Reverse Phase Layer-by-Layer Encapsulation of Highly Water Soluble Materials

The present invention refers to a method and process for the encapsulation of highly water soluble materials in the further termed "Reverse Phase Layer-by-Layer (RP-LbL) Encapsulation". State of the art polyelectrolyte self assembly Layer-by-Layer coating or encapsulation methods are only applicable to non water soluble materials. The current invention provide a novel method to extend the material spectrum to highly water soluble materials by using non-ionized polyelectrolytes in an organic phase (Reverse Phase) instead of polyelectrolyte salts in an aqueous environment of the common art. Reverse Phase LbL is applicable to encapsulate highly water soluble substances, such as proteins, sugars, ascorbic acid, fragrants, inorganic salts, amino acids and vitamins, which could not be encapsulated by the current LbL technology.

In state of the art LbL encapsulation, salts of anionic and cationic polyelectrolytes carrying negative and positive charges are dissolved into an aqueous buffer and are deposited onto an oppositely charged template material driven by coulomb interaction. Consecutively positive and negative charged polyelectrolytes are deposited until the desired layer number is achieved, whereby the entire process takes place in an aqueous phase, typically a buffer is used. LbL deposition of colloidal particles was described by WO9947253 (Fabrication of Multilayer-Coated Particles and Hollow Shells via Electrostatic Self-Assembly of Nanocomposite Multilayers on Decomposable Colloidal Templates) and WO 9947252 (Production of nanocapsules and microcapsules by layer-wise polyelectrolyte self-assembly). The technology was further developed by Neu WO0003797 (POLYELECTROLYTE COVERINGS ON BIOLOGICAL TEMPLATES) to use cells as a template, by Caruso to encapsulate non-water soluble organic substances WO0151196 (Templating of solid particles by polymer multilayers) and selected protein crystals dispersed in a buffer with high salt concentration WO0077281 (Encapsulation of crystals via multilayer coatings). WO0077281 demonstrated encapsulation of crystals, including crystals of selected proteins, however only relative poorly water soluble crystals can be encapsulated by using the method performed in aqueous phase. WO 0209864 (Encapsulation of liquid template particles) extends the LbL method to emulsions of oil droplets in water.

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All known polyelectrolyte LbL coating and encapsulation methods are performed in an aqueous phase, for example as stated in US 2006/0275375 paragraph 28-29 and its Examples, particles are used as aqueous dispersion; US20020187197 paragraph 42 uses suspension in aqueous phase and all Examples provided use aqueous solutions of the ionized polyelectrolyte. US20020187197 also explicit teaches in Claim 1 the use of charged (ionized) polyelectrolytes. The use of water limits the method to none or poorly water soluble substances, as stated in US20020187197 paragraph 25-26.

By using the present invention of "Reverse Phase Layer-by-Layer (LbL) encapsulation" a number of limitations and problems of the current art can be solved; the present invention extends the spectrum to a broad range of highly water soluble materials.
In comparison to the present art, the current invention is carried out in an organic phase and uses non-ionized polyelectrolytes.

In the following the present invention is described in detail: The present invention refers to "Reverse Phase Layer-by-Layer (LbL) encapsulation" process for the encapsulation of highly water soluble materials within self assembled polymeric capsules by using a non-ionized anionic and a non-ionized cationic polyelectrolyte dissolved in an organic solvent for deposition onto a highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form capsules of multiple layers in a Layer-by-Layer like process.
The process achieves the encapsulation of highly water soluble materials within polymeric capsules in organic phase (reverse phase) by using a non-ionized anionic and a non-ionized cationic polyelectrolyte dissolved in an organic solvent for deposition onto a highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form capsules of multiple nm thick layers in a Layer-by-Layer like process and is comprising the steps:

i) Deprotonation of a cationic polyelectrolyte to form a non-ionized polyelectrolyte and dissolving the non-ionized polyelectrolyte in an organic solvent,

ii) Protonation of an anionic polyelectrolyte to form a non-ionized polyelectrolyte and dissolving the non-ionized polyelectrolyte in an organic solvent,

iii) Providing a suspension of a highly water soluble substance in an organic solvent,

iv) Deposition of the first non-ionized polyelectrolyte onto the highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form a layer of ionized polyelectrolyte,

v) Deposition of alternating layers of non-ionized cationic and non-ionized anionic polyelectrolytes by a solid phase acid-base reaction between the preceding layer on the material surface and the non-ionized polyelectrolyte to form a multi layer capsule until the desired number of layers is achieved,

The process may further comprising the step to transfer the encapsulated material from the organic phase into another organic solvent or into an aqueous phase and/or evaporation of the organic phase, preferentially at reduced temperature and pressure to preserve the properties of the encapsulated material, to form a powder.

In the following the process is described in detail. The first step in the process is to provide a non-ionized anionic and a non-ionized cationic polyelectrolyte and to dissolve them individually into an organic solvent. The problem to overcome is the very poor or non-solubility of polyelctrolytes into organic solvents is the use of non-ioniced polyelectrolytes prepared by deprotonation of cationic polyelectrolytes and protonation of an anionic polyelectrolyte to form a non-ionized polyelectrolyte and to dissolving the non-ionized polyelectrolyte in an organic solvent. A solubility of 1-10 mg/ml is desired, however the method of the present invention can be carried out successfully with much lower concentrations because the deposition is driven by an acid-base reaction at the surface and the formed ionized polyelectrolyte is not longer soluble in the organic phase.

Then, a suspension of a highly water soluble substance in an organic solvent is prepared. Solubility of highly water soluble substances is decreased with decreasing

polarity of the organic solvent. The current invention is teaching a "Reversed Phase" system for LbL encapsulation consisting of an organic solvent instead of water used in the present art. The organic solvent is used to disperse the highly water soluble substance and to dissolve the non-ionized polyelectrolyte; the organic solvent is chosen in accordance to the desired coating material and the template to maintain non solubility of the highly water soluble substance and at the same time provide sufficient solubility for the non-ionized polyelectrolyte.

The first non-ionized polyelectrolyte is then incubated with the highly water soluble substance suspended into an organic solvent, preferentially the same solvent or solvent mixture. Deposition of the non-ionized polyelectrolyte onto the surfaces of the highly water soluble substance (the template) is driven by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form an nm thick layer of ionized polyelectrolyte. The current art LbL process is driven by coulomb forces between charged particles and oppositely charged ionized polyelectrolytes in water, wherein in the present invention non charged polyelectrolytes interact and a layer is formed by a solid phase acid-base reaction.

Then, deposition of alternating layers of non-ionized cationic and non-ionized anionic polyelectrolytes by a solid phase acid-base reaction between the preceding layer surface and the non-ionized polyelectrolyte is performed to form a multi layer capsule until the desired number of layers is achieved. Excess of non-ionized polyelectrolyte is removed by washing the particles (templates) with organic solvent. The thickness of a single resulting layer is comparable with the state of the art LbL methods of about 2 nm; a number of one to 100 layers can be deposited to reach a capsule thickness between 2 and 200 nm.

The process is applicable to highly water soluble materials with a particle size from 10 nm to 100 micrometer; particle material could be crystalline or amorphous or a mixture thereof; particles may be monodisperse or may have a range in size.

In another embodiment of the present invention the suspension of highly water soluble materials in organic solvent can be generated by first dissolving the material in water and then add organic solvent until the solubility limit of the material is reached causing the material to flocculate and to form particles; consecutively the first non-ionized

polyelectrolyte is added or the non-ionized polyelectrolyte may be present in the solvent added to the material.

After the Reverse Phase LbL encapsulation process is performed the encapsulated material can be: i) transfer to another organic solvent and used in the further as a suspension. ii) dried to create a powder, wherein drying from an organic solvent suspension has many advantages and can be performed under lower temperatures and in the vacuum or both. iii) transfer of the encapsulated material from the organic phase into an aqueous phase causing partial or full dissolution of the highly water soluble core material, whereas the dissolved core materials can be retain inside the capsule, partially release out of the capsule or totally release out the capsule.

A range of non-ionized polyelectrolytes (Polymers) can be used such as: Poly-methacrylic acid, poly-acrylicacid and other poly carboxylic-, phosphoric-, sulphuric- or sulfonicacids or other polymers with a functional group that can act as a acid, Polyethylenimine, Polyallylamine, desalted polydiallyldimethylammoniumchloride, and other aminofunctional polymers or polymers with a functional group that can act as a base, or block copolymers or mixtures thereof.

The current invention makes it possible for the first time to encapsulate crystalline glucose, ammonium citrate and BSA by LbL polyelectrolyte self assembly and is applicable to a wide range of water soluble substances. By using the process of the current invention applicable substances are: proteins, peptides, nucleic acids, oligonucleotides, carbohydrates, organic acids, inorganic salts, water or water crystals, vitamins, monosodiumglutamate, amino acids drugs, antibiotics, nutritions, pesticides, fragrants, antioxidants, dyes and fluorophores, salts or derivatives of the previous compounds or mixtures thereof.

The organic solvent has to be chosen in accordance with the non-ionized polyelectrolyte and the polarity and solubility properties of the highly water soluble substance, applicable organic solvents are: alcohols, esters, ethers, furanes, alkanes and chlorinated alkanes, aromatics or a mixture thereof, wherein the organic solvent is mixable with water or is not mixable with water.

In another embodiment of the present invention substances such as crown ethers, detergents or amphyphylic substances are added to the organic phase to improve solubility of the polyelectrolyte in the organic phase by promoting the interaction of the

relatively polar polyelectrolyte with the relative non-polar organic solvent and thereby increase the solubility. By addition of crown ethers which the oxygen atoms within the ether molecules can coordinate with cations (e.g. Na^+, K^+, $RNH3^+$ or $NH4^+$) of an ionic anionic and an ionic cationic polyelectrolytes in the interior of the ring, whereas the exterior of the ring is hydrophobic; resulting in a higher solubility of the polyelectrolyte crown ether complex in organic solvent.

In another embodiment of the present invention, a mixture of two or more organic solvents is used to improve the solubility of the non-ionized polyelectrolyte into the organic phase. Typically the solvent pair consists of organic solvents with different polarity; a typical example is ether in toluene.

Typical non-ionized polyelectrolyte and organic solvent pairs are: Polymethacrylicacid in ethanol, modified polydiallyldimethylammoniumchloride in ethanol; polyethylenimine in chloroform; Poly(ethylene/acrylic acid) in ternary solvents like perchlororthylene, IPA, and toluene; Poly(methyl methacrylate/methacrylic acid) in ethyl cellosolve; Poly(ethyl acrylate/acrylic acid) in ethanol; Poly(vinyl chloride/vinyl acetate/maleic acid) in various organic solvents, Poly(2-dimethylaminoethyl methacrylate in tert-butanol; Poly(2-vinylpyridine) in tert-butanol and/or DMF and/or other alcohols; Poly(N-vinylpyrrolidone) in alcohols and/or chloroform and/or nitroparaffins.

In another embodiment of the present invention, the encapsulated material is transferred from the organic phase into another organic solvent with low boiling point, e.g. ether chlormethane, chloroform, followed by evaporation of the organic phase at ambient pressure or at reduced pressure and low temperature to create a powder of the encapsulated material. The advantage of the current invention is the use of organic solvents instead of water; organic solvents can be evaporated at lower temperature with less energy and complications to create a powder and preserve the properties of the encapsulated material. This is of particular interest if a sensitive substance such as fragrances or biomolecules are used.

In another embodiment of the present invention, the method can be used to encapsulate water ice crystals or carbon dioxide ice crystals or other frozen highly water soluble materials. The frozen crystals, for example the water ice crystals may contain another material which was dissolved before the freezing. Only by using the method of the

current invention based on encapsulation in an organic phase frozen templates can be retained during the LbL polyelectrolyte self assembly process at temperatures between 0 to -70 degree.

In another embodiment of the present invention, the method can be used to produce a coating of the encapsulated material on a substrate. The encapsulated material is first transferred from the organic phase into another organic solvent with low boiling point followed by evaporation of the organic phase at ambient pressure or at reduced pressure in the presence of a substrate material leading to the deposition of the encapsulated material onto a substrate material surface to form a coating. For example, a coating of an encapsulated drug on a biomaterial surface may be formed by using this embodiment of the present invention.

The applicability of the method of the current invention was tested on a number of highly water soluble substances. Highly water soluble organic model substances of high molecular weight (BSA) and low molecular weight (glucose) and a salt (ammonium citrate) in combination with different non-ionized polyelectrolytes were used to experimentally demonstrate the method. Fluorescent labeled BSA (BSA-FITC) was synthesized to prove encapsulation and to study the release of the substance from the capsule by fluorescence microscopy. Fluorescent labeled non-ionized polyelectrolytes were used in some experiments to prove capsule formation and to study capsule morphology by fluorescence microscopy. The formation of multilayers was experimentally confirmed by deposition of several layers of fluorescent labeled non-ionized polyelectrolyte. An increase of fluorescent intensity with deposition of each lsayer confirmed multi layer formation by using the method of the current invention.

The process of the current invention has applications in several fields of technology and manufacturing, for example in the food industry to encapsulate fragrants and vitamins, in the cosmetic industry to encapsulate antioxidants, in the pharmaceutical industry to encapsulate drugs and to release drugs, in agriculture, pigment manufacturing and chemical industry.

The invention is further illustrated in the following figures and examples.

Figures

Figure 1 Schematic representation of the Reversed Phase LbL encapsulation process. i) Deprotonation of a cationic polyelectrolyte to form a non-ionized polyelectrolyte dissolved in an organic solvent. ii) Protonation of an anionic polyelectrolyte to form a non-ionized polyelectrolyte dissolved in an organic solvent. iii) Providing a suspension of a highly water soluble substance in an organic solvent. iv) Deposition of the first non-ionized polyelectrolyte onto the highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form a layer of ionized polyelectrolyte. v) Deposition of the second and further alternating layers of non-ionized cationic and non-ionized anionic polyelectrolytes by a solid phase acid-base reaction between the preceding layer on the material surface and the non-ionized polyelectrolyte to form a multi layer capsule until the desired number of layers is achieved. vi) The process may further comprising the step to transfer the encapsulated material from the organic phase into another organic solvent (left) or into an aqueous phase (right) and/or evaporation of the organic phase, preferentially at reduced temperature and pressure to preserve the properties of the encapsulated material, to form a powder (not shown).

Figure 2 Fluorescent micrographs demonstrating the Reverse Phase LbL Encapsulation of the highly water soluble protein bovine serum albumin (BSA) (Fig 2-a) and release of BSA after addition of water, figures 2-B to 2-J. Fluorescent labeled BSA (BSA-FITC) was used to demonstrate release.

Figure 3 Light microscopic and fluorescent micrograph series demonstrating the Reverse Phase LbL Encapsulation of Series A) Glucose; Series B) Sodium chloride and, and Series C) Ascorbic acid. Image A shows RP-LbL encapsulated crystals in ethanol before addition of water; image A-b 20 seconds after addition of water and A-c the empty capsule material after complete release of glucose. Image B shows RP-LbL encapsulated sodium chloride crystals in ethanol before addition of water; image B-b 20 seconds after addition of water and B-c the empty capsule material after complete release. Image C shows RP-LbL encapsulated crystals og ascorbic acid in ethanol before addition of water; image C-b 30 seconds after addition of water and C-c the

empty capsule material after complete release. A fluorescein labeled non-ioniced polyelectrolyte was used in the RP-LbL process to demonstrate capsule formation (images not shown).

Examples

Materials: Poly-(diallyldimethylammoniumchloride) (PDADMA) M_w 100000 to 200000 Da and Bovine Serum Albumin (BSA) and Fluoresceine Isothiocyanate (FITC) were obtained from Sigma Aldrich. Poly-methacrylic acid (PMA), M_w 100000 Da was purchased from Polysciences Inc.. Ethanol was obtained from Merck and Sodiumhydroxid from Fluka Chemika.

Preparation of the non-ionized polyelectrolyte solutions in organic solvent: PMA was first protonated with hydrochloric acid to prepare the non-ionized (ni) polyelectrolyte (niPMA); then dialyzed against water and vacuum dried. An amount of 0.25 g PMA was dissolved at 45 °C in 25 ml in pure ethanol over 24 h.

PDADMA was first modified by dissolving 1 g in 5 ml water, mixed with 10 ml of 25% sodium hydroxide solution and allowed to react over night at 55°C while stirring. The non ionized modified PDADMA (nimPDAMA) was extensively dialyzed against distilled water and dried under vacuum at 105°C. Then, 0.272 g nimPDADMA was dissolved in 25 ml pure ethanol over 24 h at 45°C.

Example I: Encapsulation of Bovine Serum Albumin as a highly water soluble high molecular weight substance

BSA-FITC with a conjugation ratio of 1:10 was prepared as described by "Bioconjugate Techniques [1], purified by dialyzes and dried at room temperature.

BSA-FITC powder was extensively milled together with pure Ethanol for 5 min by hand in a small agate mortar. The suspension was transferred into a 1.5 ml vial and centrifuged at 500 r/min for 30 s, the supernatant containing smaller BSA-FITC particles was discarded. The vial was refilled with pure ethanol again and allowed to precipitate for a few minutes. To obtain particles of almost the same size, the supernatant was used for the following experiments and the precipitate was discarded. After transferring a part of the suspension to a smaller vial, the polymer layers were assembled onto the protein particles by the sequential deposition of niPMA and nimPDADMA. The first layer was deposited by adding 50 µl aliquot of nimPDADMA (10 mg/ml) to 100 µl ethanol BSA particle suspension, occasionally shaking the suspension and allowing 15 minutes for deposition.

The excess nimPDADMA was removed by two repeated centrifugation and redispersion cycles in pure ethanol. The next layer, niPMA (10 mg/ml in ethanol), was deposited by using the same procedure as described for nimPDADMA. The process was repeated until the desired number of layers was deposited.

Example II: Encapsulation of sugar as a highly water soluble low molecular weight substance

Materials: Polyethylenimine, linear (PEI) M_w 250000 Da and Poly-methacrylic acid (PMA), M_w 100000 Da were purchased from Polysciences Inc. Glucose, Fructose, 15-crown-5 and 18-crown-6 ethers, Polyallylaminehydrochloride (PAH) M_w 15000 and polyacrylicacid sodiumsalt (PAA) M_w 2100 were obtained from Sigma Aldrich. Ethanol was obtained from Merck and chloroform was purchased from EM Sciences.

The sugar crystals, for e.g. sacharose, glucose or fructose, were extensively grinded in a small agate mortar by hand and after grinding suspended in Ethanol. To obtain particles of almost the same size, the sample was treated as described in Example 1.

After transferring a part of the suspension to another vial, the polymer layers were assembled onto the sugar crystals by the sequential deposition of niPMA in ethanol solution and niPEI dissolved in chlorform. The first layer was deposited by adding 50 µl aliquot of niPMA (10 mg/ml) to 100 µl ethanol sugar crystal suspension, occasionally shaking the suspension and allowing 15 minutes for deposition.

The excess niPMA was removed by two repeated centrifugation and redispersion cycles in pure ethanol followed by washing steps with the solvent (chloroform) of the other non-ionized polyelectrolyte. The next layer, niPEI (5 mg/ml in chloroform), was deposited by using the same procedure as described for niPMA. The process was repeated until the desired number of layers was deposited. Furthermore, the encapsulation of sugar crystals can be achieve for non ionic templates suspensions with polyelectrolytes-crownether complexes, e.g. PAH–18-crown-6-ether hydrochloride and polyacrylicacid- sodium-15-crown-5, in organic solvents can alternatively be used. In addition the process was performed with fluorescent labelled non-ioniced polyelectrolyte to proof capsule formation. The encapsulated material was released by addition of water and the fluorescence labelled remaining capsule was detected.

Example III: Encapsulation of organic acids and organic and inorganic salts as a highly water soluble low molecular weight substance

Materials: Polyethylenimine, linear (PEI) M_w 250000 Da and Poly-methacrylic acid (PMA), M_w 100000 Da were purchased from Polysciences Inc., citric acid, sodium citrate, ascorbic acid and sodium chloride were obtained from Sigma Aldrich. Ethanol was obtained from Merck and chloroform was purchased from EM Sciences.

The salt or acid crystals, for e.g. citric acid or citric acid sodium salt or ascorbic acid or sodium chloride, were extensively grinded in a small agate mortar by hand and suspended in ethanol after grinding. To obtain particles of almost the same size, the particles were treated as described in Example 1. After transferring a part of the suspension to another vial, the polymer layers were assembled onto the salt or acid crystals by the sequential deposition of niPMA in ethanol solution and niPEI dissolved in chlorform. The first layer was deposited by adding 50 µl aliquot of niPMA (10 mg/ml) to 100 µl ethanol crystal suspension, occasionally shaking the suspension and allowing 15 minutes for deposition. The excess niPMA was removed by two repeated centrifugation and redispersion cycles in pure ethanol followed by washing steps with the solvent (chloroform) of the other non ionized polyelectrolyte. The next layer, niPEI (5 mg/ml in chloroform), was deposited by using the same procedure as described for niPMA. The process was repeated until the desired number of layers was deposited.

Example IV: Encapsulation of water droplets (inverse emulsion) or ice crystals as a highly water soluble substance

A suspension of water crystals or a reverse emulsion of water droplets is first prepared in an organic solvent; most preferentially an organic solvent not mixable with water. For example a suspension of water crystals can be obtained by first preparing a reversed emulsion of water in an organic solvent and then reducing the temperature to case freezing of the water to form a suspension of ice in an organic solvent. The water may contain solubilized substances (e.g. protein, DNA or salts). Polymer layers are then assembled onto the water crystals by the sequential deposition of non-ionized polyelectrolytes dissolved in the organic phase. The excess non-ionized polyelectrolyte

is removed by two repeated centrifugation and redispersion cycles in organic solvent. The process is repeated until the desired number of layers is deposited. More desired is the encapsulation of ice crystals, because water droplets may dissolve the polyelectrolyte and no deposition of polymer to form a capsule takes place.

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Claims

1 Process for the encapsulation of highly water soluble materials within polymeric capsules in organic phase (reverse phase) by using a non-ionized anionic and a non-ionized cationic polyelectrolyte dissolved in an organic solvent for deposition onto a highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form capsules of multiple nm thick layers in a Layer-by-Layer like process comprising the steps:

i) Deprotonation of a cationic polyelectrolyte to form a non-ionized polyelectrolyte and dissolving the non-ionized polyelectrolyte in an organic solvent,

ii) Protonation of an anionic polyelectrolyte to form a non-ionized polyelectrolyte and dissolving the non-ionized polyelectrolyte in an organic solvent,

iii) Providing a suspension of a highly water soluble substance in an organic solvent,

iv) Deposition of the first non-ionized polyelectrolyte onto the highly water soluble substance suspended into an organic solvent by a solid phase acid-base reaction between the material surface and the non-ionized polyelectrolyte to form a layer of ionized polyelectrolyte,i

v) Deposition of alternating layers of non-ionized cationic and non-ionized anionic polyelectrolytes by a solid phase acid-base reaction between the preceding layer on the material surface and the non-ionized polyelectrolyte to form a multi layer capsule until the desired number of layers is achieved,

vi) Transfer of the encapsulated material from the organic phase into another organic solvent or into an aqueous phase and/or evaporation of the organic phase, preferentially at reduced temperature and pressure to preserve the properties of the encapsulated material, to form a powder.

2 Process according to claim 1, wherein the non-ionized anionic polyelectrolyte is selected but not limited to carboxy-, sulfonic-, phosphoric-, or other organic or inorganic acid functional polymers, e.g. polymethacylicacid, polyacrylicacid, polystyrenesulfonate, or co-polymers such as poly(ethylene/acrylicacid), poly(n-butyl acrylate / acrylicacid) or biodegradeable polymers and copolymers such as for example poly(dl-lactide/glycolide), poly(methyl methacrylate/methacrylic acid), poly(vinyl chloride/vinyl acetate/maleic acid) a mixture of thereof, and the non-ionized cationic polyelectrolyte is selected but not limited to base functional polymers, e.g. amino and amine functional polymers such as polyallylamine, poly(2-dimethylaminoethyl methacrylate, poly(2-vinylpyridine), poly(N-vinylpyrrolidone), desalted derivates of polydiallyldimethylammoniumchloride or other derivates N- alkyl substituted quartaner ammonium salts, polyethylenimines, chitosan.

3 Process according to claim 1, wherein the highly water soluble material is a protein, peptide, nucleic acid, oligonucleotide, carbohydrate, organic acid, inorganic salt, water or water crystals, vitamin, monosodiumglutamate, amino acid, drug, antibiotic, nutrition, pesticide, dye or fluorophore, fragrant or a salt or derivative of these substances and mixtures thereof and is dispersed into an organic solvent.

4 Process according to claim 1, wherein the organic solvent to dissolve the non-ionized anionic polyelectrolyte and the non-ionized cationic polyelectrolyte is selected from alcohols, esters, ethers, ketones, furanes, alkanes and chlorinated alkanes, aromatics or a mixture thereof, wherein the organic solvent is mixable with water or is not mixable with water.

5 Process according to claim 1, wherein the organic solvent to disperse the highly water soluble substance is selected from alcohols, esters, ethers, furanes, alkanes, chlorinated alkanes, alkenes, aromatics, amines, nitroalkanes, aldehydes, ketones, ketenes, nitriles, silicones phosphorderivates such as hexamethylphosphorsäuretriamide, heteroaromatics, isocyanates and cyanates, thiocionates and isothiocyanates and D-substituted solvents or a mixture thereof, wherein the organic solvent is mixable with water or is not mixable with water.

6 Process according to claim 1, wherein a substance or several substances are added into the organic phase to promote the solubility of the non-ionized polyelectrolytes in the organic solvent such as crown ethers, detergents, amphiphylic substances, bases, acids or mixtures thereof.

7 Process according to claim 1, wherein the highly water soluble material has a particle size from 10 nm to 100 micrometer and is crystalline or amorphous or freeze dried or spray dried or a frozen highly water soluble materials or a mixture thereof and forms a suspension in an organic solvent.

8 Process according to claim 1, wherein the encapsulated material is transferred from the organic phase into another organic solvent.

9 Process according to claim 1, wherein the encapsulated material is transferred from the organic phase into an aqueous phase causing partial or full dissolution of the highly water soluble material, whereas the dissolved core materials can be retain inside the capsule, partially release out of the capsule or totally release out the capsule.

10 Process according to claim 1, wherein the encapsulated material is transferred from the organic phase into another organic solvent with low boiling point followed by evaporation of the organic phase at ambient pressure or at reduced pressure and leading to the deposition of the material onto a surface to form a coating.

11 Use of the process of claims 1 to 10 for the production of encapsulated materials and core shell material dispersions and formulations and coatings and aerosols and powders.