CLAIMS

1. A method for preparing microcarrier particles, comprising the steps:

1) preparing a dispersed phase liquid and a continuous phase liquid, wherein:

the dispersed phase liquid contains a synthetic polymer and/or natural biological macromolecules, and a curing agent;

the continuous phase liquid contains an organic solvent and a nonionic surfactant;

2) allowing the dispersed phase liquid to flow from one side of a multi-hole plate to the other side of the multi-hole plate through a plurality of micro-wells of the multi-hole plate while allowing the continuous phase liquid to flow, parallel to the multi-hole plate, on the other side of the multi-hole plate, shearing the dispersed phase liquid passing through the multi-hole plate to form liquid microspheres in the flowing continuous phase liquid;

3) allowing the synthetic polymer and/or the natural biological macromolecules in the liquid microsphere to react with the curing agent to form particles; and

4) collecting and washing the particles;

wherein, the temperature of the continuous phase liquid in Step 2) does not exceed 0℃; and Step 3) is executed for 2-72 hours at the temperature of not higher than 0℃.

2. The method of Claim 1, wherein Step 2) is executed in a vessel comprising the multi-hole plate which separates the interior of the vessel into a first portion and a second portion, the dispersed phase liquid enters the first portion through a dispersed phase inlet arranged on the vessel and connected with the first portion and then flows into the second portion through the multi-hole plate; the continuous phase liquid enters the second portion through a continuous phase inlet arranged on the vessel and connected with the second portion; the mixed liquid containing the liquid microspheres after the dispersed phase liquid and the continuous phase liquid are mixed leaves the vessel through an outlet arranged on the vessel and connected with the second portion; and the vessel outlet and the continuous phase inlet are arranged on the opposite sides of the vessel.

3. The method of Claim 1 or 2, wherein the dispersed phase liquid enters the first portion of the vessel and flows through the multi-hole plate by gas pressurization; the continuous phase liquid enters the second portion of the vessel by a gear pump and flows parallel to the multi-hole plate.

4. The method of any one of Claims 1 to 3, wherein Step 3) is performed in a tank provided with a stirring device.

5. The method of any one of Claims 1 to 4, wherein Step 4) is performed by vacuuming in a tank provided with a filtering device.

6. The method of any one of Claims 1 to 5, wherein the micro-wells have a diameter between 0.1 μm and 500 μm.

7. The method of any one of Claims 1 to 6, wherein the micro-wells have a diameter between 30 μm and 50 μm.

8. The method of any one of Claims 1 to 7, wherein the flow of the continuous phase liquid is 5-20 times that of the dispersed phase liquid over the same time.

9. The method of any one of Claims 1 to 8, wherein the synthetic polymer is selected from at least one of polyethylene glycol, a polyethylene glycol derivative, polyethylene glycol diacrylate, polypropylene, polystyrene, polyacrylamide, polylactic acid, polyhydroxy acid, a polylactic acid-alcohol acid copolymer, polydimethylsiloxane, polyanhydride, polyacrylate, polyamide, polyamino acid, polyacetal, polycyanoacrylate, polyurethane, polypyrrole, polyester, polymethacrylate, polyethylene, polycarbonate, and a polyethylene oxide.

10. The method of any one of Claims 1 to 9, wherein the natural biological macromolecules are selected from at least one of collagen, proteoglycan, glycoprotein, gelatin, a gelatin derivative, chitin, alginate, an alginate derivative, agar, fibrinogen, matrigel, a hyaluronic acid, laminin, and fibronectin.

11. The method of any one of Claims 1 to 10, wherein the organic solvent is selected from at least one of hydrofluoroether, carbon tetrachloride, petroleum ether, cyclohexane, liquid paraffin, edible oil, soybean oil, olive oil, chloroform, dichloromethane, carbon tetrachloride, and tetrachloroethylene.

12. The method of any one of Claims 1 to 11, wherein the nonionic surfactant is selected from at least one of sorbitan fatty acid ester, fatty glyceride, laurate, alkylphenol polyoxyethylene ether, high-carbon fatty alcohol-polyoxyethylene ether, arlacel, PO-500, monooleate, and tween.

13. The method of any one of Claims 1 to 12, wherein the curing agent is selected from at least one of divinylbenzene, diisocyanate, N-hydroxysuccinimide, N,N-methylenebisacrylamide, formaldehyde, glutaraldehyde, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, calcium ions, tetramethylethylenediamine, ammonium sulfate, genipin, and transglutaminase.

14. The method of any one of Claims 1 to 13, wherein the dispersed phase liquid further contains a buffer agent selected from at least one of carboxymethylcellulose, sodium chloride, polyacrylamide, potassium chloride, polyvinylpyrrolidone, sodium sulfate, calcium chloride, sodium chloride, sodium carbonate, and sodium bicarbonate.

15. The method of any one of Claims 1 to 14, wherein the method further comprises the step of washing the particles with a cleaning agent selected from at least one of acetone, anhydrous copper sulfate, calcium chloride, sodium sulfate, anhydrous ethanol, medical alcohol, hydrofluoroether, sodium alkylbenzene sulfonate, sodium aliphatic alcohol sulfate, sodium tripolyphosphate, and deionized water.

16. The method of any one of Claims 1 to 15, wherein the ratio of the organic solvent to the nonionic surfactant in the continuous phase liquid is from 5:1 to 20:1 by weight.

17. A process system for preparing microcarrier particles, comprising:

1) an apparatus for preparing an emulsion, comprising:

a vessel;

a multi-hole plate arranged in the vessel and including a plurality of micro-wells; the multi-hole plate separating the interior of the vessel into a first portion and a second portion;

a dispersed phase inlet connected with the first portion and used for feeding a dispersed phase liquid;

a continuous phase inlet connected with the second portion and used for feeding a continuous phase liquid; and

a vessel outlet connected with the second portion.

wherein, the vessel outlet and the continuous phase inlet are arranged on opposite sides of the vessel, such that the continuous phase liquid fed from the continuous phase inlet can flow through the second portion in a direction parallel to the multi-hole plate and then flow out from the vessel outlet;

2) a first tank connected with the dispersed phase inlet and used for containing the dispersed phase liquid, wherein the first tank is further connected with a pressurizing device or a gas cylinder so as to enable the dispersed phase liquid to enter the apparatus for preparing the emulsion under pressure;

3) a second tank connected with the continuous phase inlet and provided with a cooling device, used for containing the continuous phase liquid and cooling the continuous phase liquid;

4) a third tank connected with the vessel outlet, wherein the third tank is provided with a stirrer and a cooling device and used for carrying out emulsion reaction; and

5) a fourth tank connected with the third tank, wherein the fourth tank is provided with a filtering device for collecting particles formed by the emulsion reaction.

18. The process system of Claim 17, wherein the vessel is in a cuboid shape.

19. The process system of Claim 17 or 18, wherein the number of continuous phase inlets is two or more, and the number of vessel outlets is also two or more.

20. The process system of any one of Claims 17 to 19, wherein the continuous phase inlet and the vessel outlet have the same height relative to the vessel bottom.

21. The process system of any one of Claims 17 to 20, wherein the micro-wells have a diameter between 0.1 μm and 500 μm.

22. The process system of any one of Claims 17 to 21, wherein the micro-wells have a diameter between 30 μm and 50 μm.

23. The process system of any one of Claims 17 to 22, wherein a gear pump is arranged between the continuous phase inlet and the second tank and used for feeding the continuous phase liquid from the second tank to the apparatus for preparing the emulsion.

24. The process system of any one of Claims 17 to 23, wherein it further comprises a fifth tank connected with the fourth tank, and the fifth tank is provided with a filtering device for washing the particles.

25. The process system of Claim 24, wherein the fourth tank and the fifth tank are each provided with an evacuating device.