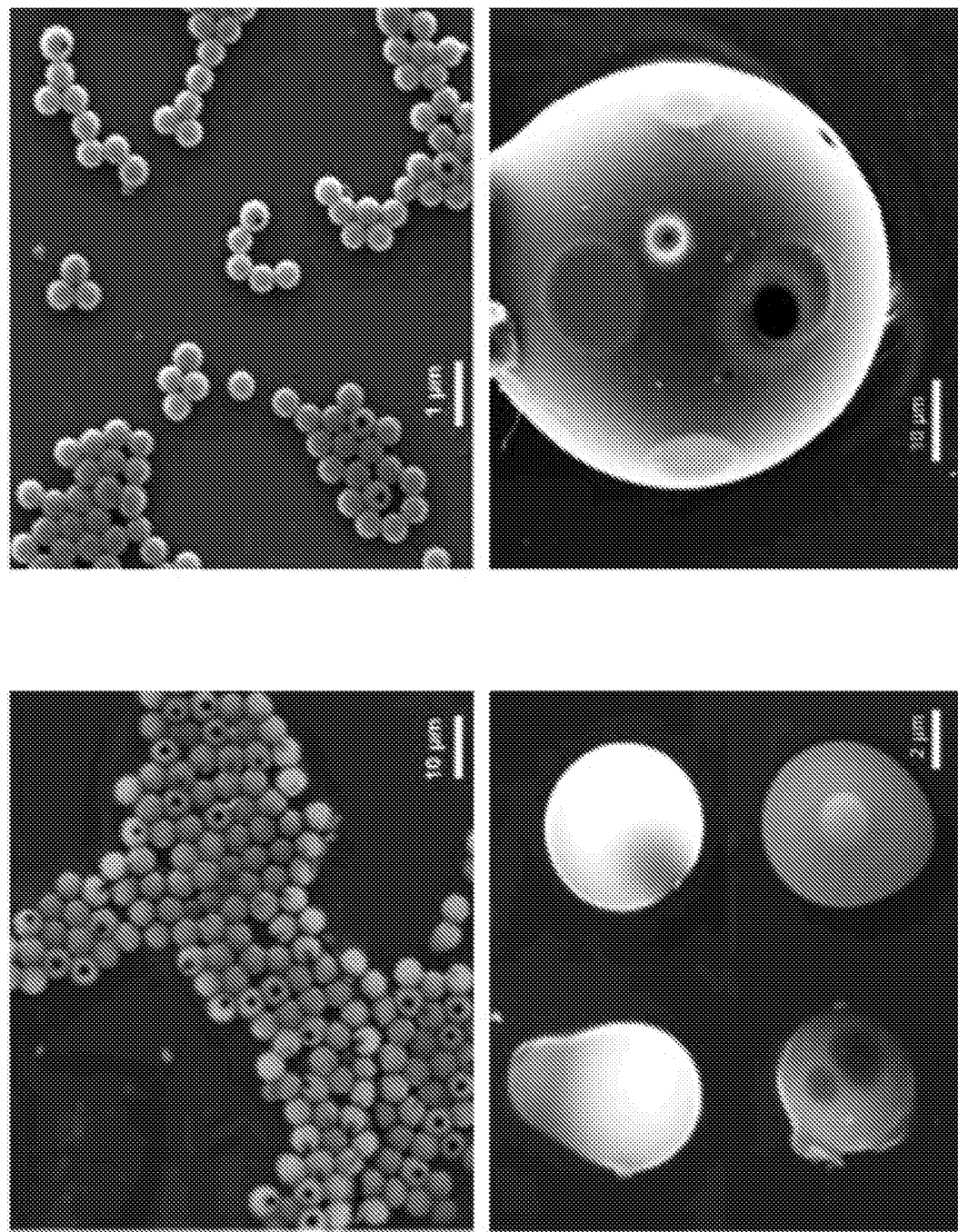


FIG.2

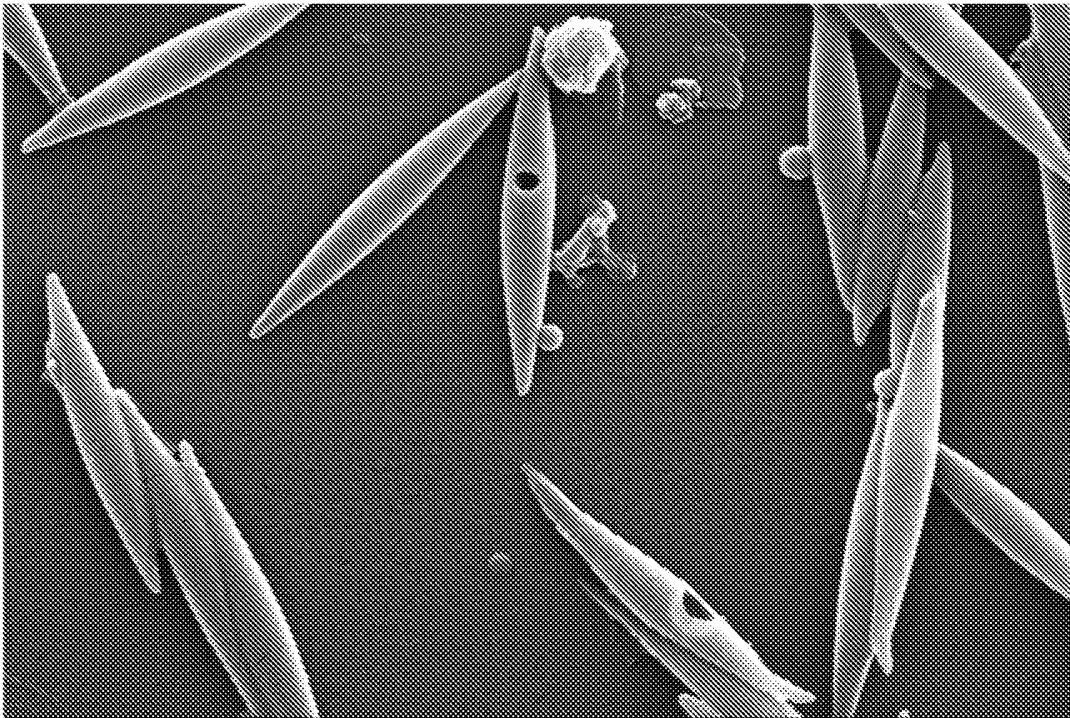


FIG.3

INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C08J9/18 C08J9/224 C08J3/12
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EP0-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

Information on patent family members

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