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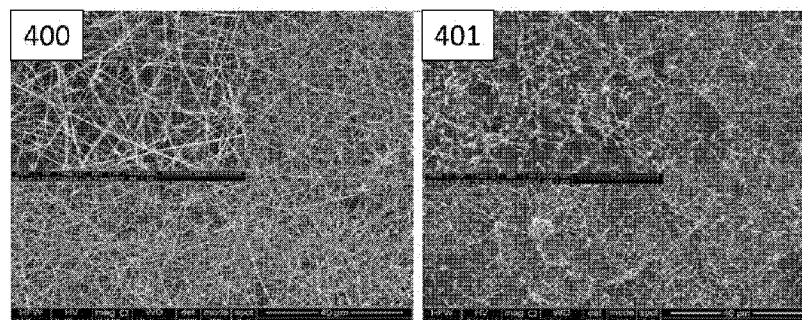
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(54) Title: ANTIBACTERIAL NANOFIBRES

FIG. 4A



(57) Abstract: Antibacterial nanofibres and methods for their preparation are described. Antibacterial nanofibres include as-spun alginate nanofibres treated with silver to generate silver-alginate nanofibres. Antibacterial nanofibres provided are useful components of wound dressings, wherein the wound dressings optionally further comprise malodor absorbing agents such as cyclodextrins.

ANTIBACTERIAL NANOFIBRES**CROSS-REFERENCE**

[0001] This application claims the benefit of U.S. Provisional Application 62/154,056, filed April 28, 2015, which is incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] An important problem associated with wound treatment is the management of infection. Infection can retard wound healing, is traumatic for the patient and can significantly increase treatment time and cost. Consequently there is a need to both prevent and treat infection resulting from wounds, preferably in conjunction with wound dressings.

SUMMARY OF THE INVENTION

[0003] Disclosed herein are methods and compositions for wound treatment in a subject including the preparation and use of compositions comprising antimicrobial agents incorporated with or coating nanofibre materials. In other embodiments, the methods and compositions incorporate an anti-odor component with the nanofibre material. In yet other embodiments, the methods and compositions incorporate both an antimicrobial and anti-odor component with the nanofibre material.

[0004] In one aspect, provided herein are methods for preparing anti-odor, antimicrobial nanofibres derived from alginate nanofibres, the method comprising a) contacting the alginate nanofibres with a first organic solution comprising calcium ions to generate calcium-alginate nanofibres; b) contacting the calcium-alginate nanofibres with a second organic solution comprising an antimicrobial agent to generate antimicrobial-alginate nanofibres; and c) combining or coating the antimicrobial-alginate nanofibres with a malodor absorbing agent to generate anti-odor, antimicrobial nanofibres. In some embodiments, the alginate nanofibres are formed by electrospinning an aqueous solution comprising from 1% to 10% by weight mixture of alginate and poly(ethylene)oxide (PEO), for example, 4% mixture of alginate and PEO. In some embodiments, the aqueous solution comprises an alginate to PEO ratio from 60:40 to 80:20, for example, 70:30. In some embodiments, the first organic solution comprises from 0.1% to 10% by weight calcium salt. For example, calcium salts include, without limitation, calcium chloride, calcium bromide, calcium fluoride, calcium iodide, calcium nitrate and calcium hydride salts. In some embodiments, the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof. Antibiotics include, without limitation, gentamicin, ofloxacin, minocycline, tetracycline, metronidazole and derivatives thereof. In some embodiments, the second organic solution comprises from 0.05% to 10% by weight silver

salt. Silver salts include, without limitation, silver nitrate, silver chloride, silver sulfate, silver lactate, silver bromide, silver acetate, and combinations thereof. In some embodiments, the antimicrobial-alginate nanofibres are coated with a malodor absorbing agent by electrospraying, electrospinning, or both electrospraying and electrospinning the malodor absorbing agent onto a surface of the antimicrobial-nonofibres. In some embodiments, the malodor absorbing agent comprises cyclodextrin. In some instances, the method comprises washing the alginate nanofibres with an organic solvent prior to contact with the first organic solution. In some instances, the method comprises washing the antimicrobial-alginate nanofibres with an organic solvent prior to combining or coating with the malodor absorbing agent. In some instances, the anti-odor, antimicrobial nanofibres have less than a 10% decrease in average fibre diameter as compared to the average fibre diameter of the alginate nanofibres. In some embodiments, at least a portion of the antimicrobial agent of the anti-odor, antimicrobial nanofibres dissociates and releases from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate. In some embodiments, at least a portion of calcium ions of the anti-odor, antimicrobial nanofibres dissociates and releases from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate. In some instances, the anti-odor antimicrobial nanofibres remain intact after soaking in an aqueous solution for 24 hours.

[0005] In one aspect, provided herein are anti-odor, antimicrobial nanofibres comprising alginate nanofibres electrospun from an aqueous solution comprising a 4% mixture of alginate and PEO in a 70:30 ratio; an antimicrobial agent; and a malodor absorbing agent. In some embodiments, the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof. In some instances, the malodor absorbing agent comprises silver ions. In some cases, at least a portion of the silver ions form particles within the anti-odor, antimicrobial nanofibres. In some cases, the silver particles have an average diameter from 150 nm to 300 nm. In some cases, at least a portion of the silver ions in anti-odor, antimicrobial nanofibres dissociate and release from the anti-odor, antimicrobial nanofibres when contacted with wound exudate. In some embodiments, the anti-odor, antimicrobial nanofibres further comprise calcium ions. In some cases, at least a portion of the calcium ions dissociate and release when the anti-odor, antimicrobial nanofibres are contacted with wound exudate. In some embodiments, the malodor absorbing agent of the anti-odor, antimicrobial nanofibres is in the form of a fibre. In some embodiments, the malodor absorbing agent is electrospun onto the alginate nanofibres. In some embodiments, the malodor absorbing agent is electrosprayed onto

the alginate nanofibres. In some embodiments, the malodor absorbing agent comprises cyclodextrin. In some examples, the cyclodextrin comprises hydroxypropyl- β -cyclodextrin (HB- β -CD). In some cases, the anti-odor, antimicrobial nanofibres do not comprise PEO. In some cases, the average nanofibre diameter of anti-odor, antimicrobial nanofibres is from 120 nm to 150 nm. In some instances, the anti-odor, antimicrobial nanofibres remain intact after soaking in an aqueous solution for 24 hours. In another aspect, provided herein is a wound dressing structure comprising anti-odor, antimicrobial nanofibres and a backing. In some embodiments, the backing is a fabric backing. In some embodiments, the backing is nylon. In some embodiments, the backing comprises carboxymethylcellulose (CMC).

[0006] In a further aspect, provided herein is a method of preparing a wound dressing structure, the method comprising: depositing alginate nanofibres on a surface of a backing, b) chemically treating the alginate nanofibres with a solution comprising calcium ions dissolved in an organic solvent to generate calcium-alginate nanofibres, c) chemically treating the calcium-alginate nanofibres with a solution comprising an antimicrobial agent dissolved in an organic solvent to generate antimicrobial-alginate nanofibres, and d) electrospinning or electrospraying fibres comprising a malodor absorbing agent onto a surface of the antimicrobial-alginate nanofibres. In some embodiments, the alginate nanofibres are deposited on the surface of the backing by electrospinning an aqueous solution comprising from 1% to 10% by weight mixture of alginate and PEO. In some embodiments, the aqueous solution comprises an alginate to PEO ratio from 60:40 to 80:20. In some embodiments, the solution comprising calcium ions comprises from 0.1% to 10% by weight calcium salt. Calcium salts include, without limitation, calcium chloride, calcium bromide, calcium fluoride, calcium iodide, calcium nitrate, and calcium hydride. In some embodiments, the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof. Antibiotics include, without limitation, gentamicin, ofloxacin, minocycline, tetracycline, metronidazole and derivatives thereof. In some instances, the solution comprising the antimicrobial agent comprises from 0.05% to 10% by weight silver salt. Silver salts include, without limitation, silver nitrate, silver chloride, silver sulfate, silver lactate, silver bromide, silver acetate, and combinations thereof. In some cases, the malodor absorbing agent comprises cyclodextrin. In some embodiments, the method further comprises washing the alginate nanofibres with an organic solvent after depositing onto the surface of the backing. In some cases, the method further comprises washing the antimicrobial-alginate nanofibres with an organic solvent prior to electrospinning or electrospraying with the malodor absorbing agent. In some cases, the antimicrobial-alginate nanofibres have less than a

10% decrease in average fibre diameter as compared to the average fibre diameter of the starting alginate nanofibre material. In some embodiments, a portion of the antimicrobial agent dissociates and releases from the wound dressing structure when the wound dressing structure is in contact with wound exudate. In some embodiments, a portion of the calcium ions dissociate and release from the wound dressing structure when the wound dressing structure is in contact with wound exudate. In some embodiments, the backing is a fabric backing. In some instances, the backing is nylon. In some instances, the backing comprises carboxymethylcellulose (CMC). In yet other embodiments, the backing comprises derivatized carboxymethylcellulose. Further provided, in one aspect, is a nanofibrous structure prepared by a method provided herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0007] **Figure 1** shows scanning electron microscope images of as-spun sodium-alginate nanofibres before and after chemical treatment; and corresponding fibre diameter distributions.

[0008] **Figure 2** is a graph depicting average particle size in an antibacterial nanofibre structure.

[0009] **Figure 3A** is an infrared spectra from 4,000 to 400 cm^{-1} of as-spun nanofibre mats before and after chemical treatment. **Figure 3B** is an infrared spectra from 3,500 to 2,000 cm^{-1} of the as-spun nanofibre mats before and after chemical treatment.

[0010] **Figure 4A** shows scanning electron microscope images of nanofibres spun from a 70:30 sodium-alginate:PEO solution (**400**) and a 80:20 sodium-alginate:PEO solution (**401**). **Figure 4B** is a graph illustrating fibre diameter distribution of the nanofibres spun from the 70:30 sodium-alginate:PEO solution as shown in Figure 4A.

[0011] **Figure 5** shows infrared spectra of as-spun PEO nanofibres (A), sodium alginate (B), and sodium alginate/PEO nanofibres (C) within a 4000-400 cm^{-1} and a 2000-1000 cm^{-1} spectral range.

[0012] **Figure 6** shows photographs and scanning electron microscope images of a base fabric before and after deposition of as-spun nanofibres.

[0013] **Figure 7** shows scanning electron microscope images of nanofibres electrosprayed with a malodor absorbing agent for different periods of time.

[0014] **Figure 8** shows a scanning electron microscope image of fibres electrospun from a solution having a blend of HP- β -CD/PEO.

[0015] **Figure 9** provides an example workflow for the preparation of a dressing structure comprising nanofibres.

[0016] **Figure 10** provides a summary of example methods for the preparation of a nanofibrous structure.

DETAILED DESCRIPTION OF THE INVENTION

[0017] Provided herein, in various embodiments, are nanofibres chemically treated with an antibacterial agent to generate antibacterial nanofibres. A suitable antibacterial agent is silver, which in its ionic form, is an effective antimicrobial against a large number of gram-negative and gram-positive bacteria, including antibiotic-resistant strains such as methicillin-resistant and vancomycin-resistant *Staphylococcus aureus* and *Enterococcus faecium*.

[0018] The antibacterial nanofibres described are useful as components of a wound dressing. In some embodiments, antibacterial nanofibres are prepared by treating nanofibres comprising biopolymers with an antibacterial agent. As an example, nanofibres are electrospun from a solution comprising one or more biopolymers and subsequently treated with an antibacterial agent. An exemplary biopolymer is alginate. Alginate is useful in a wound dressing to absorb large amounts of wound fluid while forming a gel-like substance, thus maintaining a moist microenvironment for the wound. In exemplary embodiments, antibacterial nanofibres are derived from as-spun nanofibres, wherein the as-spun nanofibres are formed by electrospinning a solution comprising a biopolymer and optionally a carrier polymer and/or a surfactant. In some embodiments, the as-spun nanofibres are formed by electrospinning a solution comprising alginate and a carrier polymer. In some cases, the carrier polymer is poly(ethylene)oxide (PEO).

[0019] In various embodiments, antibacterial nanofibres are derived from a nanofibre comprising a biopolymer suitable for end-use in a wound dressing. In some embodiments, nanofibres comprise biopolymers combined with one or more carrier polymers or carrier agents. Non-limiting examples of biopolymers and/or carriers useful as components of a nanofibre described herein include alginate, chitosan, carboxymethylcellulose (CMC), dextran, collagen, glycosaminoglycans, cellulose, poly(caprolactone), polyglactin, gelatin, PEO, polyvinyl alcohol, polyvinyl caprolactam, polyvinyl acetate, polyethylene glycol, cellulose derivatives, polyvinylpyrrolidone, poly-L-lactic acid, poly(ϵ -caprolactone), chitosan, derivatives thereof, solutions thereof, and any combination thereof. In some instances, a solution comprising a biopolymer or biopolymer and carrier is electrospun with a surfactant, for example, oxtoxynol (TritonTM X-100), polysorbate (TweenTM), stearyl alcohol, sorbitan, polyglycerol polyricinoleate, poloxamer, pentaethylene glycol monododecyl ether, oleyl alcohol, octyl glucoside, N-octyl beta-D-thioglycopyranoside, octaethylene glycol monododecyl ether, NP-40, nonoxynols, nonidet P-40, monolaurin, ethoxylate, lauryl glucoside, isoceteth-20, IGEPAL CA-630, decyl glucoside, cetomacrogol, cetostearyl alcohol, cetyl alcohol, cocamide DEA, cocamide MEP, or derivatives or combinations thereof.

[0020] In various embodiments, nanofibres are produced from an organic solution comprising a biopolymer and optionally a carrier and/or surfactant. In alternative embodiments, nanofibres are produced from an aqueous solution comprising a biopolymer and optionally a carrier and/or surfactant. In other embodiments, nanofibres are produced from a miscible aqueous-organic solution comprising a biopolymer and optionally a carrier and/or surfactant.

[0021] In some examples, nanofibres are produced by electrospinning a solution comprising from about 1% to about 50% by weight biopolymer. In some examples, nanofibres are produced by electrospinning a solution comprising from about 1% to about 50% by weight biopolymer and carrier. In some instances, the percentage by weight of biopolymer or biopolymer: carrier in the solution is from about 1% to about 50%, from about 1% to about 40%, from about 1% to about 30%, from about 1% to about 20%, from about 1% to about 10%. In some instances, the percentage by weight of biopolymer or biopolymer: carrier in the solution is 1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, or 10%. For nanofibres produced from electrospinning solutions comprising a biopolymer and a carrier, the ratio of biopolymer to carrier may be from about 20:80 to about 95:5, from about 30:70 to about 95:5, from about 40:70 to about 95:5, from about 50:70 to about 95:5, from about 60:80 to about 90:10, from about 60:80 to about 80:20. In some embodiments, the ratio of biopolymer to carrier in an electrospinning solution is 60:40, 61:39, 62:38, 63:37, 64:36, 65:35, 66:34, 67:33, 68:32, 69:31, 70:30, 71:29, 72:28, 73:27, 74:26, 75:25, 76:24, 77:23, 78:22, 79:21, or 80:20. In some implementations, nanofibres are electrospun from a 1% to 50% by weight solution of biopolymer and carrier polymer in a ratio from about 20:80 to about 95:5 biopolymer:carrier polymer. For example, the electrospun or as-spun nanofibres are produced by electrospinning a 4% by weight 70:30 biopolymer: carrier polymer solution. The as-spun nanofibres may comprise from about 20% to about 95%, preferably 50 to 90%, more preferably 60% to 80%, e.g., 70% biopolymer. In one embodiment, the as-spun nanofibres comprise from about 60% to about 80% or about 70% alginate or salt thereof. The as-spun nanofibres may comprise 5% to 80%, preferably 10% to 50%, more preferably 20% to 40%, e.g., 30% carrier polymer. In one embodiment, the as-spun nanofibres comprise from about 20% to about 40%, e.g., 30% PEO. In one example, nanofibres are produced by electrospinning a 4% by weight 70:30 alginate: carrier polymer solution, wherein the carrier polymer is optionally PEO and the solution optionally comprises a surfactant such as TritonTM X-100.

[0022] In some embodiments, the carrier is substantially removed from the nanofibres, for example, by washing the nanofibres with a solution suitable for maintaining the nanofibres insoluble, e.g., a solution comprising an organic solvent. The carrier is substantially removed, for example, when more than 90%, more than 92%, more than 94%, more than 96%, or more

than 98% of the carrier is removed from the nanofibres or when the carrier is unable to be detected by spectroscopic methods such as infrared spectroscopy. In some embodiments, the surfactant is at least partially removed from the nanofibres, for example, at least about 50% of the surfactant is removed from the nanofibres. In other embodiments, the surfactant is not substantially removed (e.g., less than about 50% is removed) from the nanofibres.

[0023] In various embodiments, antibacterial nanofibres are derived from nanofibres having an average diameter from about 50 nm to about 500 nm, from about 60 nm to about 400 nm, from about 70 nm to about 300 nm, from about 70 nm to about 200 nm, from about 80 nm to about 200 nm, from about 90 nm to about 150 nm, or from about 100 nm to about 140 nm. In embodiments, the average fibre diameter is less than about 200 nm, less than about 150 nm, or less than about 130 nm. In some embodiments, the average fibre diameter is greater than about 50 nm, greater than about 70 nm, or greater than about 90 nm.

[0024] In various embodiments, nanofibres described herein form nanofibrous structures, for example, nanofibrous mats. In some embodiments, the nanofibres comprise as-spun biopolymers. In exemplary embodiments, the nanofibres and/or nanofibrous mats are chemically treated with an antibacterial agent to generate antibacterial nanofibres. As described herein, at least in some implementations, nanofibres are inclusive of nanofibres within a nanofibrous structure.

[0025] In some embodiments, the antibacterial nanofibres or nanofibrous structures provided herein comprise one or more components useful for wound treatment. In some embodiments, a wound dressing comprising antibacterial nanofibres comprises one or more components useful for wound treatment. Non-limiting examples of components useful for wound treatment include drugs, antimicrobial compounds, lipids, triglycerides, vitamins, minerals, enzymes to minimize the development of malodorous compounds, and growth factors. Antimicrobial compounds include antiseptics (e.g., acetic acid, chlorhexidine, silver, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, polyhexamethyl biguanide, triclosan) and antibiotics (e.g., gentamicin, ofloxacin, minocycline, tetracycline, metronidazole and derivatives thereof). Non-limiting examples of growth factors include epithelial growth factor, platelet derived growth factor, and human growth hormone. Non-limiting examples of vitamins include vitamin A, vitamin C and vitamin E. Non-limiting examples of minerals include copper and zinc.

[0026] Nanofibres are often water soluble and therefore unable to sustain in aqueous environments of biomedical applications, such as wound dressings. One method to convert soluble biopolymer nanofibres to insoluble nanofibres involves complexing the biopolymer with calcium (II) ions to generate calcium-biopolymer nanofibres. Calcium-biopolymer nanofibres

may be formed by ion-exchange between calcium and a cation (e.g., sodium) in a cation-biopolymer complex (e.g., sodium-biopolymer complex). In some embodiments, an ion-exchange reaction is facilitated by soaking biopolymer nanofibres in a calcium treatment solution comprising calcium (II) ions (e.g., calcium (II) ions from calcium salts). In some embodiments, the biopolymer comprises alginate or alginate salts such as sodium alginate. Exemplary calcium salts include, without limitation, calcium chloride, calcium bromide, calcium fluoride, calcium iodide, calcium nitrate, calcium hydride, calcium sulfate, calcium phosphate, calcium oxalate, calcium nitrite, calcium molybdate, calcium benzoate and calcium carbonate. The percentage of calcium (II) ions or calcium salts in the calcium treatment solution, in many embodiments, is from about 0.1% to about 10%, from about 0.1% to about 9%, from about 0.1% to about 8%, from about 0.1% to about 7%, from about 0.1% to about 6%, from about 0.1% to about 5%, from about 0.5% to about 10%, from about 0.5% to about 9%, from about 0.5% to about 8%, from about 0.5% to about 7%, from about 0.5% to about 6%, from about 0.5% to about 5%, or from about 1% to about 5%. In exemplary embodiments, the percentage of calcium (II) ions or calcium salts in the calcium treatment solution is about 0.5%, about 1%, about 1.5%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5, or about 5%. Nanofibres may be treated with a calcium treatment solution for at least about 1 minute, at least about 2 minutes, at least about 3 minutes, at least about 4 minutes, at least about 5 minutes, at least about 6 minutes, at least about 7 minutes, at least about 8 minutes, at least about 9 minutes, at least about 10 minutes, at least about 12 minutes, at least about 15 minutes, or at least about 20 minutes. In some instances, nanofibres are treated with a calcium treatment solution for less than about 30 minutes, less than about 25 minutes, less than about 20 minutes, less than about 15 minutes, or less than about 10 minutes. In one example, nanofibres are treated with a calcium treatment solution for 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 11 minutes, 12 minutes, 13 minutes, 14 minutes, or 15 minutes.

[0027] In some embodiments, nanofibre insolubility is maintained by dissolving the calcium (II) ions in an organic solvent or an organic miscible solvent to produce the calcium treatment solution. Organic solvents or organic miscible solvents include, without limitation, ethanol, acetic acid, acetone, acetonitrile, benzene, 1-butanol, 2-butanol, 2-butanone, t-butyl alcohol, carbon tetrachloride, chlorobenzene, chloroform, cyclohexane, 1,2-dichloroethane, diethylene glycol, diethyl ether, diglyme (diethylene glycol dimethyl ether), 1,2-dimethoxy-ethane (glyme, DME), dimethyl-formamide (DMF), dimethyl sulfoxide (DMSO), 1,4-dioxane, ethyl acetate, ethylene glycol, glycerin, heptane, Hexamethylphosphoramide (HMPA), Hexamethylphosphorous triamide (HMPT), hexane, methanol, methyl t-butyl ether (MTBE),

methylen chloride, N-methyl-2-pyrrolidinone (NMP), nitromethane, pentane, 1-propanol, 2-propanol, tetrahydrofuran (THF), toluene, triethyl amine, heavy water, and any solutions (e.g., 50% organic solvent, 90% organic solvent) or combinations thereof. In one example, the calcium treatment solution comprises calcium (II) ions (e.g., calcium (II) ions from CaCl_2) dissolved in ethanol (e.g., ethanol absolute or >98% ethanol).

[0028] Antibacterial Nanofibres

[0029] The nanofibres described herein are receptive to complexing or retaining antimicrobial agents, e.g., antimicrobials such as silver. In some embodiments, nanofibres, such as as-spun nanofibres comprising a biopolymer, are chemically treated with an antibacterial treatment solution to generate antibacterial nanofibres. In some embodiments, the nanofibres for antibacterial treatment are produced by electrospinning a solution comprising a biopolymer and optionally one or more carrier polymers and/or surfactants. In some embodiments, the nanofibres are washed prior to antibacterial treatment. In some embodiments, the nanofibres are washed with a solution comprising an organic solvent, for example, ethanol. In some embodiments, the nanofibres are treated with a solution to render the nanofibres insoluble prior to antibacterial treatment. In some examples, the biopolymer comprises alginate. In some examples, the antibacterial treatment solution comprises silver. In some examples, the solution rendering the nanofibres insoluble comprises calcium (II) ions.

[0030] In some instances, nanofibres for antibacterial chemical treatment are nanofibres or nanofibrous mats in a wound dressing or a dressing structure. A dressing structure includes any structural component of a wound dressing, for example, a nanofibrous mat, a backing, an absorptive layer, and any combination thereof. A nanofibrous structure or nanofibre structure, in many instances, includes a nanofibrous mat. In other instances, a nanofibrous structure of nanofibre structure comprises nanofibres (including, in some cases, a nanofibrous mat) and a structural support, e.g., a backing.

[0031] In various embodiments, nanofibres are chemically treated, e.g., by soaking, with a silver treatment solution comprising silver (I) ions, resulting in nanofibres incorporated with silver. In some embodiments, during silver treatment, silver (I) ions are ion-exchanged with cations complexed to the biopolymers of the nanofibres to generate silver-biopolymer complexes. In exemplary embodiments, silver (I) ions are ion-exchanged with cations in cation-alginate nanofibres to generate cation-alginate complexes, wherein the cations are optionally sodium (I) ions. In some embodiments, silver (I) ions are ion-exchanged with calcium (II) ions in calcium-alginate nanofibres to generate silver-alginate complexes. In some instances, silver (I) ions are complexed with calcium-alginate nanofibres to generate silver-alginate-calcium complexes. In

some embodiments, silver (I) ions from the silver treatment solution are precipitated as particles within nanofibres, for example, by the generation of insoluble silver salts (e.g., silver chloride). In exemplary embodiments, nanofibres are sequentially treated with a calcium solution and a silver treatment solution. In some embodiments, nanofibres are washed with a solution (e.g., organic solvent) suitable for removing one or more non-biopolymer components (e.g., carriers, surfactants) in the nanofibres prior to chemical treatment with a calcium solution, silver solution or both calcium and silver solutions. Nanofibres incorporated with silver (I) ions are antibacterial nanofibres, at least in some instances.

[0032] In some embodiments, a silver treatment solution comprises a silver salt including, but not limited to silver nitrate, silver chloride, silver sulfate, silver lactate, silver bromide, silver acetate, any silver salt miscible or soluble in an organic solvent, and any combination thereof.

[0033] In some embodiments, the silver treatment solution comprises from about 0.1% to about 5%, from about 0.1% to about 4%, from about 0.1% to about 3%, from about 0.1% to about 2%, from about 0.2% to about 5%, from about 0.2% to about 4%, from about 0.2% to about 3%, from about 0.2% to about 2%, from about 0.3% to about 2%, from about 0.4% to about 2%, or from about 0.5% to about 1% silver (I) ions. In exemplary embodiments, the percentage of silver (I) ions in the silver treatment solution is about 0.5%, about 1%, about 1.5%, about 2%, about 2.5%, about 3%, about 3.5%, about 4%, about 4.5%, or about 5%. The silver treatment solution is preferably a solution of silver (I) ions dissolved in a solution that maintains the structural integrity of the nanofibres, i.e., does not dissolve the nanofibres within a reasonable period of time, e.g., 24 hours. In one example, the silver treatment solution comprises silver (I) ions dissolved in a solution comprising an organic solvent, such as ethanol. Nanofibres may be treated with a silver treatment solution for at least about 1 minute, at least about 2 minutes, at least about 3 minutes, at least about 4 minutes, at least about 5 minutes, at least about 6 minutes, at least about 7 minutes, at least about 8 minutes, at least about 9 minutes, at least about 10 minutes, at least about 12 minutes, at least about 15 minutes, or at least about 20 minutes. In some instances, nanofibres are treated with a silver treatment solution for less than about 30 minutes, less than about 25 minutes, less than about 20 minutes, less than about 15 minutes, or less than about 10 minutes. In one example, nanofibres are treated with a silver treatment solution for 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 11 minutes, 12 minutes, 13 minutes, 14 minutes, or 15 minutes.

[0034] Properties of Antibacterial Nanofibres

[0035] In various aspects, provided herein are antibacterial nanofibres suitable for use in a wound dressing, wherein the antibacterial nanofibres are prepared by chemically treating

biopolymer nanofibres. In various instances, the antibacterial nanofibres are prepared from as-spun nanofibres comprising a biopolymer and optionally a carrier and/or surfactant. In exemplary embodiments, the as-spun nanofibres comprise alginate, and optionally PEO and/or TritonTM X-100. In some embodiments, the as-spun nanofibres are treated with antimicrobial ions, for example, with a silver treatment solution, to generate the antibacterial nanofibres. In some embodiments, the as-spun nanofibres are treated with a solution configured to render the nanofibres insoluble in aqueous solution. In some embodiments, the as-spun nanofibres are treated with a calcium treatment solution prior to treatment with antimicrobial ions. The chemical composition of the antibacterial nanofibres, as well as its properties for functioning in a wound dressing (e.g., absorptivity, antimicrobial content, structural stability) are dependent, in whole or in part, on the identities and concentrations of nanofibre components prior to and after one or more treatments, as well as the identities and concentrations of reactive agents in nanofibre treatment solutions (e.g., calcium treatment solution, silver treatment solution).

[0036] Chemically treated nanofibres, as used herein, refer to nanofibres treated with a solution for rendering the nanofibres insoluble, (e.g., calcium solution), an antimicrobial solution (e.g., silver solution), or a combination thereof.

[0037] The chemical composition of antibacterial nanofibres treated with silver is dependent, at least in part, on the percentage of silver (I) ions in the silver treatment solution. In some embodiments, silver (I) ions comprises from about 5% to about 75%, from about 10% to about 75%, from about 15% to about 75%, from about 20% to about 75%, from about 25% to about 75%, from about 30% to about 75%, from about 35% to about 75%, from about 40% to about 75%, from about 45% to about 75%, from about 50% to about 75%, from about 50% to about 70%, or from about 50% to about 65% of the weight of the antibacterial nanofibres that is not attributed to elemental carbon. In some examples, the percentage of silver (I) in the treated antibacterial nanofibres is less than about 65%, less than about 60%, less than about 55%, less than about 50%, less than about 45%, less than about 40%, less than about 35%, less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, less than about 5%, or less than about 1% of the weight of the antibacterial nanofibres not attributed to elemental carbon. In other or additional examples, the percentage of silver (I) in the treated antibacterial nanofibres is greater than about 0.1%, greater than about 0.5%, greater than about 1%, greater than about 2%, greater than about 3%, greater than about 4%, greater than about 5%, greater than about 6%, greater than about 7%, greater than about 8%, greater than about 9%, greater than about 10%, greater than about 15%, greater than about 20%, greater than about

25%, or greater than about 50% of the weight of the antibacterial nanofibres not attributed to elemental carbon.

[0038] In various embodiments, silver (I) ions in antibacterial nanofibres are complexed with biopolymers (e.g., alginate), precipitated with anionic salts (e.g., chloride), or a combination thereof. In some embodiments, the silver (I) ions in the antibacterial nanofibres are released by ion exchange in an aqueous environment comprising salts, for example, a wound. In some examples, silver (I) ions exchanged into the aqueous environment are silver (I) ions that were complexed with biopolymers (e.g., alginate) in the nanofibres.

[0039] The chemical composition of antibacterial nanofibres that have been treated with calcium is dependent, at least in part, on the percentage of calcium (II) ions in the calcium treatment solution. In some embodiments, the percentage of calcium (II) in the treated antibacterial nanofibres is from about 1% to about 50%, from about 2% to about 20%, preferably less than about 20%, more preferably less than about 15% of the weight of the antibacterial nanofibres not attributed to elemental carbon.

[0040] In some embodiments, calcium in the antibacterial nanofibres, upon contact with a wound, is ion-exchanged with sodium ions in the wound to act as a hemostatic agent for facilitating wound healing. In some examples, a nanofibre comprising calcium-alginate participates in an ion-exchange with sodium in a wound to generate a sodium alginate gel. This sodium alginate gel is useful for maintaining a moist healing microenvironment for the wound.

[0041] In some embodiments, the percentage of oxygen in the treated antibacterial nanofibres is from about 5% to about 50%, preferably from about 10% to about 25%, or more preferably from about 15% to about 25% of the weight of the antibacterial nanofibres not attributed to elemental carbon.

[0042] In some embodiments, the antibacterial nanofibres have been treated with a solution of calcium chloride. In these instances, the concentration of chloride in the treated nanofibres is from about 1% to about 25% or is less than 1%. In some embodiments, the concentration of chloride in the treated antibacterial nanofibres is from about 1% to about 20%, from about 3% to about 20%, from about 5% to about 20%, from about 1% to about 10%, from about 2% to about 10%, from about 3% to about 10%, or from about 5% to about 10%. In some embodiments, the concentration of chloride in the treated antibacterial nanofibres is less than about 20%, less than about 15%, less than about 10%, less than about 9%, less than about 8%, less than about 7%, less than about 6%, or less than about 5%. In exemplary embodiments, the concentration of chloride in the treated antibacterial nanofibres is between 1% and 10% of the weight of the antibacterial nanofibres not attributed to elemental carbon.

[0043] In some embodiments, the antibacterial nanofibres are derived from chemically treated sodium-alginate nanofibres. In some embodiments, the concentration of sodium in the treated nanofibres is from about 1% to about 20% or is less than 1% of the weight of the antibacterial nanofibres not attributed to elemental carbon. In some embodiments, the concentration of sodium in the treated nanofibres is from about 1% to about 15%, from about 1% to about 10%, from about 1% to about 9%, from about 1% to about 8%, from about 1% to about 7%, from about 1% to about 6%, from about 1% to about 5%, from about 2% to about 10%, or from about 2% to about 5% of the weight of the antibacterial nanofibres not attributed to elemental carbon. In some embodiments, the concentration of sodium in the treated nanofibres is less than about 10%, less than about 9%, less than about 8%, less than about 7%, less than about 6%, or less than about 5%. In exemplary embodiments, the concentration of sodium in the treated nanofibres is between 1% and 5% of the weight of the antibacterial nanofibres not attributed to elemental carbon.

[0044] In some embodiments, the antibacterial nanofibres are derived from as-spun nanofibres prepared by electrospinning a solution comprising a biopolymer and a carrier polymer. In some embodiments, the carrier polymer is PEO. In many instances, the antibacterial nanofibres do not comprise detectable traces of carrier polymer. For example, the carrier polymer is not detected in a nanofibre by spectroscopic techniques such as infrared spectroscopy. In some embodiments, at least 90%, at least 95%, or at least 99% of the carrier polymer is not present in the antibacterial nanofibres.

[0045] In various embodiments, the morphology of the nanofibres changes after chemical treatment. For example, the average fibre diameters decrease or increase depending on the type of chemical treatment. In some examples, sequential treatment with calcium and silver solutions results in antibacterial nanofibres having smaller average fibre diameters than the nanofibres from which they were derived. In some embodiments, chemical treatment results in nanofibres having between a 1% and a 50% decrease in average fibre diameter. In some embodiments, the decrease in average fibre diameter is between about 1% and about 20%, between about 1% and about 10%, between about 1% and about 9%, between about 1% and about 8%, between about 2% and about 10%, between about 2% and about 9%, between about 2% and about 8%, or between about 3% and about 8%. In some embodiments, the decrease in average fibre diameter is less than about 10%, less than about 9%, less than about 8%, less than about 7%, less than about 6%, less than about 5%, less than about 4%, less than about 3%, less than about 2%, or less than about 1%. In some embodiments, the average fibre diameter does not substantially decrease after chemical treatment. In some embodiments, the average fibre diameter increases

after chemical treatment. In some embodiments, the average fibre diameter of chemically treated antibacterial nanofibres is from about 30 nm to about 500 nm, from about 60 nm to about 440 nm, from about 80 nm to about 200 nm, from about 100 nm to about 160 nm, from about 110 nm to about 150, from about 120 nm to about 150 nm, from about 125 nm to about 145 nm, or from about 125 nm to about 140 nm. In some embodiments, the antibacterial nanofibres were derived from sodium-alginate nanofibres, wherein the sodium-alginate nanofibres were optionally produced by electrospinning a solution comprising sodium alginate and PEO.

[0046] In some instances, treatment of nanofibres with an antibacterial agent results in antibacterial nanofibres having a wider fibre diameter distribution than nanofibres prior to treatment. In some embodiments, the nanofibres were sequentially treated with calcium and silver solutions. In some embodiments, at least about 75% of antibacterial nanofibres have fibre diameters between about 80 nm and about 200 nm, or between about 80 nm and about 160 nm. In some embodiments, at least about 50% of antibacterial nanofibres have fibre diameters between about 80 nm and 160 nm or between about 100 nm and about 140 nm.

[0047] In some instances, treatment of nanofibres with an antibacterial agent results in breakage of one or more nanofibres in a nanofibre structure. In some embodiments, the nanofibres were sequentially treated with calcium and silver solutions. In some embodiments, nanofibre breakage is correlated, at least in part, to the concentration of calcium (II) ions in a calcium treatment solution. For example, a nanofibre structure treated with a 5% solution of CaCl_2 has more broken nanofibres than a nanofibre structure treated with 1-4% solution of CaCl_2 , e.g., a 1% solution of CaCl_2 .

[0048] In some instances, treatment of nanofibres in a nanofibre structure with an antibacterial agent results in an antibacterial nanofibre structure comprising a plurality of spherical particles. In some embodiments, the nanofibres were sequentially treated with calcium and silver solutions. In some embodiments, the spherical particles comprise elemental silver and/or silver (I) ions, wherein the silver (I) ions are optionally precipitated, for example, with chloride or another anionic salt during the treatment process. In some embodiments, the spherical particles have diameters from about 100 nm to about 350 nm or from about 150 nm to about 300 nm. In another embodiment, the average diameter of spherical particles is from about 180 nm to about 250 nm, from about 190 nm to about 230 nm, or from about 200 nm to about 220 nm, wherein the standard deviation is from about 10 nm to about 50 nm.

[0049] In some instances, treatment of nanofibres with an antibacterial agent results in antibacterial nanofibres having increased resistance to solubility in aqueous environments as compared to the nanofibres from which they were derived. In some embodiments, the

nanofibres were sequentially treated with calcium and silver solutions. For example, the antibacterial nanofibres remain intact after solubility tests are performed in accordance with BS EN 13726-1:2002 section 3.7 dispersion and solubility of hydrogel dressings in water. In some embodiments, antibacterial nanofibres soaked in water or a simulated test solution (STS) remain insoluble for at least 120 minutes at room temperature (e.g., between about 20 °C and 25 °C). In some embodiments, antibacterial nanofibres soaked in water remain insoluble for at least 2 hours, at least 3 hours, at least 4 hours, at least 5 hours, at least 6 hours, at least 7 hours, at least 8 hours, at least 9 hours, at least 10 hours, at least 11 hours, at least 12 hours, at least 24 hours, or at least 48 hours. Insolubility of the soaked antibacterial nanofibres may be assessed by visual inspection. An exemplary STS is an aqueous solution comprising serum and one or more salts to mimic wound exudate. In one example, STS comprises 0.4 M sodium chloride, 0.02 M calcium chloride and 10% newborn calf serum.

[0050] Nanofibre Compositions

[0051] In various aspects, provided herein are antibacterial nanofibres suitable for use in a wound dressing, wherein the antibacterial nanofibres are prepared by chemically treating biopolymer nanofibres. In various instances, the antibacterial nanofibres are prepared from as-spun nanofibres comprising a biopolymer and optionally a carrier and/or surfactant. In some embodiments, the biopolymer comprises alginate. In some embodiments, the carrier comprises PEO. In some embodiments, the surfactant is TritonTM X-100. The nanofibres, e.g., as-spun nanofibres, are treated with antimicrobial ions, for example, with a silver treatment solution, to generate the antibacterial nanofibres. In some embodiments, the nanofibres are treated with a solution configured to render the nanofibres insoluble in aqueous solution. In some embodiments, the as-spun nanofibres are treated with a calcium treatment solution prior to treatment with antimicrobial ions.

[0052] The antibacterial nanofibres provided herein, in various embodiments, are combined with one or more elements of a wound dressing and/or are further treated with one or more agents useful in a wound dressing. In some embodiments, an agent useful in a wound dressing is a malodor absorbing agent, such as cyclodextrin.

[0053] In some embodiments, nanofibres are combined with a backing to form a composite dressing structure or nanofibrous dressing structure. In some embodiments, the nanofibres are antibacterial nanofibres. In some embodiments, the nanofibres are combined with a backing and then chemically treated to generate antibacterial nanofibres within a nanofibrous dressing structure. The composite dressing structure is suitable for use as a wound dressing or as a component of a wound dressing. A suitable backing is a mechanically stable material useful for

constructing a wound dressing. A suitable backing includes, without limitation, a nonwoven backing comprising, for example, carboxymethylcellulose (CMC). In some embodiments, nanofibres are electrospun onto a backing. In some embodiments, nanofibres or nanofibre structures are attached to a backing. In some embodiments, nanofibres are disposed between a backing and another wound dressing component or layer. In various cases, the nanofibres are alginate nanofibres, for example, as-spun alginate nanofibres. In some embodiments, the backing is useful for absorbing wound exudates, providing a barrier from bacterial penetration and foreign contamination, allowing oxygen balance in the wound, assisting in cell growth, or any combination thereof.

[0054] In various embodiments, nanofibrous dressing structures are chemically treated to generate insoluble nanofibres (e.g., calcium treatment). In some embodiments, nanofibrous dressing structures are chemically treated to generate antibacterial nanofibres (e.g., silver treatment). In some embodiments, a nanofibrous dressing structure is chemically treated with sequential solutions of calcium and silver. In some embodiments, nanofibres are chemically treated with sequential solutions of calcium and silver and then deposited, attached, or otherwise combined with a backing to generate an antibacterial nanofibrous dressing structure. In some examples, the nanofibrous dressing structures comprise nanofibres and a backing. In some examples, the nanofibres are alginate nanofibres, for example, as-spun alginate nanofibres.

[0055] In various embodiments, an antibacterial nanofibrous dressing structure is prepared by a) depositing a biopolymer solution onto a backing to generate a nanofibrous structure, b) contacting the nanofibrous structure with a calcium solution to generate calcium-biopolymer nanofibres, and c) contacting the calcium-biopolymer nanofibres with a silver solution to generate an antibacterial nanofibrous dressing structure comprising silver-biopolymer nanofibres. In some instances, the biopolymer solution is deposited onto the backing by electrospinning. In some instances, the biopolymer solution is electrospun to form as-spun nanofibres. In some instances, the biopolymer solution comprises a biopolymer and optionally a carrier and/or surfactant. In some examples, the biopolymer comprises alginate. In some cases, the carrier is PEO. In some cases, the surfactant is TritonTM X-100. In some embodiments, the nanofibrous structure is washed with an organic solvent prior to contacting with the calcium solution. In some embodiments, the calcium solution comprises calcium (II) ions dissolved in an organic solvent, e.g., ethanol. In some embodiments, the silver solution comprises silver (I) ions dissolved in an organic solvent, e.g., ethanol. In various implementations, the method further comprises contacting the antibacterial nanofibrous dressing structure with an organic solvent to remove precipitated and unreacted salts. In some implementations, the method further

comprises drying the antibacterial nanofibrous dressing structure. In some embodiments, the backing comprises CMC. In various implementations, the antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0056] In some embodiments, an antibacterial nanofibrous dressing structure is prepared by a) combining nanofibres with a backing to generate a nanofibrous structure, b) contacting the nanofibrous structure with a calcium solution to generate calcium-complexed nanofibres, and c) contacting the calcium-complexed nanofibres with a silver solution to generate an antibacterial nanofibrous dressing structure comprising silver-complexed nanofibres. In some embodiments, the nanofibres are as-spun nanofibres. In some embodiments, the nanofibres comprise a biopolymer and optionally a carrier and/or surfactant. In some embodiments, the nanofibres are as-spun from a solution comprising a biopolymer and optionally a carrier and/or surfactant. In some examples, the biopolymer comprises alginate. In some cases, the carrier is PEO. In some cases, the surfactant is TritonTM X-100. In some embodiments, the nanofibrous structure is washed with an organic solvent prior to contacting with the calcium solution. In some embodiments, the calcium solution comprises calcium (II) ions dissolved in an organic solvent, e.g., ethanol. In some embodiments, the silver solution comprises silver (I) ions dissolved in an organic solvent, e.g., ethanol. In various implementations, the method further comprises contacting the antibacterial nanofibrous dressing structure with an organic solvent to remove precipitated and unreacted salts. In some implementations, the method further comprises drying the antibacterial nanofibrous dressing structure. In some embodiments, the backing comprises CMC. In various implementations, the antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0057] In some embodiments, an antibacterial nanofibrous dressing structure is prepared by a) chemically treating nanofibres with an antibacterial agent to generate antibacterial nanofibres and b) combining the antibacterial nanofibres with a backing. In some cases, the nanofibres are chemically treated by i) application of a solution rendering the nanofibres insoluble and ii) application of a solution comprising an antibacterial agent. In some embodiments, the antibacterial agent is silver. In some embodiments, the backing comprises CMC. In various implementations, the antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0058] In some embodiments, a nanofibrous structure described herein is treated with a calcium solution. In some embodiments, a nanofibrous structure comprises a backing comprising CMC. In some examples, a nanofibrous structure comprising CMC has been treated with a calcium solution, resulting in calcium-CMC complexes. In some embodiments, a nanofibrous structure comprises alginate nanofibres, wherein treatment of the nanofibres (prior to after combining with a backing) with a calcium solution results in calcium-alginate complexes. In some instances, calcium-CMC complexes and/or calcium-alginate complexes occur through ion-exchange. These ion-exchange reactions may be equilibrium reactions, with a constant flux of ion exchange.

[0059] In some embodiments, a nanofibrous structure described herein is treated with a silver solution. In some embodiments, a nanofibrous structure comprises a backing comprising CMC. In some examples, a nanofibrous structure comprising CMC has been treated with a silver solution, resulting in silver-CMC complexes. In some embodiments, a nanofibrous structure comprises alginate nanofibres, wherein treatment of the nanofibres (prior to or after combining with a backing) with a silver solution results in silver-alginate complexes. In some instances, silver-CMC complexes and/or silver-alginate complexes occur through ion-exchange. These ion-exchange reactions may be equilibrium reactions, with a constant flux of ion exchange.

[0060] In various embodiments, nanofibres (including nanofibrous mats, nanofibres in nanofibrous structures, nanofibres in a wound dressing or wound dressing component) are combined with or coated with a malodor absorbing agent to generate nanofibres having malodor absorption properties. In some cases, the nanofibres are antibacterial nanofibres. In some cases, the nanofibres are combined or coated with a malodor absorbing agent and then treated to generate antibacterial nanofibres having malodor absorption properties. Malodorous nanofibres are useful as a component in a nanofibrous wound dressing. Exemplary malodor absorbing agents include cyclodextrins. In some embodiments, the malodor absorbing agent is electrospun onto the nanofibres. In some embodiments, the malodor absorbing agent is electrosprayed onto the nanofibres. In some embodiments, the malodor absorbing agent is attached to or placed next to the nanofibres, for example, as layers in a wound dressing.

[0061] An exemplary malodor absorbing agent comprises a cyclodextrin. Cyclodextrins include α -, β -, γ -cyclodextrins and combinations thereof. In some embodiments, the malodor absorbing agent is hydroxypropyl- β -cyclodextrin (HP- β -CD).

[0062] In various embodiments, an anti-odor, antibacterial nanofibrous dressing structure is prepared by a) depositing a biopolymer solution onto a backing to generate a nanofibrous structure, b) contacting the nanofibrous structure with a calcium solution to generate calcium-

biopolymer nanofibres, c) contacting the calcium-biopolymer nanofibres with a silver solution to generate an antibacterial nanofibrous structure comprising silver-biopolymer nanofibres, and d) depositing a malodor absorbing agent onto a surface of the antibacterial nanofibrous structure to generate an anti-odor, antibacterial nanofibrous dressing structure. In some instances, the biopolymer solution is deposited onto the backing by electrospinning. In some instances, the biopolymer solution is electrospun to form as-spun nanofibres. In some instances, the biopolymer solution comprises a biopolymer and optionally a carrier and/or surfactant. In some examples, the biopolymer comprises alginate. In some cases, the carrier is PEO. In some cases, the surfactant is TritonTM X-100. In some embodiments, the nanofibrous structure is washed with an organic solvent prior to contacting with the calcium solution. In some embodiments, the calcium solution comprises calcium (II) ions dissolved in an organic solvent, e.g., ethanol. In some embodiments, the silver solution comprises silver (I) ions dissolved in an organic solvent, e.g., ethanol. In various implementations, the method further comprises contacting the antibacterial nanofibrous dressing structure with an organic solvent to remove precipitated and unreacted salts. In some implementations, the method further comprises drying the antibacterial nanofibrous dressing structure. In some embodiments, the backing comprises CMC. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospinning. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospraying. In some examples, the malodor absorbing agent is a cyclodextrin, such as HP- β -CD. In various implementations, the anti-odor, antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0063] In some embodiments, an anti-odor, antibacterial nanofibrous dressing structure is prepared by a) combining nanofibres with a backing to generate a nanofibrous structure, b) contacting the nanofibrous structure with a calcium solution to generate calcium-complexed nanofibres, c) contacting the calcium-complexed nanofibres with a silver solution to generate an antibacterial nanofibrous structure comprising silver-complexed nanofibres, and d) depositing a malodor absorbing agent onto a surface of the antibacterial nanofibrous structure to generate an anti-odor, antibacterial nanofibrous dressing structure. In some embodiments, the nanofibres are as-spun nanofibres. In some embodiments, the nanofibres comprise a biopolymer and optionally a carrier and/or surfactant. In some embodiments, the nanofibres are as-spun from a solution comprising a biopolymer and optionally a carrier and/or surfactant. In some examples, the biopolymer comprises alginate. In some cases, the carrier is PEO. In some cases the surfactant is TritonTM X-100. In some embodiments, the nanofibrous structure is washed with an organic

solvent prior to contacting with the calcium solution. In some embodiments, the calcium solution comprises calcium (II) ions dissolved in an organic solvent, e.g., ethanol. In some embodiments, the silver solution comprises silver (I) ions dissolved in an organic solvent, e.g., ethanol. In various implementations, the method further comprises contacting the antibacterial nanofibrous dressing structure with an organic solvent to remove precipitated and unreacted salts. In some implementations, the method further comprises drying the antibacterial nanofibrous dressing structure. In some embodiments, the backing comprises CMC. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospinning. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospraying. In some examples, the malodor absorbing agent is a cyclodextrin, such as HP- β -CD. In various implementations, the anti-odor, antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0064] In some embodiments, an anti-odor, antibacterial nanofibrous dressing structure is prepared by a) chemically treating nanofibres with an antibacterial agent to generate antibacterial nanofibres, b) combining the antibacterial nanofibres with a backing to generate an antibacterial nanofibrous structure, and c) depositing a malodor absorbing agent onto a surface of the antibacterial nanofibrous structure to generate an anti-odor, antibacterial nanofibrous dressing structure. In some cases, the nanofibres are chemically treated by i) application of a solution rendering the nanofibres insoluble and ii) application of a solution comprising an antibacterial agent. In some embodiments, the antibacterial agent is silver. In some embodiments, the backing comprises CMC. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospinning. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibrous structure by electrospraying. In some examples, the malodor absorbing agent is a cyclodextrin, such as HP- β -CD. In various implementations, the anti-odor, antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0065] In some embodiments, an anti-odor, antibacterial nanofibrous dressing structure is prepared by a) chemically treating nanofibres with an antibacterial agent to generate antibacterial nanofibres, b) depositing a malodor absorbing agent onto a surface of the antibacterial nanofibres to generate anti-odor antibacterial nanofibres, and c) combining the anti-odor antibacterial nanofibres with a backing to generate an anti-odor, antibacterial nanofibrous dressing structure. In some cases, the nanofibres are chemically treated by i) application of a

solution rendering the nanofibres insoluble and ii) application of a solution comprising an antibacterial agent. In some embodiments, the antibacterial agent is silver. In some embodiments, the backing comprises CMC. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibres by electrospinning. In some instances, the malodor absorbing agent is deposited onto the antibacterial nanofibres by electrospraying. In some examples, the malodor absorbing agent is a cyclodextrin, such as HP- β -CD. In various implementations, the anti-odor, antibacterial nanofibrous dressing structure is combined with one or more additional wound dressing components and or wound dressing additives to generate a wound dressing.

[0066] In some embodiments, nanofibres are electrosprayed with a solution comprising a malodor absorbing agent. These nanofibres include, without limitation, nanofibrous mats, nanofibres in nanofibrous structures and nanofibres in a wound dressing or a wound dressing component. Nanofibrous structures include, without limitation, nanofibrous structures comprising nanofibres and a backing (e.g., a CMC comprising backing). These nanofibres also include antibacterial nanofibres described herein (e.g., silver treated nanofibres). In some embodiments, the nanofibres comprise alginate. In some embodiments, the malodor absorbing agent is HP- β -CD. The solution comprising a malodor absorbing agent (e.g., HP- β -CD) may comprise between about 1% and about 90%, between about 5% and about 80%, between about 10% and about 80%, between about 20% and about 80%, between about 20% and about 70%, between about 30% and 80%, between about 30% and 70%, between about 20% and about 60%, between about 20% and about 50%, between about 30% and about 60%, between about 30% and about 50%, or between about 35% to about 45% by weight malodor absorbing agent. In one example, the solution comprising a malodor absorbing agent (e.g., HP- β -CD) comprises 40% by weight malodor absorbing agent. Solution feed rates for electrospraying a solution comprising a malodor absorbing agent (e.g., HP- β -CD) onto nanofibres include, in at least in some embodiments, feed rates between about 0.1 ml/hour to about 5 ml/hour, between about 0.2 ml/hour to about 5 ml/hour, between about 0.3 ml/hour to about 5 ml/hour, between about 0.2 ml/hour to about 4 ml/hour, between about 0.3 ml/hour to about 4 ml/hour, between about 0.3 ml/hour to about 3 ml/hour, between about 0.3 ml/hour to about 2 ml/hour, between about 0.4 ml/hour to about 5 ml/hour, between about 0.4 ml/hour to about 4 ml/hour, between about 0.4 ml/hour to about 3 ml/hour, between about 0.4 ml/hour to about 2 ml/hour, between about 0.5 ml/hour to about 5 ml/hour, between about 0.5 ml/hour to about 4 ml/hour, between about 0.5 ml/hour to about 3 ml/hour, between about 0.5 ml/hour to about 2 ml/hour, between about 0.8 ml/hour to about 1.5 ml/hour, or between about 0.8 ml/hour to about 1.2 ml/hour. In one

example, the feed rate is about 1.0 ml/hour. A working distance for electrospraying a solution comprising a malodor absorbing agent (e.g., HP- β -CD) onto nanofibres include, in at least in some embodiments, a distance between about 10 cm and about 30 cm, between about 10 cm and about 25 cm, between about 10 cm and about 20 cm, between about 12 cm and about 20 cm, between about 10 cm and about 18 cm, between about 12 cm and about 18 cm. In one example, the working distance from the syringe of the electrospray device to the nanofibres is about 16 cm. In some embodiments, the solution comprising a malodor absorbing agent (e.g., HP- β -CD) is electrosprayed with an applied voltage between 2 kV and 30 kV, between 4 kV and 25 kV, between 4 kV and 20 kV, between 5 kV and 25 kV, between 5 kV and 20 kV, between 7 kV and 20 kV, or between 7 kV and 15 kV. In one example, a solution comprising a malodor absorbing agent (e.g., HP- β -CD) is electrosprayed with an applied voltage of about 12 kV. In some embodiments, the amount of a solution comprising a malodor absorbing agent (e.g., HP- β -CD) electrosprayed onto an antibacterial nanofibre structure having a size less than about 500 cm², less than about 400 cm², less than about 300 cm², less than about 200 cm², less than about 100 cm², or less than about 50 cm², is from about 0.5 ml to about 30 ml, from about 0.5 ml to about 25 ml, from about 0.5 ml to about 20 ml, from about 0.5 ml to about 15 ml, from about 0.5 ml to about 10 ml, from about 0.5 ml to about 8 ml, from about 0.5 ml to about 5 ml, or from about 1 ml to about 5 ml solution comprising a malodor absorbing agent. The time to electrospray a solution comprising a malodor absorbing agent (e.g., HP- β -CD) onto nanofibres may be from about 30 minutes to 6 hour, from about 1 hour to about 4 hour. In some embodiments, the electrospray time is 1 hour, 2 hours, or 4 hours. In some embodiments, the electrosprayed malodor absorbing agent (e.g., HP- β -CD) generates fibres. In some embodiments, the average malodorous fibre diameter depositing by electrospraying onto nanofibres is from about 300 nm to about 1,800 nm, from about 400 nm to about 1,600 nm, from about 500 nm to about 1,500 nm, from about 500 nm to about 1,200 nm, from about 500 nm to about 1,000 nm, from about 600 nm to about 1,000 nm, from about 600 nm to about 900 nm, or from about 700 nm to about 900 nm. In one example, the average electrosprayed malodor absorbing agent fibre diameter is about 850 nm.

[0067] In some embodiments, nanofibres are deposited with an electrospun solution comprising a malodor absorbing agent. These nanofibres include, without limitation, nanofibrous mats, nanofibres in nanofibrous structures and nanofibres in a wound dressing or a wound dressing component. Nanofibrous structures include, without limitation, nanofibrous structures comprising nanofibres and a backing (e.g., a CMC comprising backing). These nanofibres also include antibacterial nanofibres described herein (e.g., silver treated nanofibres). In some

embodiments, the nanofibres comprise alginate. In some embodiments, the malodor absorbing agent is HP- β -CD. In some embodiments, the solution comprising a malodor absorbing agent (e.g., HP- β -CD) further comprises a carrier, for example, PEO. The solution comprising a malodor absorbing agent may comprise between about 1% and about 70%, between about 1% and about 60%, between about 1% and about 50%, between about 1% and about 40%, between about 1% and about 30%, between about 1% and 20%, between about 1% and 15%, between about 2% and about 15%, or between about 4% and about 12% by weight malodor absorbing agent. In some examples, the solution comprising a malodor absorbing agent comprises 40% by weight malodor absorbing agent. In some embodiments, the solution comprising a malodor absorbing agent comprises a malodor absorbing agent and a carrier. In some embodiments, the solution comprising a malodor absorbing agent has a malodor absorbing agent:carrier ratio of 30-95 agent to 70-5 carrier, 40-90 agent to 60-10 carrier, 50-90 agent to 50-10 carrier. In some embodiments, the agent:carrier ratio is 50:50, 60:40, 70:30, 80:20 or 90:10. Solution feed rates for electrospinning a solution comprising a malodor absorbing agent onto nanofibres include, in at least in some implementations, feed rates between about 0.1 ml/hour to about 5 ml/hour, between about 0.2 ml/hour to about 5 ml/hour, between about 0.3 ml/hour to about 5 ml/hour, between about 0.2 ml/hour to about 4 ml/hour, between about 0.3 ml/hour to about 4 ml/hour, between about 0.3 ml/hour to about 3 ml/hour, between about 0.3 ml/hour to about 2 ml/hour, between about 0.4 ml/hour to about 5 ml/hour, between about 0.4 ml/hour to about 4 ml/hour, between about 0.4 ml/hour to about 3 ml/hour, between about 0.4 ml/hour to about 2 ml/hour, between about 0.5 ml/hour to about 5 ml/hour, between about 0.5 ml/hour to about 4 ml/hour, between about 0.5 ml/hour to about 3 ml/hour, between about 0.5 ml/hour to about 2 ml/hour, between about 0.8 ml/hour to about 1.5 ml/hour, or between about 0.8 ml/hour to about 1.2 ml/hour. In one example, the feed rate is about 1.0 ml/hour. A working distance for electrospinning a solution comprising a malodor absorbing agent onto nanofibres include, in at least in some implementations, a distance between about 10 cm and about 30 cm, between about 10 cm and about 25 cm, between about 10 cm and about 20 cm, between about 12 cm and about 20 cm, between about 10 cm and about 18 cm, between about 12 cm and about 18 cm. In one example, the working distance from the syringe of the electrospinning device to the nanofibres is about 12 cm. In some embodiments, the solution comprising a malodor absorbing agent is electrospun with an applied voltage between 2 kV and 30 kV, between 4 kV and 25 kV, between 4 kV and 20 kV, between 5 kV and 25 kV, between 5 kV and 20 kV, between 7 kV and 20 kV, or between 7 kV and 15 kV. In one example, the solution comprising a malodor absorbing agent is electrospun with an applied voltage of about 12 kV. In some embodiments, the amount of

solution comprising a malodor absorbing agent electrospun onto a nanofibre structure having a size less than about 500 cm^2 , less than about 400 cm^2 , less than about 300 cm^2 , less than about 200 cm^2 , less than about 100 cm^2 , or less than about 50 cm^2 ; is from about 0.5 ml to about 30 ml, from about 0.5 ml to about 25 ml, from about 0.5 ml to about 20 ml, from about 0.5 ml to about 15 ml, from about 0.5 ml to about 10 ml, from about 0.5 ml to about 8 ml, from about 0.5 ml to about 5 ml, or from about 1 ml to about 5 ml solution comprising a malodor absorbing agent. In some embodiments, the electrospun solution comprising a malodor absorbing agent (HP- β -CD) generates fibres. In some embodiments, the average malodor absorbing agent fibre diameter depositing by electrospinning onto nanofibres is from about 50 nm to about 1,800 nm, from about 50 nm to about 1,500 nm, from about 50 nm to about 1,000 nm, from about 50 nm to about 800 nm, from about 50 nm to about 700 nm, from about 50 nm to about 600 nm, from about 50 nm to about 500 nm, from about 50 nm to about 400 nm, from about 50 nm to about 300 nm, from about 100 nm to about 300 nm, or from about 150 nm to about 300 nm. In one example, the electrospun average malodor absorbing agent fibre diameter is about 200 nm, about 210 nm, about 220 nm, about 230 nm, about 240 nm, about 250 nm, about 260 nm, about 270 nm, about 280 nm, about 290 nm or about 300 nm.

[0068] Throughout this disclosure, various embodiments are presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of any embodiments.

Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range to the tenth of the unit of the lower limit unless the context clearly dictates otherwise.

[0069] The terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting of any embodiment. As used herein, the singular forms “a,” “an” and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. It will be further understood that the terms “comprises” and/or “comprising,” when used in this specification, specify the presence of stated features, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, integers, steps, operations, elements, components, and/or groups thereof. As used herein, the term “and/or” includes any and all combinations of one or more of the associated listed items.

[0070] The following examples are set forth to illustrate more clearly the principle and practice of embodiments disclosed herein to those skilled in the art and are not to be construed as

limiting the scope of any claimed embodiments. Unless otherwise stated, all parts and percentages are on a weight basis.

EXAMPLES

[0071] Example 1: Preparation and characterization of antibacterial nanofibres derived from alginate nanofibres

[0072] Methods of preparing antibacterial nanofibres: Antibacterial nanofibre mats were prepared by chemical modification of as-spun sodium-alginate/PEO nanofibre mats. The as-spun nanofibres were generated by electrospinning an aqueous solution comprising 4% by weight sodium-alginate and PEO in a 70:30 ratio. The resulting as-spun nanofibres were bead free, as shown by Field Gun Emission Scanning Electron Microscopy (SEM) in Figure 1, panel A1. As-spun sodium-alginate/PEO nanofibres were soaked in a petri-dish containing about 25 mL ethanol absolute. The petri-dish was gently shaken for 10 minutes while the PEO dissolved from the nanofibres. The soaked as-spun nanofibres were transferred to a second petri-dish comprising CaCl_2 in ethanol absolute for a second 10 minute soak. This second soak allowed for the exchange of sodium and calcium ions to generate calcium-alginate nanofibres. The calcium-alginate nanofibres were transferred to a third petri-dish comprising AgNO_3 in ethanol absolute for a third 10 minute soak. This third soak provided another ion exchange to generate silver-alginate nanofibres. The silver-alginate nanofibres were washed in ethanol absolute to remove precipitated and unreacted salts and subsequently dried at room temperature (20 °C). The concentrations of CaCl_2 and AgNO_3 used are shown in Table 1.

[0073] Table 1: Reaction conditions for four sets of chemically treated as-spun sodium-alginate/PEO nanofibres.

Sample Nomenclature	Treated with CaCl_2 in ethanol absolute solution		Treated with AgNO_3 in ethanol absolute solution	
	CaCl_2 concentration	Treatment time	AgNO_3 concentration	Treatment time
T0.5/1.0Ag/Ca	1.0%	10 min	0.5%	10 min
T1.0/1.0Ag/Ca	1.0%	10 min	1.0%	10 min
T0.5/5.0Ag/Ca	5.0%	10 min	0.5%	10 min
T1.0/5.0Ag/Ca	5.0%	10 min	1.0%	10 min

[0074] Characterization of antibacterial nanofibres: The morphology and characterization of antibacterial nanofibres were investigated by Field Gun Emission Scanning Electron Microscope

(SEM) and Energy Dispersion X-ray (EDX) (Philips XL30 FEG-SEM) and Fourier Transform Infrared Spectroscopy (FTIR) (NICOLET5700 FT-IR, Thermo Electron Corporation).

[0075] Antibacterial nanofibre mats (0.5cm x 0.5cm) were adhered on a specimen stub by carbon tape specific for SEM. The adhered mats were coated with carbon using *gatan* Precision Etching Coating System (model 682). SEM images were captured at 2,000x, 10,000x, 20,000x magnifications. SEM operating parameters were set at 6 kV accelerating voltage and a spot size of 3. Fibre diameters were manually measured using the line-drawing feature in ImageJ (ImageJ 2004) software from 50 randomly selected fibres in the 10,000x and 20,000x magnification images at 3 different focal points. For EDX analysis, scanning was performed at 2,000x magnification with 10 kV accelerating voltage and a spot size of 3.

[0076] SEM images showing nanofibre morphology before and after chemical treatment are provided in Figure 1 (panels A1-E1). Corresponding fibre size distribution for each nanofibre mat is shown in Figure 1 (panels A2-E2). Figure 1, panel A1 is an image of as-spun sodium-alginate/PEO prior to chemical modification. Figure 1, panel B1 is an image of a silver-alginate nanofibre mat after treatment with 1.0% CaCl₂ and 0.5% AgNO₃. Figure 1, panel C1 is an image of a silver-alginate nanofibre mat after treatment with 1.0 % CaCl₂ and 1.0% AgNO₃. Figure 1, panel D1 is an image of a silver-alginate nanofibre mat after treatment with 5.0% CaCl₂ and 0.5% AgNO₃. Figure 1, panel E1 is an image of a silver-alginate nanofibre mat after treatment with 5.0% CaCl₂ and 1.0% AgNO₃. The nanofibres prior to chemical treatment are more uniform in size than the nanofibres after chemical treatment. The structure of the T0.5/1.0/Ag/Ca and T1.0/1.0/Ag/Ca nanofibres are maintained after treatment, while the T0.05/5.0/Ag/Ca and T1.0/5.0/Ag/Ca have broken nanofibres.

[0077] As shown in Figure 1 (panels A2-E2), the average diameter of the nanofibres decreased after chemical treatment and the fibre size distribution increased after chemical treatment. The average nanofibre diameter of the as-spun sodium-alginate/PEO nanofibre mat prior to chemical treatment is 141 nm with a standard deviation of 29 nm. The average nanofibre diameter of the treated T0.5/1.0Ag/Ca nanofibre mat is 131 nm with a standard deviation of 56 nm. The average nanofibre diameter of the treated T1.0/1.0Ag/Ca nanofibre mat is 130 nm with a standard deviation of 68 nm. The average nanofibre diameter of the treated T0.5/5.0Ag/Ca nanofibre mat is 136 nm with a standard deviation of 71 nm. The average nanofibre diameter of the treated T1.0/5.0Ag/Ca nanofibre mat is 134 nm with a standard deviation of 76 nm.

[0078] The SEM images of the treated and untreated nanofibre mats constructed in this example reveal the appearance of particles throughout the mats after treatment. See Figure 1 (panels A1-E1). As shown in these images, as the concentration of silver in the silver treatment solution

increased from 0.5% to 1.0%, so did the particle size. Likewise, as the concentration of calcium in the calcium treatment solution increased from 1% to 5%, so did the particle size. Nanofibre particle sizes were manually measured using a line-drawing feature in ImageJ (ImageJ 2004) software from 50 randomly selected particles in the 10,000x and 20,000x magnification images of the chemically treated samples. Figure 2 is a graph illustrating the particle size distribution in the four chemically treated nanofibre mats. The average diameter of the measured silver particles is 210 nm with a standard deviation of 32 nm.

[0079] EDX analysis was carried out to determine the composition of non-carbon elements in the four sets of chemically treated nanofibre mats, the results of which are shown in Table 2. The percentage of silver in the nanofibres decreases in proportion to an increase in the percentage of calcium (II) ions in the calcium treatment solution.

[0080] Table 2: Elemental composition in the four sets of silver-alginate nanofibres as determined by EDX.

Sample	Silver (Ag)	Calcium (Ca)	Sodium (Na)	Chlorine (Cl)	Oxygen (O)
T0.5/1.0Ag/Ca	61.42 wt. %	5.80 wt. %	4.47 wt. %	5.24 wt. %	23.06 wt. %
T1.0/1.0Ag/Ca	59.81 wt. %	11.7 wt. %	3.93 wt. %	8.51 wt. %	16.04 wt. %
T0.5/5.0Ag/Ca	51.63 wt. %	11.44 wt. %	9.03 wt. %	8.58 wt. %	19.31 wt. %
T1.0/5.0Ag/Ca	50.56 wt. %	17.71 wt. %	2.59 wt. %	16.98 wt. %	12.16 wt. %

[0081] Fourier Transform Infrared Spectroscopy (FTIR) was performed to observe the spectral peak variation between the sodium-alginate/PEO nanofibres and the treated alginate nanofibres (samples T0.5/1.0Ag/Ca, T1.0/1.0Ag/Ca, T0.5/5.0Ag/Ca and T1.0/5.0Ag/Ca).

[0082] FTIR spectra from 4,000 to 400 cm^{-1} obtained for the as-spun nanofibre mats before and after chemical treatment is shown in Figure 3A. Spectra from 3,500 to 2,000 cm^{-1} are shown in Figure 3B. The spectra include 32 scans at a resolution of 4 cm^{-1} .

[0083] As shown in Figure 3B, the peak at 2883 cm^{-1} in the pre-treatment sample (sodium-alginate/PEO nanofibre, **310**) represents the $-\text{CH}_2$ group from PEO. This peak is diminished or not detectable in the treated samples (**320**, **330**, **340**, **350**), indicating successful removal of PEO from the treated nanofibres.

[0084] The peaks between 3346 and 3336 cm^{-1} correspond to hydrogen bonds of the $-\text{OH}$ group. The $-\text{OH}$ peak is shifted in the treated samples. The $-\text{OH}$ peak in the pre-treatment sample **310** occurs at 3346 cm^{-1} . The $-\text{OH}$ peak in the T0.5/1.0Ag/Ca sample **320** occurs at 3336 cm^{-1} . The $-\text{OH}$ peak in the T1.0/1.0Ag/Ca sample **330** occurs at 3340 cm^{-1} . The $-\text{OH}$

peak in the T0.5/5.0Ag/Ca sample **340** occurs at 3340 cm^{-1} . The -OH peak in the T1.0/5.0Ag/Ca sample **350** occurs at 3336 cm^{-1} .

[0085] The solubility of the chemically modified nanofibre mats was tested in accordance with BS EM 13726-1:2002 section 3.7 dispersion and solubility of hydrogel dressings. Nanofibre mats ($0.2\text{cm} \times 0.2\text{cm}$) were placed in a petri-dish in 20 mL of water for 24 hours at $37\text{ }^{\circ}\text{C}$. The mats were visually assessed after 24 hours. Nanofibre mats ($0.2\text{cm} \times 0.2\text{cm}$) were similarly placed in a petri-dish in 20 mL of STS comprising 0.4 M NaCl, 0.02 M CaCl_2 , and 10% newborn calf serum. The nanofibre mats were soaked in STS for 24 hours at room temperature. The fibre content was visually observed to assess nanofibre solubility. The nanofibres remained intact after soaking for 24 hours in water or STS.

[0086] Example 2: Preparation of alginate nanofibres

[0087] Preparation of spinning solution: A 4% by weight 70:30 sodium-alginate/PEO solution for electrospinning was prepared by dissolving 0.7 g sodium-alginate and 0.3 g PEO in 23.875 g distilled water. To improve the homogeneity of the spinning solution, 0.5% by weight TritonTM X-100 was added. A 4% by weight 80:20 sodium-alginate/PEO solution was similarly prepared.

[0088] The spinning solution was stored in the dark for 20 days at room temperature and its viscosity measured at days 1, 5, 10 and 20 using a BROOKFIELD viscometer. The viscosity of the sodium-alginate/PEO solution decreased over the period of storage, as such, sodium-alginate/PEO spinning solutions were electrospun within five days of preparation. The viscosities were 2284 cP at day 1, 2184 cP at day 5, 1579 cP at day 10, and 202 cP at day 20.

[0089] Electrospinning: A horizontal electrospinning device was used to prepare sodium-alginate nanofibres. The process parameters were set to 12-20 cm working distance, 1.0-0.3 ml/h feed rate, and 9-12 kV applied voltage. The electrospun fibres were collected on aluminum foil. After 1 hour of electrospinning, the foil and deposited fibres were collected and dried for 24 hours at room temperature to remove residual solvents. Process parameters were varied as shown in Table 3. Final process parameters utilized to generate as-spun sodium-alginate/PEO nanofibres were 16 cm working distance, 0.4 ml/hour flow rate and a 10.5 kV applied voltage.

[0090] Table 3: Electrospinning process parameters to generate sodium-alginate/PEO nanofibres.

Observation no.	Working distance	Feed rate	Applied voltage	Observations
1	16 cm	0.5 ml/h	9 kV	Stable jet, uniform deposition but slowly formed droplet
2	16 cm	0.5 ml/h	10 kV	Stable jet, uniform deposition but slowly formed droplet
3	16 cm	0.5 ml/h	11 kV	Stable jet, uniform deposition but slowly produced droplets
4	16 cm	0.4 ml/h	9 kV	Stable jet and uniform deposition but slowly formed droplets
5	16 cm	0.4ml/h	10 kV	Stable jet and uniform deposition
6	16 cm	0.4 ml/h	11 kV	Stable jet and uniform deposition
7	16 cm	0.3 ml/h	9 kV	Stable jet and uniform deposition but slowly formed droplets
8	16 cm	0.3 ml/h	10 kV	Stable jet and uniform deposition
9	16 cm	0.3 ml/h	11 kV	Stable jet, uniform deposition
10	16 cm	0.4 ml/h	10.5 kV	Stable jet, uniform deposition (Optimized process parameters)

[0091] Characterization of as-spun sodium-alginate/PEO nanofibres: The morphology and structure of the electrospun or as-spun sodium-alginate/PEO nanofibres were observed by SEM. The elemental analysis of the as-spun sodium-alginate/PEO nanofibres was analyzed by FTIR. The solubility of the as-spun sodium-alginate/PEO nanofibres was tested in accordance with BS EN 13726-1:2002 section 3.7 dispersion and solubility of hydrogel dressings. These procedures were performed essentially as described in Example 1.

[0092] Figure 4A shows the SEM images of as-spun nanofibres from the 4% by weight 70:30 sodium-alginate:PEO solution (**400**) and the 4% by weight 80:20 sodium-alginate:PEO solution (**401**). The average diameter of the as-spun nanofibres from the 4% by weight 70:30 sodium-alginate:PEO solution was 124 nm with a standard deviation of 35 nm, as shown in Figure 4B. The as-spun nanofibres from the 4% by weight 70:30 sodium-alginate:PEO solution were uniform and bead-free.

[0093] Figure 5 shows FTIR spectra of pure PEO (panel A), sodium-alginate (panel B) and sodium-alginate/PEO (panel C) nanofibres within a 4000-400 cm^{-1} and 2000-1000 cm^{-1} spectral range. The spectrum for PEO (panel A) has peaks at 1100 cm^{-1} and 843 cm^{-1} corresponding to

ether group asymmetric stretch and bending vibrations. The spectra for sodium-alginate (panel B) has peaks at 3336 cm^{-1} corresponding to hydroxyl group stretching, 1593 cm^{-1} for carboxylate group symmetrical stretching and 1410 cm^{-1} for carboxylate group symmetrical stretching. The asymmetrical absorption band for the ether group of PEO was shifted from 1100 cm^{-1} to 1095 cm^{-1} in the sodium-alginate/PEO nanofibre. The asymmetrical absorption band for the carboxylate group of sodium-alginate was shifted from 1593 cm^{-1} to 1612 cm^{-1} in the sodium-alginate/PEO nanofibre.

[0094] The solubility of the as-spun sodium-alginate/PEO nanofibres in water and STS were assessed as in Example 1. The nanofibres dissolved in either water or STS within 2 to 3 minutes of soaking.

[0095] Example 3: Construction of a composite dressing structure comprising as-spun alginate nanofibres

[0096] Electrospun nanofibres, such as those prepared in Example 2, were deposited on the surface of a Na-CMC nonwoven base.

[0097] A Na-CMC nonwoven fabric was applied to a collector in an electrospinning device and a 4% by weight 70:30 sodium-alginate/PEO solution was electrospun as described in Example 2. The Na-CMC fabric was deposited with sodium-alginate/PEO nanofibres to generate a composite dressing structure. The morphology of as-spun nanofibres deposited on foil and on Na-CMC was visualized by SEM, as shown in Figure 6 (panels A-D). Figure 6, panel A shows a photograph of the Na-CMC base fabric, panel B shows a SEM image of the Na-CMC base fabric, panel C shows a photograph of the Na-CMC base fabric deposited with as-spun sodium-alginate/PEO nanofibres, and panel D shows a SEM image of the Na-CMC base fabric deposited with as-spun sodium-alginate/PEO nanofibres. These images indicate no morphological difference between the Na-CMC fabric before and after deposition of as-spun nanofibres to its surface.

[0098] Example 4: Antibacterial nanofibrous dressing structure

[0099] The composite dressing structure of Example 3 was chemically treated to generate an antibacterial nanofibrous dressing structure.

[00100] A 10 cm x 10 cm composite dressing structure of Example 3 was soaked in a petri-dish containing ethanol absolute for 10 minute with gentle shaking to dissolve PEO. The ethanol washed sample was transferred to a petri-dish containing a calcium solution (1.0% or 5% by weight CaCl_2 in ethanol absolute) and allowed to soak for 10 minutes. During this calcium treatment step, an ion exchange reaction occurred between the sodium (I) ions from sodium-alginate nanofibres and calcium (II) ions from the calcium solution to generate insoluble

calcium-alginate nanofibres. Similarly, sodium (I) ions from the Na-CMC fabric may exchange with calcium (II) ions from the calcium solution. The sample was then transferred to a petri-dish containing a silver solution (0.5% or 1% by weight AgNO_3 in ethanol absolute) and allowed to soak for 10 minutes. During this silver treatment step, an ion exchange reaction occurred between sodium (I) ions from sodium-alginate nanofibres, calcium (II) ions from calcium-alginate and silver (I) ions from the silver solution to generate nanofibres having sodium-alginate, calcium-alginate and silver-alginate. Similarly, sodium (I) ions from the Na-CMC fabric and calcium (II) ions from Ca-CMC fabric may exchange with silver (I) ions from the silver solution. The sample was then washed in ethanol absolute to remove precipitated and unreacted salts. The sample was dried at room temperature (about 20 °C).

[00101] This process was repeated using different concentrations of CaCl_2 and AgNO_3 as shown in Table 1. Figure 1 (panels B1-E1) show SEM images showing the morphology of nanofibres deposited on a Na-CMC backing following treatment with calcium and silver treatment solutions.

[00102] Example 5: Antibacterial nanofibrous dressing structure deposited with a malodor absorbing agent by electrospraying

[00103] Antibacterial nanofibrous dressing structures prepared in Example 4 were electrosprayed with the malodor absorbing agent hydroxypropyl- β -cyclodextrin (HP- β -CD). Figure 7 shows images of nanofibrous dressing structures prepared using a 1.0% CaCl_2 solution and a 0.5% AgNO_3 solution.

[00104] Electrospraying process parameters were adjusted to 0.5 – 2 ml/h feed rate, 7-15 kV applied voltage and 12-20 cm working distance to obtain uniform dispersion of HP- β -CD particles on a collector comprising aluminum foil. Electrosprayed HP- β -CD particles collected on aluminum foil were dried and characterized to optimize process parameters. The electrospraying process was optimized at 1.0 ml/h feed rate, 12 kV applied voltage and 16 cm working distance.

[00105] HP- β -CD particles were deposited on the antibacterial nanofibrous dressing structures prepared in Example 4 using optimized process parameters. Figure 7 (panels A-C) show SEM images showing the surface morphology of the electrosprayed nanofibrous dressings of Example 4. The dressing shown in Figure 7, panel A was electrosprayed for 1 hour, the dressing shown in panel B was electrosprayed for 2 hours, and the dressing shown in panel C was electrosprayed for 4 hours.

[00106] Example 6: Antibacterial nanofibrous dressing structure deposited with a malodor absorbing agent by electrospinning

[00107] Antibacterial nanofibrous dressing structures prepared in Example 4 are combined with the malodor absorbing agent hydroxypropyl- β -cyclodextrin (HP- β -CD) by electrospinning a HP- β -CD solution onto the nanofibrous surface of the dressing structures. The HP- β -CD solution comprises the carrier polymer PEO.

[00108] A series of spinning solutions having 4-12% by weight 50:50 HP- β -CD:PEO were prepared in water. Another series of spinning solutions having 8% by weight 50:50 to 90:10 HP- β -CD:PEO were prepared in water.

[00109] Electrospinning process parameters were adjusted to 0.5-2.5 ml/h feed rate, 5-11 kV applied voltage and 8-16 cm working distance to obtain smooth fibres. Electrospun HP- β -CD particles were collected on aluminum foil, dried for 24 hours, and characterized to optimize process parameters. The electrospinning process was optimized at 1.0 ml/h feed rate, 12 kV applied voltage and 16 cm working distance.

[00110] Electrospinning of HP- β -CD/PEO was carried out with varying mass ratios and concentrations at 1 ml/h feed rate, 12 cm working distance, and 7 kV applied voltage to obtain smooth nanofibres. Table 4 provides spinning solution compositions and properties of HP- β -CD/PEO electrospun nanofibres deposited on foil.

[00111] Table 4: Summary of electrospun HP- β -CD/PEO fibre characteristics.

Polymer conc. (% wt.)	HP- β -CD/PEO ratio	Fibre diameter range (nm)	Average diameter (nm)	Fibre morphology	Diameter of nanofibres web (cm)
8	50:50	240-289	264	Smooth fibres	9.2
8	60:40	189-301	244	Smooth fibres	10.5
8	70:30	128-390	236	Few beads	15.5
8	80:20	80-1628	208	Mainly beads	-
8	90:10	-	-	Mainly beads	-
4	50:50	60-972	268	Mainly beads	-
6	50:50	177-362	248	Smooth fibres	12.5
8	50:50	240-289	264	Smooth fibres	9.2
10	50:50	194-302	254	Smooth fibres	7.4
12	50:50	128-328	281	Branched fibres	5.7

[00112] The morphology of the electrospun HP- β -CD/PEO fibres is shown in the SEM images (2,000x, insert 10,000x) of Figure 8 (panels A-D). The fibres in Figure 8 were electrospun from an 8% solution having 50:50 (panel A), 60:40 (panel B), 70:30 (panel C), and 80:20 (panel D) HP- β -CD/PEO blend ratios.

[00113] Electrospun HP- β -CD particles are collected on a nanofibrous dressing structure of Example 4 using the optimized process parameters.

[00114] Example 7: Dressing structure comprising antibacterial nanofibres

[00115] A scheme of a proposed dressing structure is shown in Figure 9. Electrospun nanofibres, such as those prepared in Example 2, are deposited on the surface of a backing to generate a nanofibrous dressing construct using the method described in Example 3. The dressing construct is chemically treated as in Example 4 to generate an antibacterial nanofibrous dressing structure. The antibacterial nanofibrous dressing construct is electrosprayed with HP- β -CD as described in Example 5 to generate the final dressing. The final dressing structure comprises a sodium-CMC base fabric, a nanofibrous mesh comprising antibacterial silver-alginate, and a HP- β -CD coating.

[00116] Example 8: Methods for preparing dressing structures comprising antibacterial nanofibres

[00117] A schematic summarizing the methods described in Example 1 through Example 7 is provided in Figure 10.

[00118] Example 9: Assessment of dressing structures and dressing structure components

[00119] Compositions produced by the methods described in Examples 1 through 7 are summarized in Table 5.

[00120] Table 5. Summary of wound dressing compositions.

Tests	Set	Sets of samples
Mass per unit area	Set -1	Base fabric
Thickness		Chemically treated (T0.5/1.0Ag/Ca) sample
Fluid absorption and retention		Final (F0.5/1.0Ag/Ca(2h)) sample
Lateral wicking	Set -2	Base fabric
Shrinkage		Chemically treated (T0.5/5.0Ag/Ca) sample
		Final (F0.5/5.0Ag/Ca(2h)) sample
	Set -3	Base fabric
		Chemically treated (T1.0/1.0Ag/Ca) sample
		Final (F1.0/1.0Ag/Ca(2h)) sample
	Set -4	Base fabric
		Chemically treated (T1.0/5.0Ag/Ca) sample
		Final (F1.0/5.0Ag/Ca(2h)) sample

[00121] The average mass per unit area of the dressing compositions were assessed in accordance with BS EN 12127:1998 test method. Table 6 presents the average mass per 100

cm² for different compositions. The mass per unit area increased in the chemically treated compositions compared to the base fabric.

[00122] Table 6. Mass per unit area of wound dressing compositions.

Sample	Mass/unit area (g/100cm ²)	% +/- respect to base fabric
Base fabric	1.043	-
T0.5/1.0Ag/Ca	1.096	+5.08%
F0.5/1.0Ag/Ca(2h)	1.320	+26.55%
T0.5/5.0Ag/Ca	1.384	+32.69%
F0.5/5.0Ag/Ca(2h)	1.429	+37%
T1.0/1.0Ag/Ca	1.111	+6.51%
F1.0/1.0Ag/Ca(2h)	1.398	+34.03%
T1.0/5.0Ag/Ca	1.856	+77.94%
F1.0/5.0Ag/Ca(2h)	1.906	+82.74%

[00123] The thickness of the dressing compositions were assessed in accordance with BS EN ISO 9073-2:1997. The tests were carried out with 0.0 weight (without additional weight, i.e. normal state of the tester) and 100 g weight (with 100 g known weight). Table 7 presents the average thickness and relative changes in the thickness of different compositions. The addition of a HP- β -CD coating to a dressing composition increased the overall dressing composition thickness. Calcium had an effect on composition thickness.

[00124] Table 7: Average thickness of wound dressing compositions.

Sample	Thickness (mm) at 0.0 wt.	% +/- respect to base dressing	Thickness (mm) at 100g wt.	% +/- respect to base fabric	Difference between 0.0 wt. and 100g wt.
Base dressing	1.550	-	1.083	-	-30%
T0.5/1.0Ag/Ca	1.633	+ 5.35%	1.167	+7.75%	-29%
F0.5/1.0Ag/Ca(2h)	1.967	+26.9%	1.383	+27.7%	-30%
T0.5/5.0Ag/Ca	1.883	+21.48%	1.667	+53.92%	-12%
F0.5/5.0Ag/Ca(2h)	2.133	+37.6%	1.700	+56.97%	-20%
T1.0/1.0Ag/Ca	1.650	+6.45%	1.233	+13.85%	-25%
F1.0/1.0Ag/Ca(2h)	1.800	+16.1%	1.417	+30.84%	-21%
T1.0/5.0Ag/Ca	1.883	+21.48%	1.583	+46.16%	-16%
F1.0/5.0Ag/Ca(2h)	2.133	+37.6%	1.750	+61.58%	-18%

[00125] The average absorption and retention properties of the wound dressing compositions were determined in accordance with BS EN 13726-1:2002 section 3.2 free swell absorptive capacity. Absorption refers to how much fluid is absorbed by each composition. Retention refers to how much of the fluid is retained in the composition under a certain pressure. Table 8 provides a summary of the fluid handling properties of the wound dressing compositions. The average absorption and retention of the base fabric were found to be higher than the chemically treated compositions and the final dressings. The concentrations of silver and calcium ions during chemical treatment negatively affected the absorption and retention ability of compositions.

[00126] Table 8: Absorption and retention of fluids in wound dressing compositions.

Sample	Absorption (g/g)	Retention (g/g)	% Retention*	Absorption (g/100cm ²)	Retention (g/100cm ²)
Base fabric	17.50	11.85	67.72	18.01	12.2
T0.5/1.0Ag/Ca	14.58	10.03	68.8	15.97	10.98
F0.5/1.0Ag/Ca(2h)	14.37	8.10	56.37	18.97	10.7
T0.5/5.0Ag/Ca	13.77	7.95	57.74	19.06	11
F0.5/5.0Ag/Ca(2h)	12.23	6.79	55.52	17.47	9.7
T1.0/1.0Ag/Ca	14.84	8.36	56.34	16.48	9.28
F1.0/1.0Ag/Ca(2h)	13.24	7.47	56.42	18.5	10.45
T1.0/5.0Ag/Ca	8.73	5.42	62.09	16.21	10.07
F1.0/5.0Ag/Ca(2h)	11.03	6.30	57.12	20.97	11.97

* % Retention = [Retention (g/g)/Absorption (g/g) × 100]

[00127] Vertical wicking of the wound dressing compositions was tested in accordance with BS 3424-18:1986 standard test method. Table 9 provides a summary of the wicking behavior of the wound dressing compositions. The average wicking height of the compositions treated with calcium and silver solutions was higher than the average wicking height of the base fabric. The addition of HP- β -CD had little or negligible effect on the average wicking height of a composition.

[00128] Table 9: Lengthwise and traverse wicking test for wound dressing compositions.

Sample	Lengthwise (mm)	Transverse (mm)	Average (mm)
Base fabric	18.67	18.00	18.34
T0.5/1.0AgCa	25.67	28.67	27.17
F0.5/1.0AgCa(2h)	27.67	28.67	28.17
T0.5/5.0AgCa	38.67	45.33	42
F0.5/5.0AgCa(2h)	39.67	47.00	43.33
T1.0/1.0AgCa	26.33	27.67	27
F1.0/1.0AgCa(2h)	25.67	27.67	26.67
T1.0/5.0AgCa	45.00	46.00	45.5
F1.0/5.0AgCa(2h)	46.00	51.33	48.66

[00129] The shrinkage behavior of the wound dressing compositions was assessed. Table 10 provides the area shrinkage of wound dressing compositions. Electro spraying HP- β -CD on a composition had a positive effect on the dimensional stability of that composition. The concentration of calcium in the chemical treatment process negatively affected the dimensional stability of the wound dressing compositions.

[00130] Table 10: Area shrinkage of hydrated and dried wound dressing compositions.

Sample	Hydrated (%)	Dried (%)
Base fabric	31.27	46.83
T0.5/1.0Ag/Ca	31.27	62.54
F0.5/1.0Ag/Ca(2h)	33.27	36.08
T0.5/5.0Ag/Ca	20.50	43.85
F0.5/5.0Ag/Ca(2h)	24.92	38.66
T1.0/1.0Ag/Ca	27.75	55.16
F1.0/1.0Ag/Ca(2h)	28.45	35.33
T1.0/5.0Ag/Ca	15.98	24.16
F1.0/5.0Ag/Ca(2h)	25.58	29.23

[00131] Example 10: Silver-release from antibacterial dressing structures

[00132] The antibacterial nanofibrous dressing structures electro sprayed with HP- β -CD from Example 5 were tested for their silver-release properties. A 2 cm x 2 cm sample of each dressing structure was immersed in 20 mL of solution A (0.4 M NaCl, 0.02 M CaCl₂, distilled water) in a glass bottle and incubated at 37 °C for 7 days. 10 mL samples of the solution were withdrawn at 24 intervals during the incubation period. A fresh 10 mL aliquot of solution A was supplemented to the incubated sample each time a sample was drawn. The silver content in the

withdrawn samples was determined using Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES). The amount of silver released from each dressing structure is shown in Table 11.

[00133] Table 11. Silver release from antibacterial dressing structures.

Sample no.	Sample size	Silver release amount (ppm)						
		1-day	2-day	3-day	4-day	5-day	6-day	7-day
F0.5/1.0Ag/Ca(2h)	30	1.4	1.6	1.1	1.1	1.0	1.0	1.0
F0.5/5.0Ag/Ca(2h)		1.5	1.5	1.4	1.3	1.4	1.3	1.4
F1.0/1.0Ag/Ca(2h)		1.4	1.4	1.4	1.4	1.4	1.4	1.4
F1.0/5.0Ag/Ca(2h)		1.4	1.5	1.5	1.5	1.5	1.5	1.5

[00134] Example 11: Malodor absorbency of antibacterial dressing structures.

[00135] The antibacterial nanofibrous dressing structures electro electrospayed with HP- β -CD from Example 5 were tested for their ability to absorb malodors. Dressing structure samples (2 cm x 2 cm) were exposed to a malodorous environment comprising 0.5 ml of a stimulated test solution (0.4 M NaCl, 0.02 M CaCl₂, 10% newborn calf serum, 2% diethylamine). A sample of a commercial product was similarly tested (CarboFLEX®, ConvaTec). Ten randomly selected individuals assessed the smell intensity of each sample by rating the smell from 0 to 10. A score of 0 indicated “no smell” and a score of 10 indicated “maximum smell”. The results of the smell assessment for dressing structures is shown in Table 12. Samples which were electrospayed with HP- β -CD for longer periods of time (4 hours versus 1 or 2 hours) had lower smell ratings.

[00136] Table 11: Malodor absorbency of antibacterial dressing structures electrospayed with HP- β -CD.

Dressing sample	Rating (1 day incubation time)	Rating (7 days incubation time)	Specification (Level of malodour)	Grade
F0.5/1.0Ag/Ca(1h)	6.9	7.5	Moderate	Fair
F0.5/1.0Ag/Ca(2h)	6.1	6.6	Moderate	Fair
F0.5/1.0Ag/Ca(4h)	5.1	4.7	Minimal	Good
CarboFlex	4.3	4.9	Minimal	Good

[00137] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing

the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of preparing anti-odor, antimicrobial nanofibres derived from alginate nanofibres, the method comprising: a) contacting the alginate nanofibres with a first organic solution comprising calcium ions to generate calcium-alginate nanofibres; b) contacting the calcium-alginate nanofibres with a second organic solution comprising an antimicrobial agent to generate antimicrobial-alginate nanofibres; and c) combining or coating the antimicrobial-alginate nanofibres with a malodor absorbing agent to generate anti-odor, antimicrobial nanofibres.
2. The method of claim 1, wherein the alginate nanofibres are formed by electrospinning an aqueous solution comprising from 1% to 10% by weight mixture of alginate and PEO.
3. The method of claim 2, wherein the aqueous solution comprises an alginate to PEO ratio from 60:40 to 80:20.
4. The method of claim 1, wherein the first organic solution comprises from 0.1% to 10% by weight calcium salt.
5. The method of claim 4, wherein the calcium salt is selected from calcium chloride, calcium bromide, calcium fluoride, calcium iodide, calcium nitrate, and calcium hydride.
6. The method of claim 1, wherein the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof.
7. The method of claim 6, wherein the antibiotic is selected from gentamicin, ofloxacin, minocycline, tetracycline, metronidazole and derivatives thereof.
8. The method of claim 6, wherein the second organic solution comprises from 0.05% to 10% by weight silver salt.
9. The method of claim 8, wherein the silver salt is selected from the group consisting of silver nitrate, silver chloride, silver sulfate, silver lactate, silver bromide, silver acetate, and combinations thereof.
10. The method of claim 1, wherein the antimicrobial-alginate nanofibres are coated with the malodor absorbing agent by electrospraying or electrospinning the malodor absorbing agent onto a surface of the antimicrobial-nanofibres.
11. The method of claim 1, wherein the malodor absorbing agent comprises cyclodextrin.
12. The method of claim 1, wherein the alginate nanofibres are washed with an organic solvent prior to contact with the first organic solution.

13. The method of claim 1, wherein the calcium-alginate nanofibres are washed with an organic solvent prior to contact with the second organic solution.
14. The method of claim 1, wherein the antimicrobial-alginate nanofibres are washed with an organic solvent prior to combining or coating with the malodor absorbing agent.
15. The method of claim 1, wherein the anti-odor, antimicrobial nanofibres have less than a 10% decrease in average fibre diameter as compared to the average fibre diameter of the alginate nanofibres.
16. The method of claim 1, wherein a portion of the antimicrobial agent dissociates and releases from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate.
17. The method of claim 1, wherein a portion of the calcium ions dissociate and release from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate.
18. The method of claim 1, wherein the anti-odor, antimicrobial nanofibres remain intact after soaking in an aqueous solution for 24 hours.
19. Anti-odor, antimicrobial nanofibres comprising a) alginate nanofibres electrospun from an aqueous solution comprising a 4% mixture of alginate:PEO in a 70:30 ratio; b) an antimicrobial agent; and c) a malodor absorbing agent.
20. The anti-odor, antimicrobial nanofibres of claim 19, wherein the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof.
21. The anti-odor, antimicrobial nanofibres of claim 20, wherein the antimicrobial agent comprises silver ions.
22. The anti-odor, antimicrobial nanofibres of claim 19, wherein the malodor absorbing agent is in the form of a fibre.
23. The anti-odor, antimicrobial nanofibres of claim 19, wherein the malodor absorbing agent is electrospun onto the alginate nanofibres.
24. The anti-odor, antimicrobial nanofibres of claim 19, wherein the malodor absorbing agent is electrosprayed onto the alginate nanofibres.
25. The anti-odor, antimicrobial nanofibres of claim 19, wherein the malodor absorbing agent comprises cyclodextrin.
26. The anti-odor, antimicrobial nanofibres of claim 25, wherein the cyclodextrin comprises hydroxypropyl- β -cyclodextrin (HB- β -CD).

27. The anti-odor, antimicrobial nanofibres of claim 19, wherein the anti-odor, antimicrobial nanofibres do not comprise PEO.
28. The anti-odor, antimicrobial nanofibres of claim 19, wherein the average nanofibre diameter is from 120 nm to 150 nm.
29. The anti-odor, antimicrobial nanofibres of claim 21, wherein at least a portion of the silver ions form particles within the anti-odor, antimicrobial nanofibres.
30. The anti-odor, antimicrobial nanofibres of claim 29, wherein the average diameter of the particles is from 150 nm to 300 nm.
31. The anti-odor, antimicrobial nanofibres of claim 21, wherein a portion of the silver ions dissociate and release from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate.
32. The anti-odor, antimicrobial nanofibres of claim 19, further comprising calcium ions.
33. The anti-odor, antimicrobial nanofibres of claim 32, wherein a portion of the calcium ions dissociate and release from the anti-odor, antimicrobial nanofibres when the anti-odor, antimicrobial nanofibres are in contact with wound exudate.
34. A wound dressing structure comprising the anti-odor, antimicrobial nanofibres of claim 18 and a backing.
35. The wound dressing structure of claim 34, wherein the backing is a fabric backing.
36. The wound dressing structure of claim 34, wherein the backing is nylon.
37. The wound dressing structure of claim 34, wherein the backing comprises carboxymethylcellulose (CMC).
38. A method of preparing a wound dressing structure, the method comprising: depositing alginate nanofibres on a surface of a backing, b) chemically treating the alginate nanofibres with a solution comprising calcium ions dissolved in an organic solvent to generate calcium-alginate nanofibres, c) chemically treating the calcium-alginate nanofibres with a solution comprising an antimicrobial agent dissolved in an organic solvent to generate antimicrobial-alginate nanofibres, and d) electrospinning or electrospraying fibres comprising a malodor absorbing agent onto a surface of the antimicrobial-alginate nanofibres.
39. The method of claim 38, wherein the alginate nanofibres are deposited on the surface of the backing by electrospinning an aqueous solution comprising from 1% to 10% by weight mixture of alginate and PEO.
40. The method of claim 39, wherein the aqueous solution comprises an alginate to PEO ratio from 60:40 to 80:20.

41. The method of claim 38, wherein the solution comprising calcium ions comprises from 0.1% to 10% by weight calcium salt.
42. The method of claim 41, wherein the calcium salt is selected from calcium chloride, calcium bromide, calcium fluoride, calcium iodide, calcium nitrate, and calcium hydride.
43. The method of claim 38, wherein the antimicrobial agent comprises silver, acetic acid, chlorhexidine, iodine, hydrogen peroxide, sodium hypochlorite, potassium permanganate, triclosan, an antibiotic, or a combination thereof.
44. The method of claim 43, wherein the antibiotic is selected from gentamicin, ofloxacin, minocycline, tetracycline, metronidazole and derivatives thereof.
45. The method of claim 43, wherein the solution comprising the antimicrobial agent comprises from 0.05% to 10% by weight silver salt.
46. The method of claim 45, wherein the silver salt is selected from the group consisting of silver nitrate, silver chloride, silver sulfate, silver lactate, silver bromide, silver acetate, and combinations thereof.
47. The method of claim 38, wherein the malodor absorbing agent comprises cyclodextrin.
48. The method of claim 38, further comprising washing the alginate nanofibres with an organic solvent after depositing onto the surface of the backing.
49. The method of claim 38, further comprising washing the calcium-alginate nanofibres with an organic solvent prior to chemical treatment with the solution comprising the antimicrobial agent.
50. The method of claim 38, further comprising washing the antimicrobial-alginate nanofibres with an organic solvent prior to electrospinning or electrospraying with the malodor absorbing agent.
51. The method of claim 38, wherein the antimicrobial-alginate nanofibres have less than a 10% decrease in average fibre diameter as compared to the average fibre diameter of the alginate nanofibres.
52. The method of claim 38, wherein a portion of the antimicrobial agent dissociates and releases from the wound dressing structure when the wound dressing structure is in contact with wound exudate.
53. The method of claim 38, wherein a portion of the calcium ions dissociate and release from the wound dressing structure when the wound dressing structure is in contact with wound exudate.
54. The method of claim 38, wherein the backing is a fabric backing.
55. The method of claim 38, wherein the backing is nylon.

56. The method of claim 38, wherein the backing comprises carboxymethylcellulose (CMC).
57. A nanofibrous structure prepared by the method of claim 38.

FIG. 1

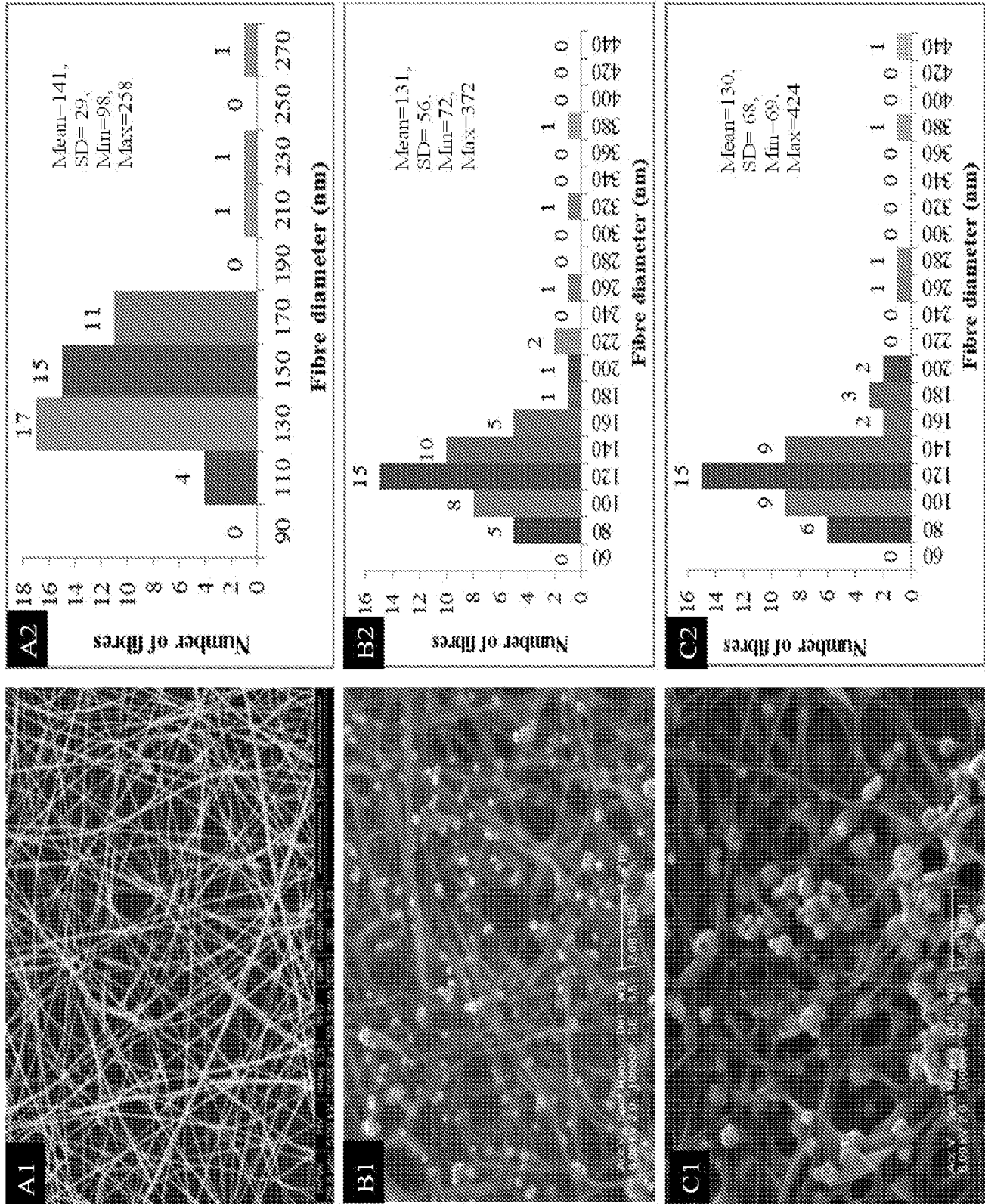


FIG. 1
Continued

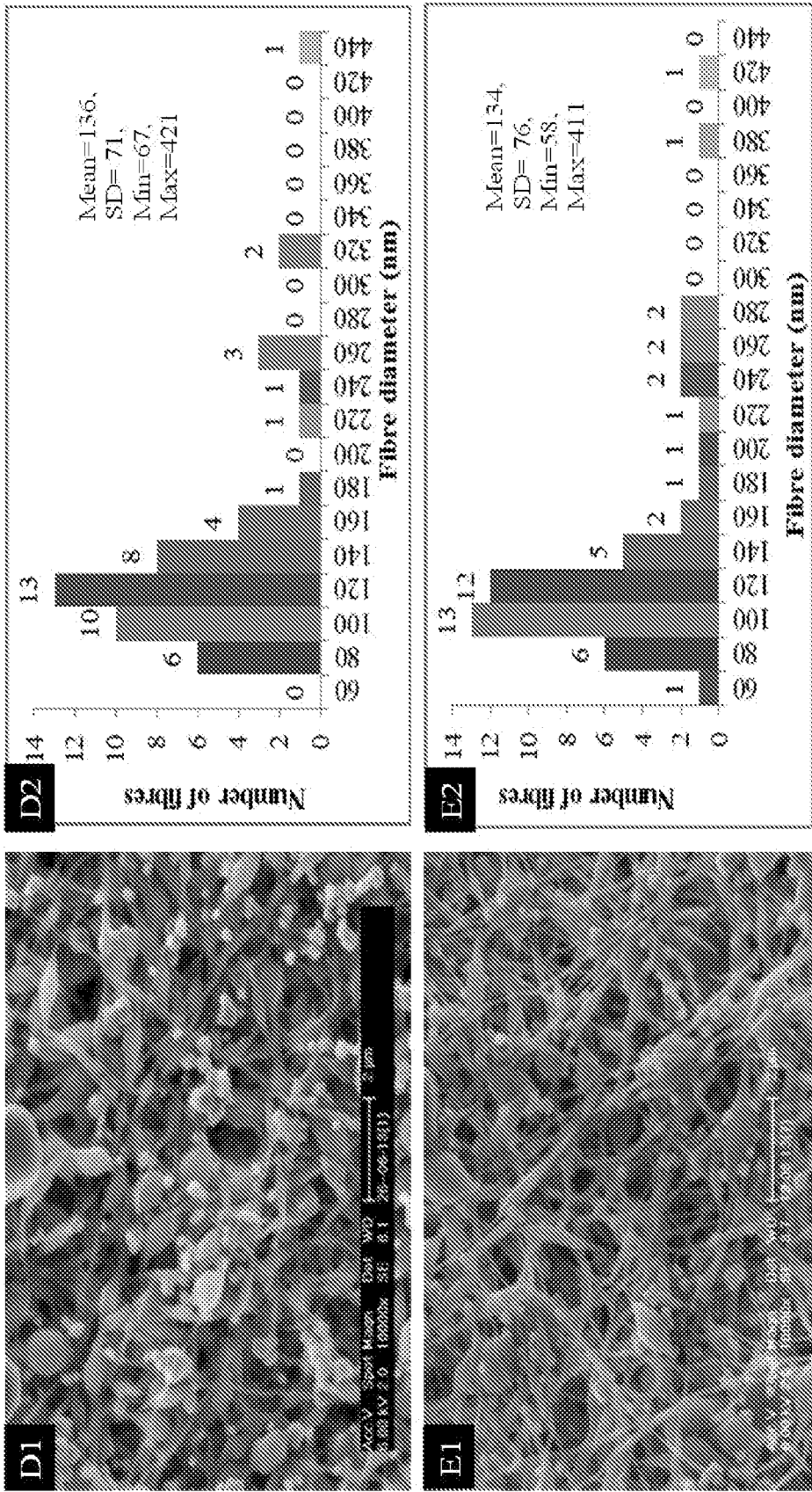


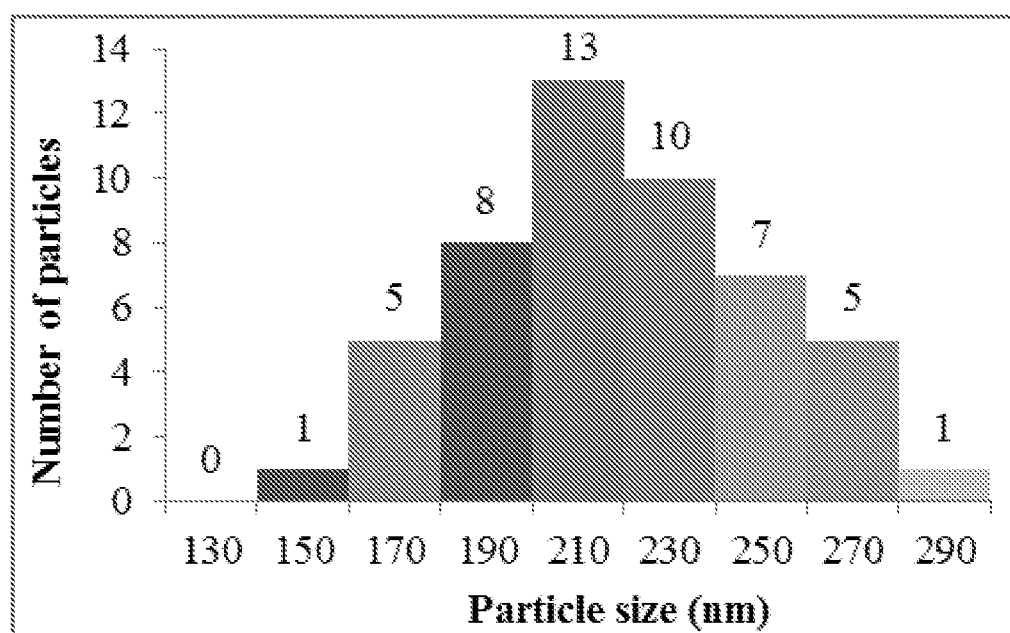
FIG. 2

FIG. 3A

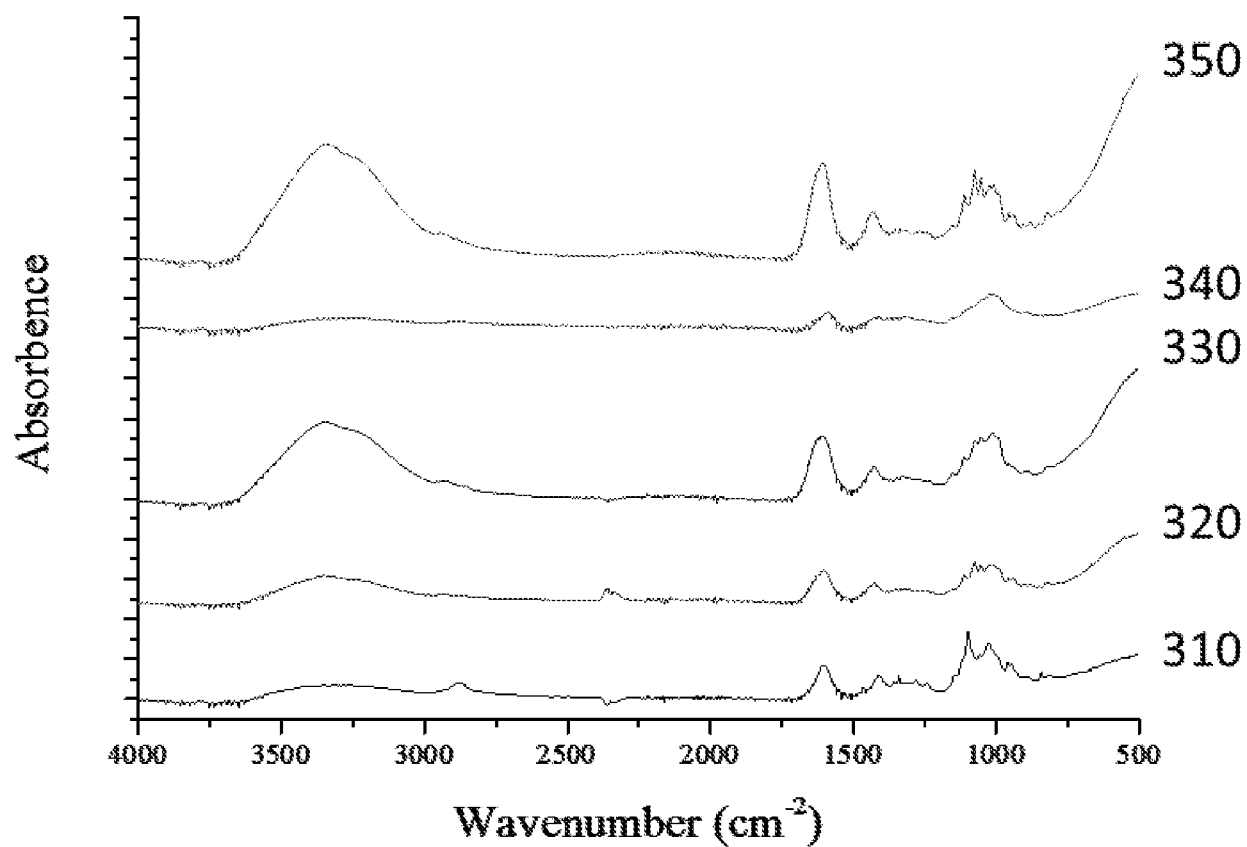


FIG. 3B

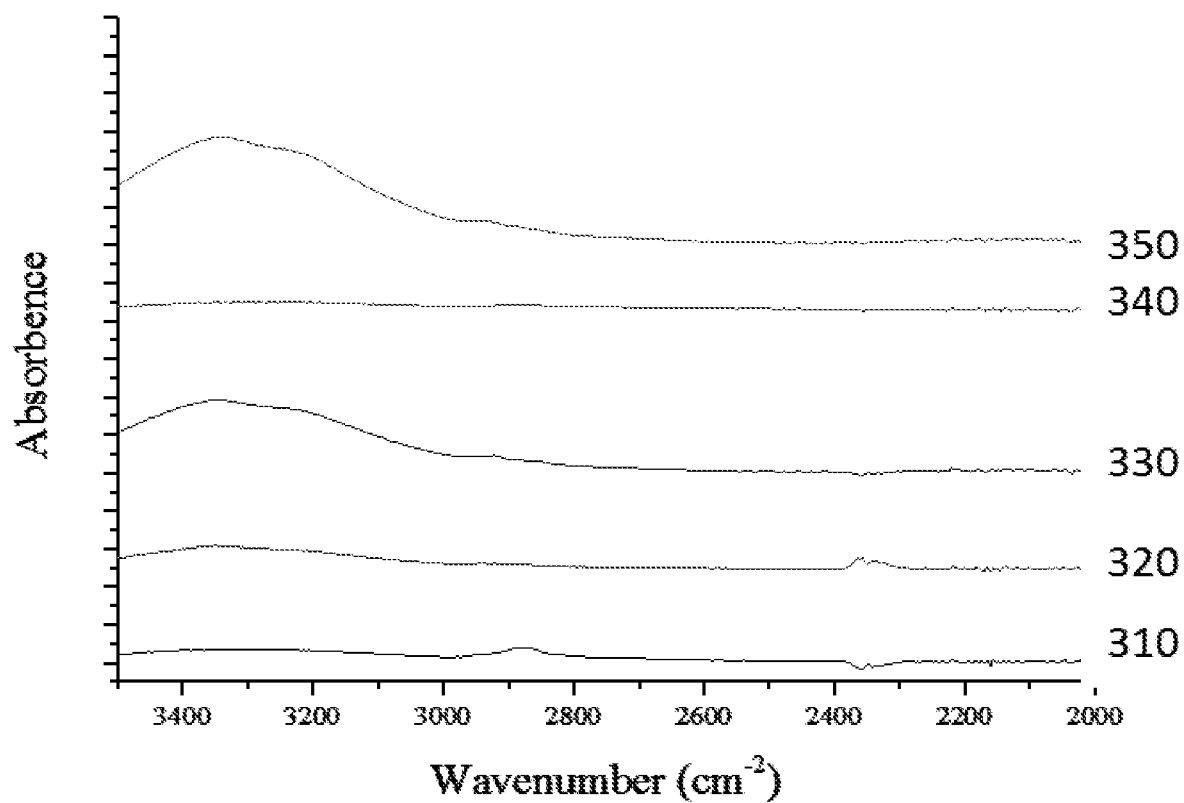


FIG. 4A

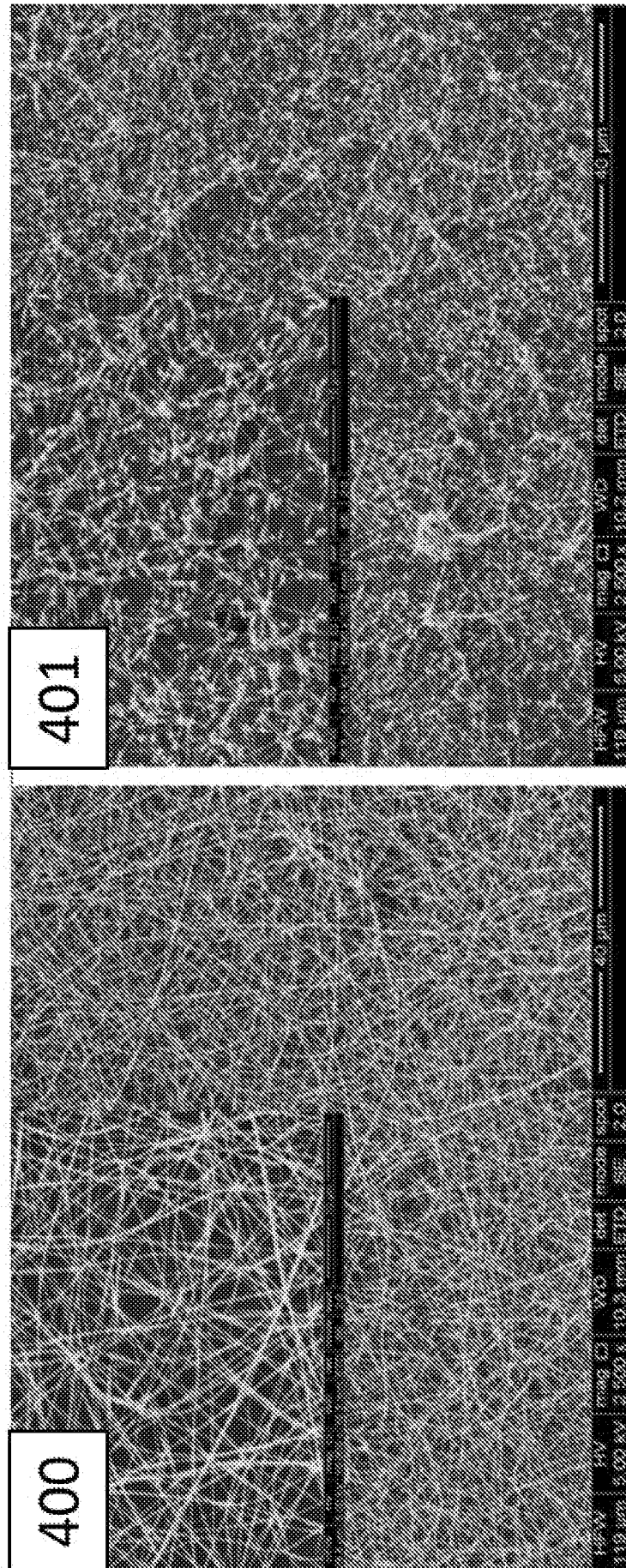


FIG. 4B

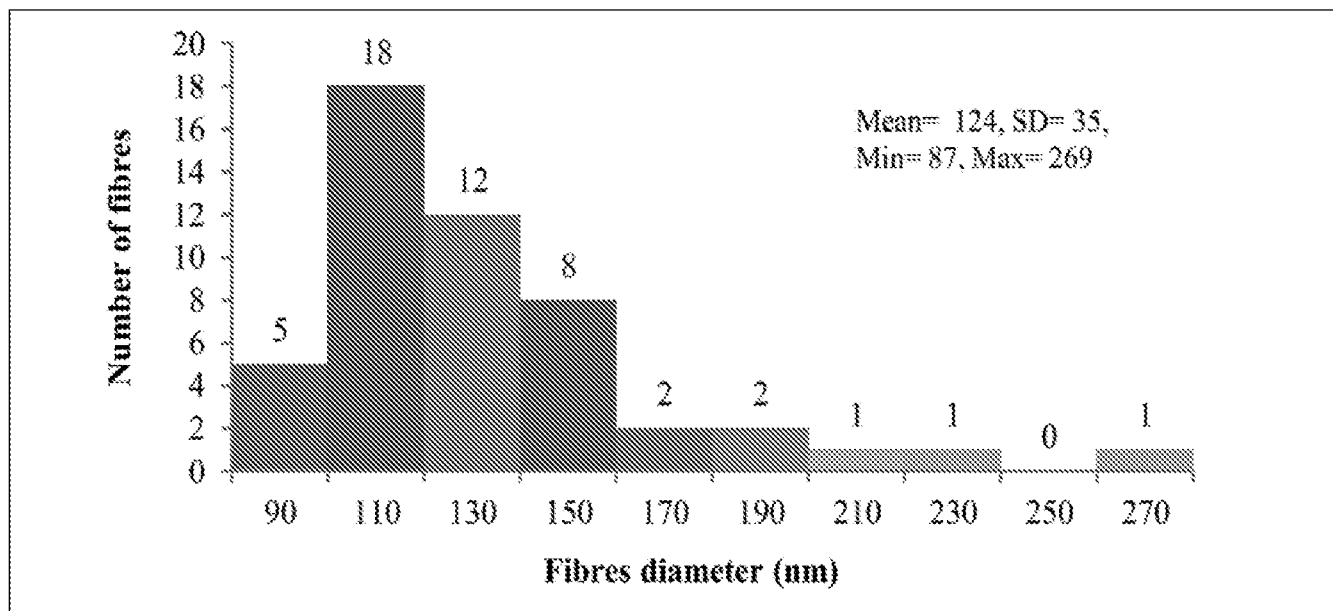


FIG. 5

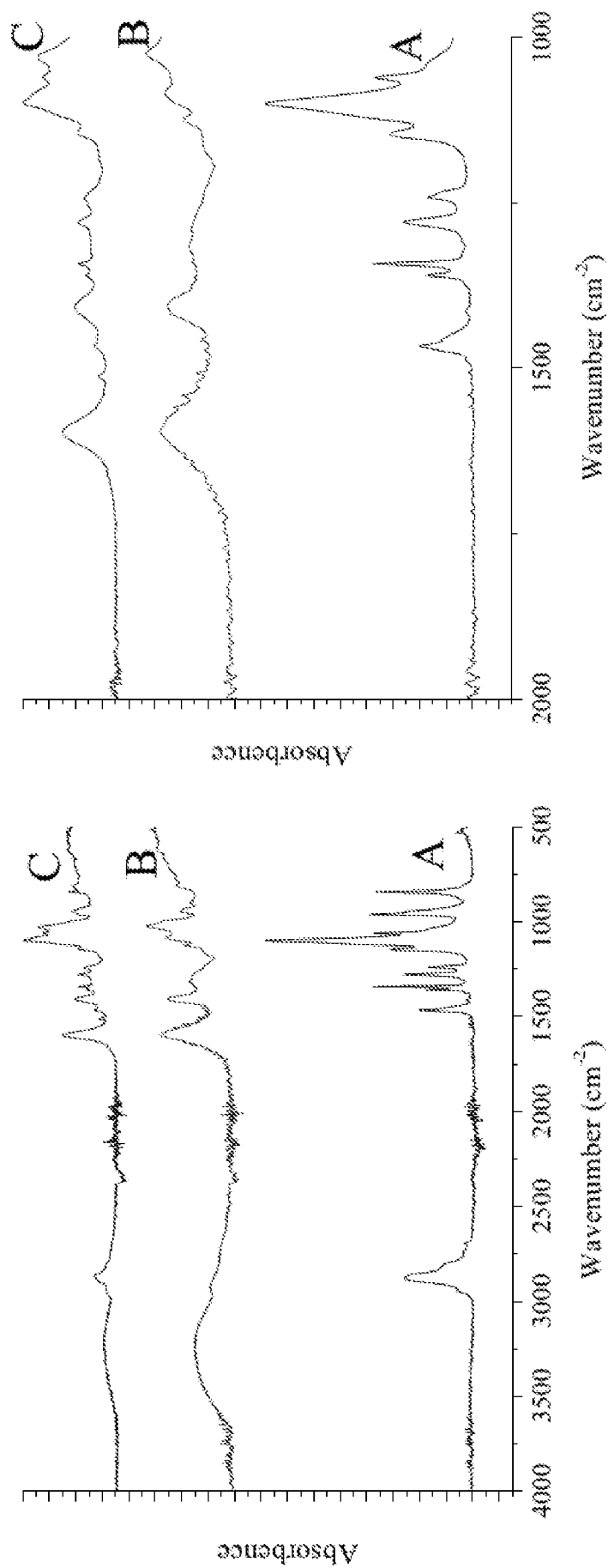


FIG. 6

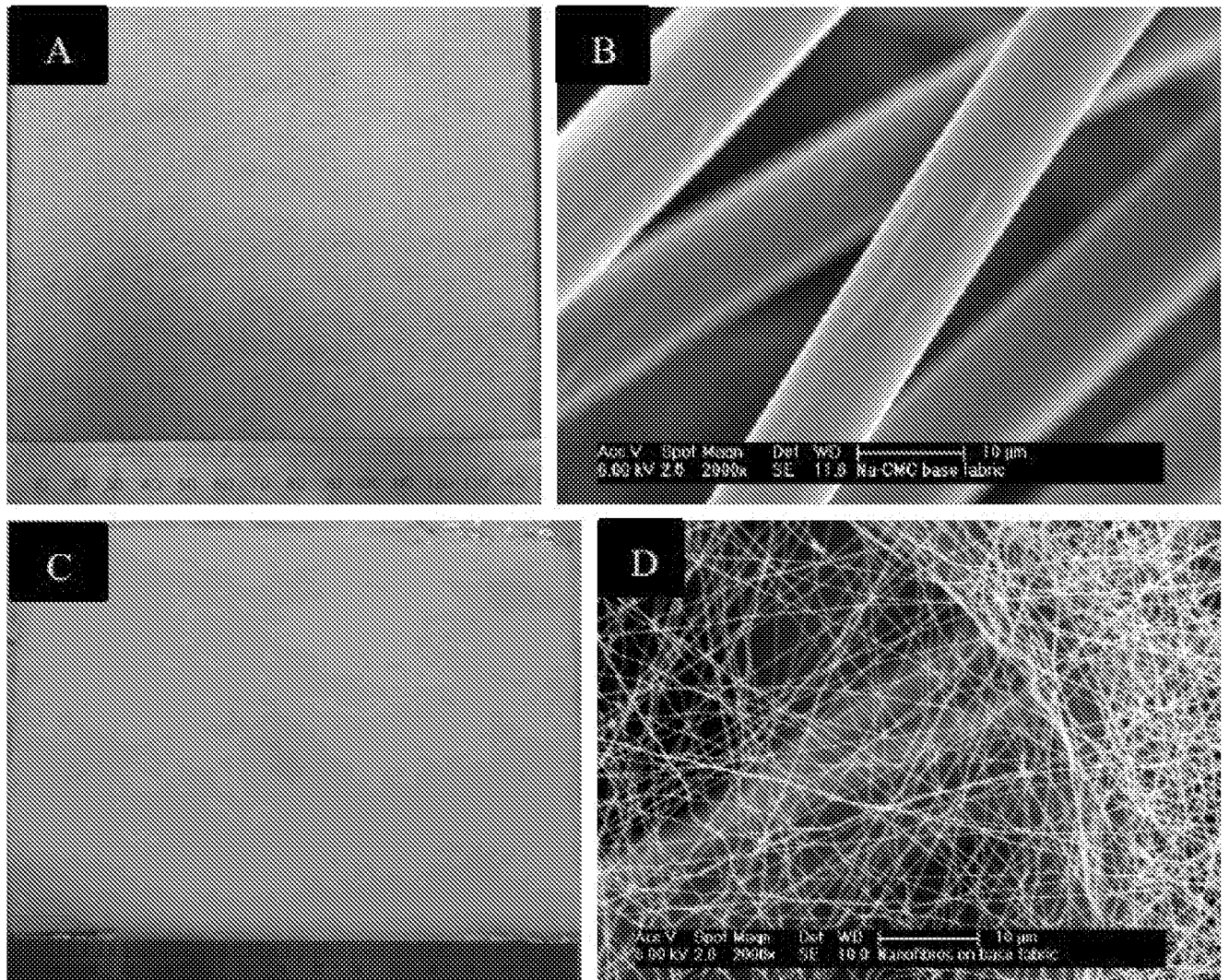


FIG. 7

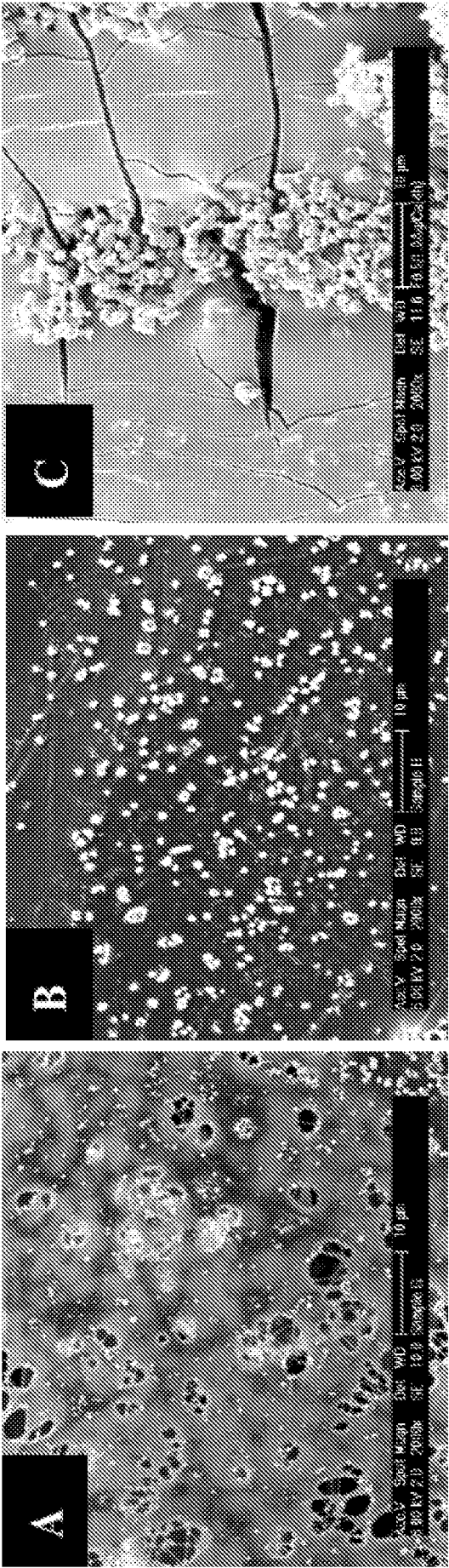


FIG. 8

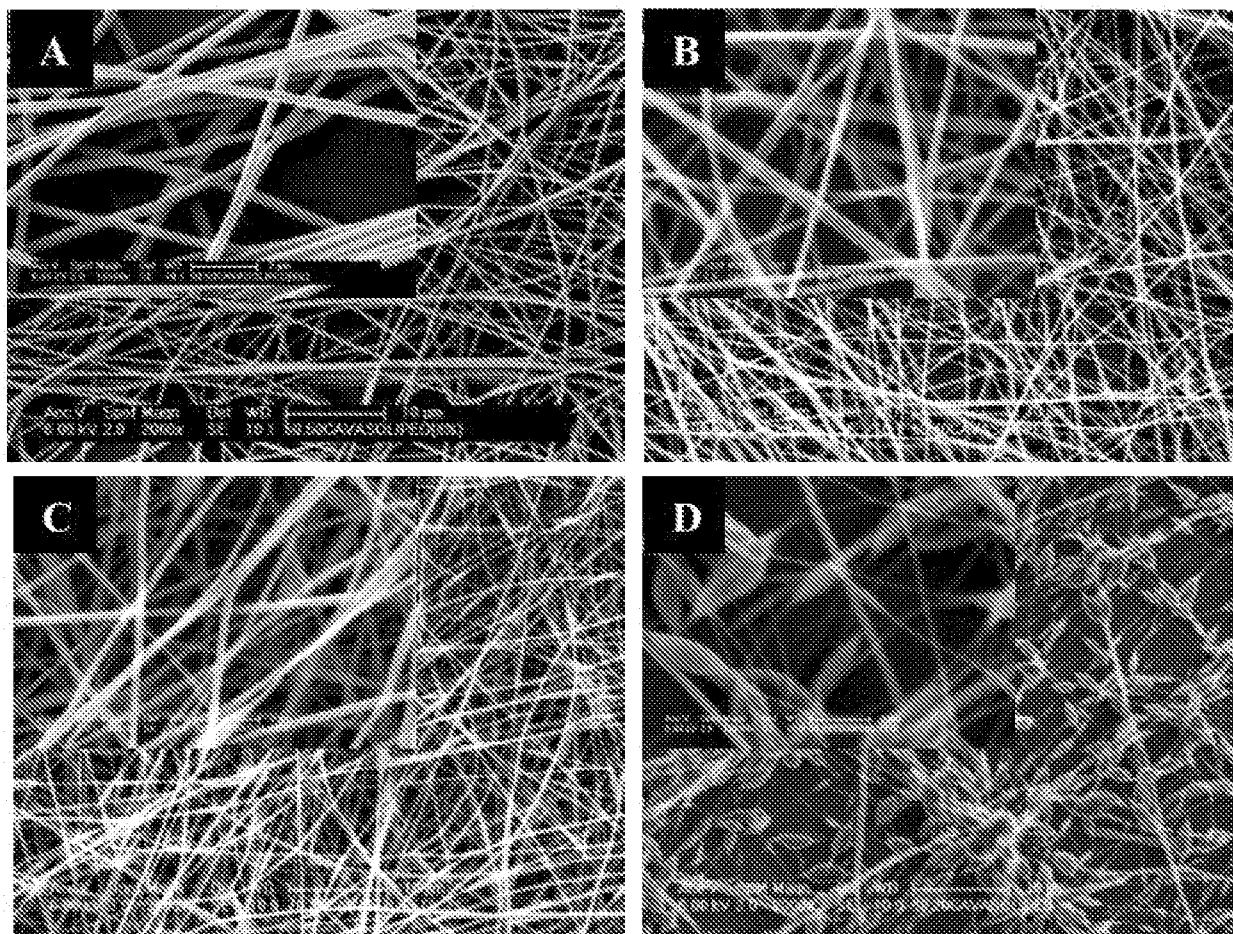


FIG. 9

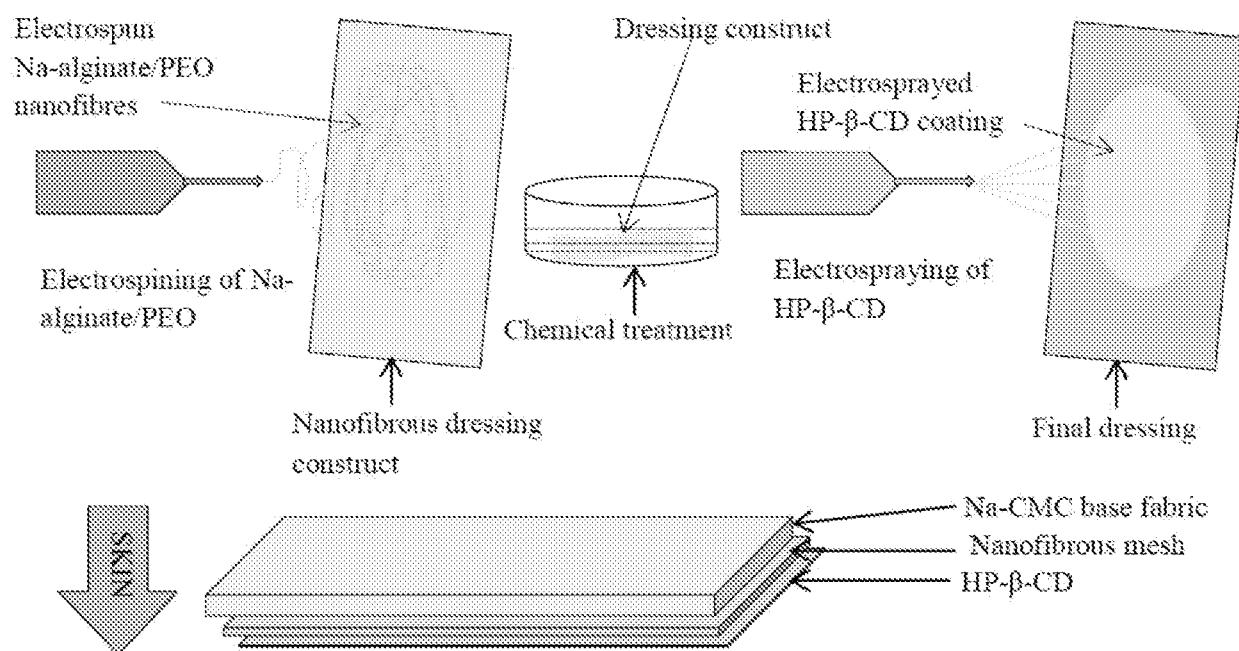
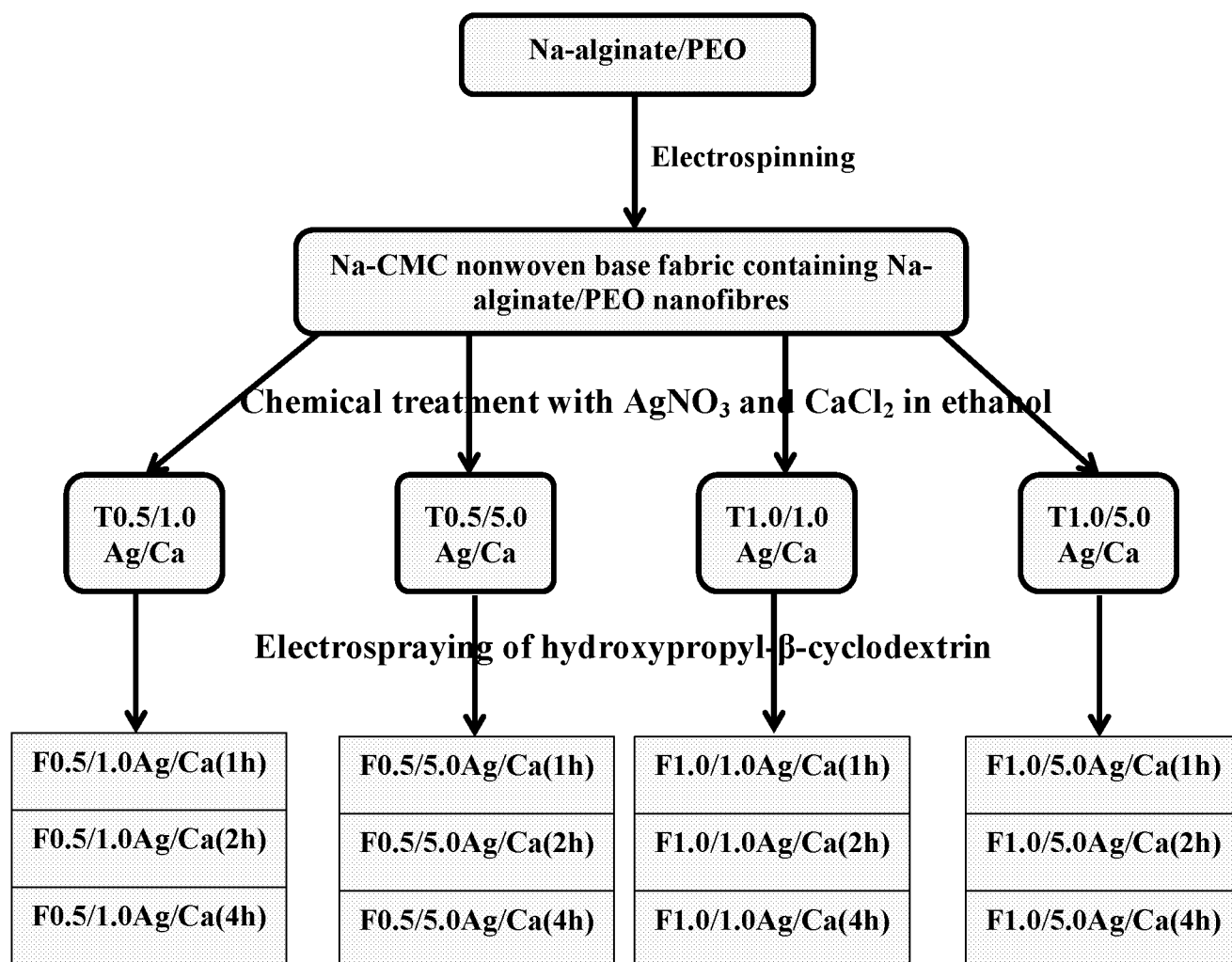
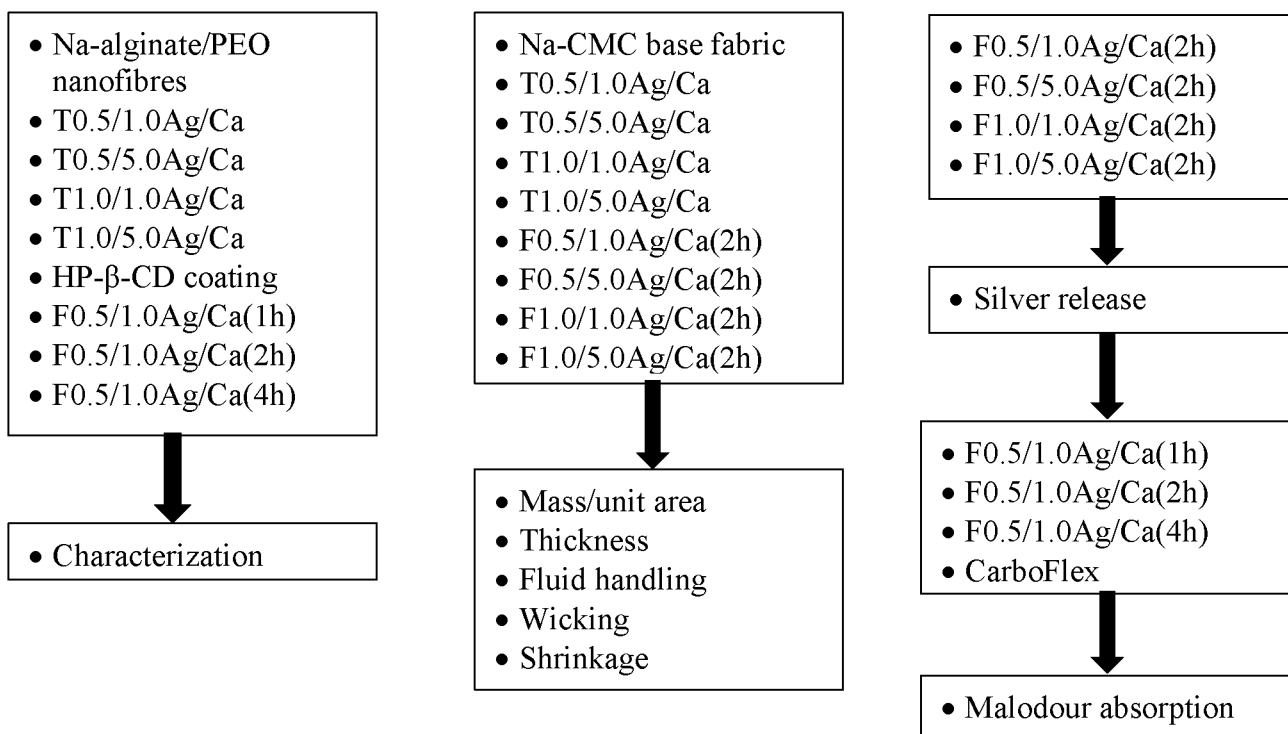


FIG. 10



Corresponding tests & assessments



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/029862

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61L 15/42; A61L 15/28; A61L 15/24; A61L 15/26; A61L 15/62 (2016.01)

CPC - A61L 15/42; A61L 15/28; A61L 15/24; A61L 15/26; A61L 15/62 (2016.05)

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)

IPC(8) - A61L 15/24; A61L 15/26; A61L 15/28; A61L 15/42; A61L 15/62 (2016.01)

CPC - A61L 15/24; A61L 15/26; A61L 15/28; A61L 15/42; A61L 15/62 (2016.05)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

IPC(8) - A61L 15/24; A61L 15/26; A61L 15/28; A61L 15/42; A61L 15/62; CPC - A61L 15/24; A61L 15/26; A61L 15/28; A61L 15/42; A61L 15/62 (keyword delimited)

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

Orbit.com, Google Patents, Google Scholar, Public AppFT and PatFT

Search terms used: calcium, alginate, fiber, silver, odor, polyethylene oxide, hydroxypropyl-β-cyclodextrin, electrospin, backing, diameter, wound, dressing.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2012/0141558 A1 (ZHANG et al) 07 June 2012 (07.06.2012) entire document	1-14, 16-50, 52-57
Y	US 2014/0335200 A1 (ZHANGJIAGANG NELLNANO TECHNOLOGY CO LTD) 13 November 2014 (13.11.2014) entire document	1-14, 16-37
Y	US 2010/0018641 A1 (BRANHAM et al) 28 January 2010 (28.01.2010) entire document	1-14, 16-18, 23, 24, 31, 34-37, 56
Y	WO 1992/022285 A1 (VIADERM PHARMACEUTICALS INC) 23 December 1992 (23.12.1992) entire document	7, 14, 38-50, 52-57
Y	US 2002/0081930 A1 (JACKSON et al) 27 June 2002 (27.06.2002) entire document	26, 47
Y	US 2013/0018336 A1 (LABORATOIRES URGO) 17 January 2013 (17.01.2013) entire document	38-50, 52-57
Y	US 6,753,454 B1 (SMITH et al) 22 June 2004 (22.06.2004) entire document	38-50, 52-57

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

☐ See patent family annex.

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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Date of the actual completion of the international search

15 June 2016

Date of mailing of the international search report

28 JUL 2016

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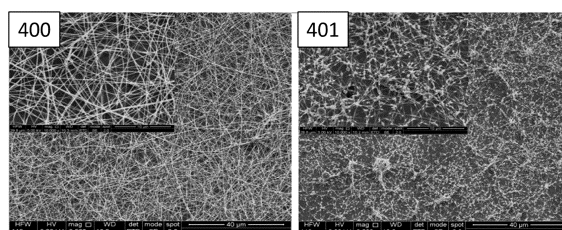
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(54)发明名称

抗菌纳米纤维

(57)摘要

本发明描述抗菌纳米纤维及其制备方法。抗菌纳米纤维包括用银处理以产生银-藻酸盐纳米纤维的初纺藻酸盐纳米纤维。提供的抗菌纳米纤维是伤口敷料的有用组分,其中伤口敷料任选进一步包含恶臭吸收剂,例如环糊精。



1. 一种制备从藻酸盐纳米纤维得到的防臭、抗微生物纳米纤维的方法,所述方法包括:
a) 使藻酸盐纳米纤维与包含钙离子的第一有机溶液接触,以产生钙-藻酸盐纳米纤维;b) 使钙-藻酸盐纳米纤维与包含抗微生物剂的第二有机溶液接触,以产生抗微生物-藻酸盐纳米纤维;和c) 用恶臭吸收剂结合或涂覆抗微生物-藻酸盐纳米纤维,以产生防臭、抗微生物纳米纤维。

2. 权利要求1的方法,其中所述藻酸盐纳米纤维通过电纺包含1%重量至10%重量藻酸盐和PEO的混合物的水溶液形成。

3. 权利要求2的方法,其中所述水溶液包括60:40至80:20的藻酸盐:PEO比。

4. 权利要求1的方法,其中所述第一有机溶液包含0.1%重量至10%重量钙盐。

5. 权利要求4的方法,其中所述钙盐选自氯化钙、溴化钙、氟化钙、碘化钙、硝酸钙和氢氧化钙。

6. 权利要求1的方法,其中所述抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。

7. 权利要求6的方法,其中所述抗生素选自庆大霉素、氧氟沙星、米诺环素、四环素、甲硝唑及其衍生物。

8. 权利要求6的方法,其中所述第二有机溶液包含0.05%重量至10%重量银盐。

9. 权利要求8的方法,其中所述银盐选自硝酸银、氯化银、硫酸银、乳酸银、溴化银、乙酸银及其组合。

10. 权利要求1的方法,其中通过将恶臭吸收剂电喷或电纺到抗微生物纳米纤维表面上,用恶臭吸收剂涂覆抗微生物-藻酸盐纳米纤维。

11. 权利要求1的方法,其中所述恶臭吸收剂包括环糊精。

12. 权利要求1的方法,其中在与第一有机溶液接触之前用有机溶剂洗涤藻酸盐纳米纤维。

13. 权利要求1的方法,其中在与第二有机溶液接触之前用有机溶剂洗涤钙-藻酸盐纳米纤维。

14. 权利要求1的方法,其中在用恶臭吸收剂结合或涂覆之前用有机溶剂洗涤抗微生物-藻酸盐纳米纤维。

15. 权利要求1的方法,其中与所述藻酸盐纳米纤维的平均纤维直径比较,所述防臭、抗微生物纳米纤维的平均纤维直径减小小于10%。

16. 权利要求1的方法,其中在防臭、抗微生物纳米纤维与伤口渗出物接触时,部分抗微生物剂从防臭、抗微生物纳米纤维分离并释放。

17. 权利要求1的方法,其中在防臭、抗微生物纳米纤维与伤口渗出物接触时,部分钙离子从防臭、抗微生物纳米纤维分离并释放。

18. 权利要求1的方法,其中在水溶液中浸泡24小时后,防臭、抗微生物纳米纤维保持完整。

19. 一种防臭、抗微生物纳米纤维,所述纳米纤维包含a) 从包含4%的具有70:30藻酸盐:PEO比的混合物的水溶液电纺的藻酸盐纳米纤维;b) 抗微生物剂;和c) 恶臭吸收剂。

20. 权利要求19的防臭、抗微生物纳米纤维,其中所述抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。

21. 权利要求20的防臭、抗微生物纳米纤维,其中所述抗微生物剂包括银离子。
22. 权利要求19的防臭、抗微生物纳米纤维,其中所述恶臭吸收剂为纤维形式。
23. 权利要求19的防臭、抗微生物纳米纤维,其中所述恶臭吸收剂电纺到藻酸盐纳米纤维上。
24. 权利要求19的防臭、抗微生物纳米纤维,其中所述恶臭吸收剂电喷到藻酸盐纳米纤维上。
25. 权利要求19的防臭、抗微生物纳米纤维,其中所述恶臭吸收剂包括环糊精。
26. 权利要求25的防臭、抗微生物纳米纤维,其中所述环糊精包括羟丙基- β -环糊精(HP- β -CD)。
27. 权利要求19的防臭、抗微生物纳米纤维,其中所述防臭、抗微生物纳米纤维不包括PEO。
28. 权利要求19的防臭、抗微生物纳米纤维,其中平均纳米纤维直径为120nm至150nm。
29. 权利要求21的防臭、抗微生物纳米纤维,其中至少部分银离子在防臭、抗微生物纳米纤维内形成颗粒。
30. 权利要求29的防臭、抗微生物纳米纤维,其中所述颗粒的平均直径为150nm至300nm。
31. 权利要求21的防臭、抗微生物纳米纤维,其中在防臭、抗微生物纳米纤维与伤口渗出物接触时,部分银离子从防臭、抗微生物纳米纤维分离并释放。
32. 权利要求19的防臭、抗微生物纳米纤维,所述纳米纤维进一步包含钙离子。
33. 权利要求32的防臭、抗微生物纳米纤维,其中在防臭、抗微生物纳米纤维与伤口渗出物接触时,部分钙离子从防臭、抗微生物纳米纤维分离并释放。
34. 一种伤口敷料结构,所述伤口敷料结构包括权利要求18的防臭、抗微生物纳米纤维和背衬。
35. 权利要求34的伤口敷料结构,其中所述背衬为织物背衬。
36. 权利要求34的伤口敷料结构,其中所述背衬为尼龙。
37. 权利要求34的伤口敷料结构,其中所述背衬包括羧甲基纤维素(CMC)。
38. 一种制备伤口敷料结构的方法,所述方法包括:在背衬表面上沉积藻酸盐纳米纤维;b) 用包含溶于有机溶剂的钙离子的溶液化学处理藻酸盐纳米纤维,以产生钙-藻酸盐纳米纤维;c) 用包含溶于有机溶剂的抗微生物剂的溶液化学处理钙-藻酸盐纳米纤维,以产生抗微生物-藻酸盐纳米纤维;和d) 使包含恶臭吸收剂的纤维电纺或电喷到抗微生物-藻酸盐纳米纤维表面上。
39. 权利要求38的方法,其中通过电纺包含1%重量至10%重量藻酸盐和PEO的混合物的水溶液,使藻酸盐纳米纤维沉积到背衬表面上。
40. 权利要求39的方法,其中所述水溶液包括60:40至80:20藻酸盐:PEO比。
41. 权利要求38的方法,其中所述包含钙离子的溶液包含0.1%重量至10%重量钙盐。
42. 权利要求41的方法,其中所述钙盐选自氯化钙、溴化钙、氟化钙、碘化钙、硝酸钙和氢化钙。
43. 权利要求38的方法,其中所述抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。

44. 权利要求43的方法,其中所述抗生素选自庆大霉素、氧氟沙星、米诺环素、四环素、甲硝唑及其衍生物。

45. 权利要求43的方法,其中所述包含抗微生物剂的溶液包含0.05%重量至10%重量银盐。

46. 权利要求45的方法,其中所述银盐选自硝酸银、氯化银、硫酸银、乳酸银、溴化银、乙酸银及其组合。

47. 权利要求38的方法,其中所述恶臭吸收剂包括环糊精。

48. 权利要求38的方法,所述方法进一步包括在沉积到背衬表面上后用有机溶剂洗涤藻酸盐纳米纤维。

49. 权利要求38的方法,所述方法进一步包括在用包含抗微生物剂的溶液化学处理前用有机溶剂洗涤钙-藻酸盐纳米纤维。

50. 权利要求38的方法,所述方法进一步包括在用恶臭吸收剂电纺或电喷之前用有机溶剂洗涤抗微生物-藻酸盐纳米纤维。

51. 权利要求38的方法,其中与所述藻酸盐纳米纤维的平均纤维直径比较,所述抗微生物-藻酸盐纳米纤维的平均纤维直径减小小于10%。

52. 权利要求38的方法,其中在伤口敷料结构与伤口渗出物接触时,部分抗微生物剂从伤口敷料结构分离并释放。

53. 权利要求38的方法,其中在伤口敷料结构与伤口渗出物接触时,部分钙离子从伤口敷料结构分离并释放。

54. 权利要求38的方法,其中所述背衬为织物背衬。

55. 权利要求38的方法,其中所述背衬为尼龙。

56. 权利要求38的方法,其中所述背衬包括羧甲基纤维素(CMC)。

57. 一种通过权利要求38的方法制备的纳米纤维结构。

抗菌纳米纤维

[0001] 交叉引用

本申请要求2015年4月28日提交的美国临时申请62/154,056的权益,所述申请全文通过引用结合到本文中。

[0002] 发明背景

与伤口治疗有关的一个重要问题是控制感染。感染可妨碍伤口愈合,对患者有创伤性,并且可显著增加治疗时间和成本。因此,需要预防和治疗由伤口引起的感染,优选与伤口敷料结合。

[0003] 发明概述

本文公开用于受试者伤口治疗的方法和组合物,包括制备和使用包含用纳米纤维材料结合或涂覆的抗微生物剂的组合物。在其它实施方案中,方法和组合物用纳米纤维材料结合防臭组分。在其它实施方案中,方法和组合物用纳米纤维材料结合抗微生物和防臭组分二者。

[0004] 在一个方面,本文提供制备从藻酸盐纳米纤维得到的防臭、抗微生物纳米纤维的方法,方法包括a)使藻酸盐纳米纤维与包含钙离子的第一有机溶液接触,以产生钙-藻酸盐纳米纤维;b)使钙-藻酸盐纳米纤维与包含抗微生物剂的第二有机溶液接触,以产生抗微生物-藻酸盐纳米纤维;和c)用恶臭吸收剂结合或涂覆抗微生物-藻酸盐纳米纤维,以产生防臭、抗微生物纳米纤维。在一些实施方案中,通过电纺包含1%重量至10%重量藻酸盐和聚氧化乙烯(PEO)的混合物的水溶液,例如4%藻酸盐和PEO的混合物,形成藻酸盐纳米纤维。在一些实施方案中,水溶液包括60:40至80:20藻酸盐:PEO比,例如70:30。在一些实施方案中,第一有机溶液包含0.1%重量至10%重量钙盐。例如,钙盐不加限制地包括氯化钙、溴化钙、氟化钙、碘化钙、硝酸钙和氢化钙盐。在一些实施方案中,抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。抗生素不加限制地包括庆大霉素、氧氟沙星、米诺环素、四环素、甲硝唑及其衍生物。在一些实施方案中,第二有机溶液包含0.05%重量至10%重量银盐。银盐不加限制地包括硝酸银、氯化银、硫酸银、乳酸银、溴化银、乙酸银及其组合。在一些实施方案中,通过将恶臭吸收剂电喷、电纺或电喷并电纺到抗微生物-纳米纤维表面上,用恶臭吸收剂涂覆抗微生物-藻酸盐纳米纤维。在一些实施方案中,恶臭吸收剂包括环糊精。在一些情况下,方法包括在与第一有机溶液接触之前用有机溶剂洗涤藻酸盐纳米纤维。在一些情况下,方法包括在用恶臭吸收剂结合或涂覆之前用有机溶剂洗涤抗微生物-藻酸盐纳米纤维。在一些情况下,与藻酸盐纳米纤维的平均纤维直径比较,防臭、抗微生物纳米纤维的平均纤维直径减小小于10%。在一些实施方案中,在防臭、抗微生物纳米纤维与伤口渗出物接触时,防臭、抗微生物纳米纤维的至少部分抗微生物剂从防臭、抗微生物纳米纤维分离并释放。在一些实施方案中,在防臭、抗微生物纳米纤维与伤口渗出物接触时,防臭、抗微生物纳米纤维的至少部分钙离子从防臭、抗微生物纳米纤维分离并释放。在一些情况下,在水溶液中浸泡24小时后,防臭、抗微生物纳米纤维保持完整。

[0005] 在一个方面,本文提供防臭、抗微生物纳米纤维,该纳米纤维包含从包含4%的具有70:30藻酸盐和PEO比的混合物的水溶液电纺的藻酸盐纳米纤维;抗微生物剂;和恶臭吸收

剂。在一些实施方案中,抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。在一些情况下,恶臭吸收剂包括银离子。在一些情况下,至少部分银离子在防臭、抗微生物纳米纤维内形成颗粒。在一些情况下,银离子具有150nm至300nm平均直径。在一些情况下,在与伤口渗出物接触时,防臭、抗微生物纳米纤维中的至少部分银离子从防臭、抗微生物纳米纤维分离并释放。在一些实施方案中,防臭、抗微生物纳米纤维进一步包含钙离子。在一些情况下,在防臭、抗微生物纳米纤维与伤口渗出物接触时,至少部分钙离子分离并释放。在一些实施方案中,防臭、抗微生物纳米纤维的恶臭吸收剂为纤维形式。在一些实施方案中,恶臭吸收剂电纺到藻酸盐纳米纤维上。在一些实施方案中,恶臭吸收剂电喷到藻酸盐纳米纤维上。在一些实施方案中,恶臭吸收剂包括环糊精。在一些实例中,环糊精包括羟丙基-β-环糊精(HP-β-CD)。在一些情况下,防臭、抗微生物纳米纤维不包含PEO。在一些情况下,防臭、抗微生物纳米纤维的平均纳米纤维直径为120nm至150nm。在一些情况下,在水溶液中浸泡24小时后,防臭、抗微生物纳米纤维保持完整。在另一个方面,本文提供一种伤口敷料结构,该伤口敷料结构包括防臭、抗微生物纳米纤维和背衬。在一些实施方案中,背衬为织物背衬。在一些实施方案中,背衬为尼龙。在一些实施方案中,背衬包括羧甲基纤维素(CMC)。

[0006] 在另一个方面,本文提供一种制备伤口敷料结构的方法,所述方法包括:在背衬表面上沉积藻酸盐纳米纤维;b)用包含溶于有机溶剂的钙离子的溶液化学处理藻酸盐纳米纤维,以产生钙-藻酸盐纳米纤维;c)用包含溶于有机溶剂的抗微生物剂的溶液化学处理钙-藻酸盐纳米纤维,以产生抗微生物-藻酸盐纳米纤维;和d)使包含恶臭吸收剂的纤维电纺或电喷到抗微生物-藻酸盐纳米纤维表面上。在一些实施方案中,通过电纺包含1%重量至10%重量藻酸盐和PEO的混合物的水溶液,使藻酸盐纳米纤维沉积到背衬表面上。在一些实施方案中,水溶液包括60:40至80:20的藻酸盐:PEO比。在一些实施方案中,包含钙离子的溶液包含0.1%重量至10%重量钙盐。钙盐不加限制地包括氯化钙、溴化钙、氟化钙、碘化钙、硝酸钙和氢化钙。在一些实施方案中,抗微生物剂包括银、乙酸、氯己定、碘、过氧化氢、次氯酸钠、高锰酸钾、三氯生、抗生素或其组合。抗生素不加限制地包括庆大霉素、氧氟沙星、米诺环素、四环素、甲硝唑及其衍生物。在一些情况下,包含抗微生物剂的溶液包含0.05%重量至10%重量银盐。银盐不加限制地包括硝酸银、氯化银、硫酸银、乳酸银、溴化银、乙酸银及其组合。在一些情况下,恶臭吸收剂包括环糊精。在一些实施方案中,方法进一步包括在沉积到背衬表面上后用有机溶剂洗涤藻酸盐纳米纤维。在一些情况下,方法进一步包括在用恶臭吸收剂电纺或电喷之前用有机溶剂洗涤抗微生物-藻酸盐纳米纤维。在一些情况下,与起始藻酸盐纳米纤维材料的平均纤维直径比较,抗微生物-藻酸盐纳米纤维的平均纤维直径减小小于10%。在一些实施方案中,在伤口敷料结构与伤口渗出物接触时,部分抗微生物剂从伤口敷料结构分离并释放。在一些实施方案中,在伤口敷料结构与伤口渗出物接触时,部分钙离子从伤口敷料结构分离并释放。在一些实施方案中,该背衬为织物背衬。在一些情况下,背衬为尼龙。在一些情况下,背衬包括羧甲基纤维素(CMC)。在其它实施方案中,背衬包括衍生的羧甲基纤维素。在一个方面,本文还提供通过本文提供方法制备的纳米纤维结构。

[0007] 附图简述

图1显示在化学处理之前和之后初纺钠-藻酸盐纳米纤维的扫描电子显微镜图像和相应纤维直径分布。

[0008] 图2为描绘抗菌纳米纤维结构中平均粒径的图解。

[0009] 图3A为化学处理之前和之后初纺纳米纤维垫的4,000至400 cm^{-1} 的红外光谱。图3B为化学处理之前和之后初纺纳米纤维垫的3,500至2,000 cm^{-1} 的红外光谱。

[0010] 图4A显示从70:30钠-藻酸盐:PEO溶液(400)和80:20钠-藻酸盐:PEO溶液(401)纺成的纳米纤维的扫描电子显微镜图像。图4B为图示说明从图4A中所示70:30钠-藻酸盐:PEO溶液纺成的纳米纤维的纤维直径分布的图解。

[0011] 图5显示在4000–400 cm^{-1} 和2000–1000 cm^{-1} 光谱范围内初纺PEO纳米纤维(A)、藻酸钠(B)和藻酸钠/PEO纳米纤维(C)的红外光谱。

[0012] 图6显示在初纺纳米纤维沉积之前和之后基础织物的相片和扫描电子显微镜图像。

[0013] 图7显示对于不同时间阶段用恶臭吸收剂电喷的纳米纤维的扫描电子显微镜图像。

[0014] 图8显示从具有HP- β -CD/PEO的混合物的溶液电纺的纤维的扫描电子显微镜图像。

[0015] 图9提供制备包含纳米纤维的敷料结构的实例工作流程。

[0016] 图10提供制备纳米纤维结构的实例方法汇总。

[0017] 发明详述

在不同的实施方案,本文提供用抗菌剂化学处理纳米纤维以产生抗菌纳米纤维。适合抗菌剂为银,在为离子形式时,这是一种抗很多格兰氏阴性菌和格兰氏阳性菌(包括耐抗生素菌株,例如耐甲氧西林和耐万古霉素的金黄色葡萄球菌和粪肠球菌)的有效抗微生物剂。

[0018] 所述抗菌纳米纤维可用作伤口敷料的组分。在一些实施方案,通过用抗菌剂处理包含生物聚合物的纳米纤维制备抗菌纳米纤维。例如,从包含一种或多种生物聚合物的溶液电纺纳米纤维,随后用抗菌剂处理。示例性生物聚合物为藻酸盐。藻酸盐可用于在伤口敷料中吸收大量伤口流体,同时形成胶状物质,因此,保持伤口的潮湿微环境。在示例性实施方案中,从初纺纳米纤维得到抗菌纳米纤维,其中通过电纺包含生物聚合物和任选载体聚合物和/或表面活性剂的溶液,形成初纺纳米纤维。在一些实施方案中,通过电纺包含藻酸盐和载体聚合物的溶液,形成初纺纳米纤维。在一些情况下,载体聚合物为聚氧化乙烯(PEO)。

[0019] 在多种实施方案中,从包含适合最终用于伤口敷料的生物聚合物的纳米纤维得到抗菌纳米纤维。在一些实施方案,纳米纤维包含与一种或多种载体聚合物或载剂结合的生物聚合物。用作本文所述纳米纤维组分的生物聚合物和/或载体的非限制实例包括藻酸盐、脱乙酰壳多糖、羧甲基纤维素(CMC)、葡聚糖、胶原、糖胺聚糖、纤维素、聚(己内酯)、羟乙乳酸聚酯、明胶、PEO、聚乙烯醇、聚乙烯基己内酰胺、聚乙酸乙烯酯、聚乙二醇、纤维素衍生物、聚乙烯吡咯烷酮、聚L-乳酸、聚(ϵ -己内酯)、脱乙酰壳多糖、其衍生物、溶液及其任何组合。在一些情况下,包含生物聚合物或生物聚合物和载体的溶液与表面活性剂电纺,例如 oxtoxynol (TritonTMX-100)、聚山梨酯(TweenTM)、硬脂醇、脱水山梨糖醇、聚甘油聚蓖麻油酸酯、泊洛沙姆、四缩(五乙二醇)单十二烷基醚、油基醇、辛基葡糖苷、N-辛基 β -D-硫基吡喃葡糖苷、七缩(八乙二醇)单十二烷基醚、NP-40、壬基醇醚、nonidet P-40、甘油单月桂酸酯、乙氧基化物、月桂基葡糖苷、异鲸蜡醇聚醚-20、IGEPAL CA-630、癸基葡糖苷、聚西托醇、十六醇十八醇混合物、鲸蜡醇、椰油酰胺DEA、椰油酰胺MEP或其衍生物或组合。

[0020] 在多种实施方案中,从包含生物聚合物和任选载体和/或表面活性剂的有机溶液制备纳米纤维。在供选实施方案中,从包含生物聚合物和任选载体和/或表面活性剂的水溶液制备纳米纤维。在其它实施方案中,从包含生物聚合物和任选载体和/或表面活性剂的混溶性水-有机溶液制备纳米纤维。

[0021] 在一些实例中,通过电纺包含约1%重量至约50%重量生物聚合物的溶液制备纳米纤维。在一些实例中,通过电纺包含约1%重量至约50%重量生物聚合物和载体的溶液制备纳米纤维。在一些情况下,溶液中生物聚合物或生物聚合物:载体的重量百分数为约1%重量至约50%重量,约1%重量至约40%重量,约1%重量至约30%重量,约1%重量至约20%重量,约1%重量至约10%重量。在一些情况下,溶液中生物聚合物或生物聚合物:载体的重量百分数为约1%、2%、3%、4%、5%、6%、7%、8%、9%或10%。对于从电纺包含生物聚合物和载体的溶液制备的纳米纤维,生物聚合物:载体之比可以为约20:80至约95:5,约30:70至约95:5,约40:70至约95:5,约50:70至约95:5,约60:80至约90:10,约60:80至约80:20。在一些实施方案中,电纺溶液中生物聚合物:载体之比为60:40、61:39、62:38、63:37、64:36、65:35、66:34、67:33、68:32、69:31、70:30、71:29、72:28、73:27、74:26、75:25、76:24、77:23、78:22、79:21或80:20。在一些实施方案中,从1%重量至50%重量的具有约20:80至约95:5生物聚合物:载体聚合物的生物聚合物和载体聚合物的溶液电纺纳米纤维。例如,通过电纺4%重量70:30生物聚合物:载体聚合物溶液制备电纺或初纺纳米纤维。初纺纳米纤维可包含约20%重量至约95%重量生物聚合物,优选50至90%重量,更优选60%重量至80%重量,例如70%重量生物聚合物。在一个实施方案中,初纺纳米纤维包含约60%重量至约80%或约70%重量藻酸或其盐。初纺纳米纤维可包含5%至80%载体聚合物,优选10%至50%,更优选20%至40%,例如30%载体聚合物。在一个实施方案中,初纺纳米纤维包含约20%至约40%PEO,例如30%PEO。在一个实例中,通过电纺4%重量70:30藻酸盐:载体聚合物溶液制备纳米纤维,其中载体聚合物任选为PEO,溶液任选包含表面活性剂,例如Triton™ X-100。

[0022] 在一些实施方案中,从纳米纤维基本去除载体,例如,通过用适合保持纳米纤维不溶的溶液洗涤纳米纤维,例如,包含有机溶剂的溶液。例如,在从纳米纤维去除大于90%、大于92%、大于94%、大于96%或大于98%载体时,或在载体不能通过光谱方法例如红外光谱检测时,载体基本被去除。在一些实施方案中,至少部分从纳米纤维去除表面活性剂,例如,从纳米纤维去除至少约50%表面活性剂。在其它实施方案中,未从纳米纤维基本去除表面活性剂(例如,去除小于约50%)。

[0023] 在不同实施方案中,抗菌纳米纤维从平均直径为约50nm至约500nm、约60nm至约400nm、约70nm至约300nm、约70nm至约200nm、约80nm至约200nm、约90nm至约150nm或约100nm至约140nm的纳米纤维得到。在实施方案中,平均纤维直径小于约200nm,小于约150nm,或小于约130nm。在一些实施方案中,平均纤维直径大于约50nm,大于约70nm,或大于约90nm。

[0024] 在不同实施方案中,本文所述纳米纤维形成纳米纤维结构,例如,纳米纤维垫。在一些实施方案中,纳米纤维包含初纺生物聚合物。在示例性实施方案中,用抗菌剂化学处理纳米纤维和/或纳米纤维垫,以产生抗菌纳米纤维。如本文所述,至少在一些实施方案中,纳米纤维包括纳米纤维结构内的纳米纤维。

[0025] 在一些实施方案,本文提供的抗菌纳米纤维或纳米纤维结构包含一种或多种可用

于伤口处理的组分。在一些实施方案,包含抗菌纳米纤维的伤口敷料包含一种或多种可用于伤口处理的组分。可用于伤口处理的组分的非限制实例包括药物、抗微生物化合物、脂类、甘油三酯、维生素、矿物、最大限度地减少恶臭化合物出现的酶和生长因子。抗微生物化合物包括抗菌剂(例如,乙酸、氯己定、银、碘、过氧化氢、次氯酸钠、高锰酸钾、聚六甲基双胍、三氯生)和抗生素(例如,庆大霉素、氧氟沙星、米诺环素、四环素、甲硝唑及其衍生物)。生长因子的非限制实例包括上皮生长因子、血小板衍生生长因子和人生长激素。维生素的实例包括维生素A、维生素C和维生素E。矿物的非限制实例包括铜和锌。

[0026] 纳米纤维通常为水溶性,因此,不能保持在生物医疗应用的水性环境中,例如伤口敷料。使可溶性生物聚合物纳米纤维转化成不溶性纳米纤维的一种方法包括使生物聚合物与钙(II)离子络合,以产生钙-生物聚合物纳米纤维。通过在钙和阳离子-生物聚合物络合物(例如钠-生物聚合物络合物)中的阳离子(例如,钠)之间离子交换,可生成钙-生物聚合物纳米纤维。在一些实施方案中,通过在包含钙(II)离子(例如,来自钙盐的钙(II)离子)的钙处理溶液中浸泡生物聚合物纳米纤维,促进离子交换反应。在一些实施方案中,生物聚合物包括藻酸或藻酸盐,例如藻酸钠。示例性钙盐不加限制地包括氯化钙、溴化钙、氟化钙、碘化钙、硝酸钙、氢化钙、硫酸钙、磷酸钙、草酸钙、亚硝酸钙、钼酸钙、苯甲酸钙和碳酸钙。在很多实施方案中,钙处理溶液中钙(II)离子或钙盐的百分数为约0.1%至约10%、约0.1%至约9%、约0.1%至约8%、约0.1%至约7%、约0.1%至约6%、约0.1%至约5%、约0.5%至约10%、约0.5%至约9%、约0.5%至约8%、约0.5%至约7%、约0.5%至约6%、约0.5%至约5%或约1%至约5%。在示例性实施方案中,钙处理溶液中钙(II)离子或钙盐的百分数为约0.5%、约1%、约1.5%、约2%、约2.5%、约3%、约3.5%、约4%、约4.5或约5%。可用钙处理溶液处理纳米纤维至少约1分钟、至少约2分钟、至少约3分钟、至少约4分钟、至少约5分钟、至少约6分钟、至少约7分钟、至少约8分钟、至少约9分钟、至少约10分钟、至少约12分钟、至少约15分钟或至少约20分钟。在一些情况下,用钙处理溶液处理纳米纤维小于约30分钟、小于约25分钟、小于约20分钟、小于约15分钟或小于约10分钟。在一个实例中,用钙处理溶液处理纳米纤维5分钟、6分钟、7分钟、8分钟、9分钟、10分钟、11分钟、12分钟、13分钟、14分钟或15分钟。

[0027] 在一些实施方案中,通过将钙(II)离子溶于有机溶剂或有机混溶性溶剂产生钙处理溶液,保持纳米纤维不溶性。有机溶剂或有机混溶性溶剂不加限制地包括乙醇、乙酸、丙酮、乙腈、苯、1-丁醇、2-丁醇、2-丁酮、叔丁醇、四氯化碳、氯苯、氯仿、环己烷、1,2-二氯乙烷、一缩(二乙二醇)、乙醚、二甘醇二甲醚(二乙二醇二甲醚)、1,2-二甲氧基乙烷(乙二醇二甲醚,DME)、二甲基甲酰胺(DMF)、二甲亚砜(DMSO)、1,4-二氧杂环己烷、乙酸乙酯、乙二醇、甘油、庚烷、六甲基磷酰胺(HMPA)、六甲基亚磷酰三胺(HMPT)、己烷、甲醇、甲基·叔丁基醚(MTBE)、二氯甲烷、N-甲基-2-吡咯烷酮(NMP)、硝基甲烷、戊烷、1-丙醇、2-丙醇、四氢呋喃(THF)、甲苯、三乙胺、重水及其任何溶液(例如,50%有机溶剂、90%有机溶剂)或其组合。在一个实例中,钙处理溶液包括溶于乙醇(例如,无水乙醇或>98%乙醇)的钙(II)离子(例如,来自CaCl₂的钙(II)离子)。

[0028] 抗菌纳米纤维

本文所述纳米纤维易络合或保持抗微生物剂,例如,抗微生物物质,例如银。在一些实施方案中,用抗菌处理溶液化学处理纳米纤维,例如包含生物聚合物的初纺纳米纤维,以产生抗菌纳米纤维。在一些实施方案中,通过电纺包含生物聚合物和任选一种或多种载体聚

合物和/或表面活性剂的溶液制备用于抗菌处理的纳米纤维。在一些实施方案中,在抗菌处理之前洗涤纳米纤维。在一些实施方案中,用包含有机溶剂(例如,乙醇)的溶液洗涤纳米纤维。在一些实施方案中,在抗菌处理之前用溶液处理纳米纤维,以给予纳米纤维不溶性。在一些实例中,生物聚合物包括藻酸盐。在一些实例中,抗菌处理溶液包含银。在一些实例中,给予纳米纤维不溶性的溶液包含钙(II)离子。

[0029] 在一些情况下,用于抗菌化学处理的纳米纤维为伤口敷料或敷料结构中的纳米纤维或纳米纤维垫。敷料结构包括伤口敷料的任何结构组件,例如纳米纤维垫、背衬、吸收层及其任何组合。在很多情况下,纳米纤维性结构或纳米纤维结构包括纳米纤维垫。在其它情况下,纳米纤维性结构或纳米纤维结构包括纳米纤维(在一些情况下,包括纳米纤维垫)和结构载体(例如,背衬)。

[0030] 在多种实施方案中,例如通过用包含银(I)离子的银处理溶液浸泡,化学处理纳米纤维,得到结合银的纳米纤维。在一些实施方案中,在银处理期间,银(I)离子与络合到纳米纤维的生物聚合物的阳离子离子交换,产生银-生物聚合物络合物。在示例性实施方案中,银(I)离子与阳离子-藻酸盐纳米纤维中的阳离子离子交换,以产生阳离子-藻酸盐络合物,其中阳离子任选为钠(I)离子。在一些实施方案中,银(I)离子与钙-藻酸盐纳米纤维中的钙(II)离子离子交换,以产生银-藻酸盐络合物。在一些情况下,银(I)离子与钙-藻酸盐纳米纤维络合产生银-藻酸盐-钙络合物。在一些实施方案中,来自银处理溶液的银(I)离子在纳米纤维内沉淀为颗粒,例如,通过产生不溶性银盐(例如,氯化银)。在示例性实施方案中,依次用钙溶液和银处理溶液处理纳米纤维。在一些实施方案中,在用钙溶液、银溶液或钙和银溶液二者化学处理之前,用适合去除纳米纤维中一种或多种非生物聚合物组分(例如,载体、表面活性剂)的溶液(例如,有机溶剂)洗涤纳米纤维。至少在一些情况下,结合银(I)离子的纳米纤维为抗菌纳米纤维。

[0031] 在一些实施方案中,银处理溶液包括银盐,不加限制地包括硝酸银、氯化银、硫酸银、乳酸银、溴化银、乙酸银、混溶于或可溶于有机溶剂的任何银盐及其任何组合。

[0032] 在一些实施方案中,银处理溶液包含约0.1%至约5%、约0.1%至约4%、约0.1%至约3%、约0.1%至约2%、约0.2%至约5%、约0.2%至约4%、约0.2%至约3%、约0.2%至约2%、约0.3%至约2%、约0.4%至约2%或约0.5%至约1%银(I)离子。在示例性实施方案中,银处理溶液中银(I)离子的百分数为约0.5%、约1%、约1.5%、约2%、约2.5%、约3%、约3.5%、约4%、约4.5或约5%。银处理溶液优选为溶于保持纳米纤维结构完整性的溶液中的银(I)离子的溶液,即,在合理时间段例如24小时内不溶解纳米纤维。在一个实例中,银处理溶液包含溶于含有机溶剂(例如,乙醇)的溶液中的银(I)离子。可用银处理溶液处理纳米纤维至少约1分钟、至少约2分钟、至少约3分钟、至少约4分钟、至少约5分钟、至少约6分钟、至少约7分钟、至少约8分钟、至少约9分钟、至少约10分钟、至少约12分钟、至少约15分钟或至少约20分钟。在一些情况下,用银处理溶液处理纳米纤维小于约30分钟、小于约25分钟、小于约20分钟、小于约15分钟或小于约10分钟。在一个实例中,用银处理溶液处理纳米纤维5分钟、6分钟、7分钟、8分钟、9分钟、10分钟、11分钟、12分钟、13分钟、14分钟或15分钟。

[0033] 抗菌纳米纤维的性质

在多个方面,本文提供适用于伤口敷料的抗菌纳米纤维,其中通过化学处理生物聚合物纳米纤维制备抗菌纳米纤维。在多种情况下,从包含生物聚合物和任选载体和/或表面活

性剂的初纺纤维制备抗菌纳米纤维。在示例性实施方案中,初纺纳米纤维包含藻酸盐和任选PEO和/或Triton™ X-100。在一些实施方案中,用抗微生物离子处理初纺纳米纤维,例如,用银处理溶液,以产生抗菌纳米纤维。在一些实施方案中,用配置为给予纳米纤维在水溶液中不溶性的溶液处理初纺纳米纤维。在一些实施方案中,在用抗微生物离子处理之前用钙处理溶液处理初纺纳米纤维。抗微生物纳米纤维的化学组成及其用于伤口敷料中作用的性质(例如,吸收性、抗微生物内容物、结构稳定性)完全或部分取决于一种或多种处理之前和之后纳米纤维组分的同一性和浓度及纳米纤维处理溶液中反应剂的同一性和浓度(例如,钙处理溶液、银处理溶液)。

[0034] 本文所用经化学处理纳米纤维指用给予纳米纤维不溶性的溶液(例如,钙溶液)、抗微生物溶液(例如,银溶液)或其组合处理的纳米纤维。

[0035] 用银处理的抗微生物纳米纤维的化学组成至少部分取决于银处理溶液中银(I)离子的百分数。在一些实施方案中,银(I)离子占不归入单质碳的抗菌纳米纤维重量的约5%至约75%、约10%至约75%、约15%至约75%、约20%至约75%、约25%至约75%、约30%至约75%、约35%至约75%、约40%至约75%、约45%至约75%、约50%至约75%、约50%至约70%或约50%至约65%。在一些实例中,经处理抗菌纳米纤维中银(I)的百分数为不归入单质碳的抗菌纳米纤维重量的小于约65%、小于约60%、小于约55%、小于约50%、小于约45%、小于约40%、小于约35%、小于约30%、小于约25%、小于约20%、小于约15%、小于约10%、小于约5%或小于约1%。在其它或另外的实例中,经处理抗菌纳米纤维中银(I)的百分数为不归入单质碳的抗菌纳米纤维重量的大于约0.1%、大于约0.5%、大于约1%、大于约2%、大于约3%、大于约4%、大于约5%、大于约6%、大于约7%、大于约8%、大于约9%、大于约10%、大于约15%、大于约20%、大于约25%或大于约50%。

[0036] 在多种实施方案中,抗菌纳米纤维中的银(I)离子与生物聚合物(例如,藻酸盐)络合,用阴离子盐(例如,氯化物)沉淀,或其组合。在一些实施方案中,抗菌纳米纤维中的银(I)离子通过在含盐的水性环境(例如,伤口)中离子交换释放。在一些实例中,交换进入水性环境的银(I)离子为与纳米纤维中生物聚合物(例如,藻酸盐)络合的银(I)离子。

[0037] 已用钙处理的抗菌纳米纤维的化学组成至少部分取决于钙处理溶液中钙(II)离子的百分数。在一些实施方案中,经处理抗菌纳米纤维中钙(II)的百分数为不归入单质碳的抗菌纳米纤维重量的约1%至约50%、约2%至约20%、优选小于约20%,更优选小于约15%。

[0038] 在一些实施方案中,在与伤口接触时,抗菌纳米纤维中的钙与伤口中的钠离子离子交换,作为促进伤口愈合的止血剂。在一些实例中,包含钙-藻酸盐的纳米纤维在与伤口中的钠离子交换中沉淀,产生藻酸钠凝胶。该藻酸钠凝胶可用于保持伤口的潮湿愈合微环境。

[0039] 在一些实施方案中,经处理抗菌纳米纤维中氧的百分数为不归入单质碳的抗菌纳米纤维重量的约5%至约50%,优选约10%至约25%,或优选约15%至约25%。

[0040] 在一些实施方案中,抗菌纳米纤维已用氯化钙溶液处理。在这些情况下,经处理纳米纤维中氯化物的浓度为约1%至约25%,或小于约1%。在一些实施方案中,经处理抗菌纳米纤维中氯化物的浓度为约1%至约20%、约3%至约20%、约5%至约20%、约1%至约10%、约2%至约10%、约3%至约10%或约5%至约10%。在一些实施方案中,经处理抗菌纳米纤维中氯化物的浓度小于约20%、小于约15%、小于约10%、小于约9%、小于约8%、小于约7%、小于约6%或小于约

5%。在示例性实施方案中,经处理抗菌纳米纤维中氯化物的浓度在不归入单质碳的抗菌纳米纤维重量的1%和10%之间。

[0041] 在一些实施方案中,抗菌纳米纤维从经化学处理的钠-藻酸盐纳米纤维得到。在一些实施方案中,经处理纳米纤维中钠的浓度为不归入单质碳的抗菌纳米纤维重量的约1%至约20%或小于1%。在一些实施方案中,经处理纳米纤维中钠的浓度为不归入单质碳的抗菌纳米纤维重量的约1%至约15%、约1%至约10%、约1%至约9%、约1%至约8%、约1%至约7%、约1%至约6%、约1%至约5%、约2%至约10%或约2%至约5%。在一些实施方案中,经处理纳米纤维中钠的浓度小于约10%重量、小于约9%、小于约8%、小于约7%、小于约6%或小于约5%。在示例性实施方案中,经处理纳米纤维中钠的浓度在不归入单质碳的抗菌纳米纤维重量的1%和5%之间。

[0042] 在一些实施方案中,从通过电纺包含生物聚合物和载体聚合物的溶液制备的初纺纳米纤维得到抗菌纳米纤维。在一些实施方案中,载体聚合物为PEO。在很多情况下,抗菌纳米纤维不包含可检测微量的载体聚合物。例如,通过光谱技术例如红外光谱,在纳米纤维中检测不到载体聚合物。在一些实施方案中,在抗菌纳米纤维中不存在至少90%、至少95%或至少99%载体聚合物。

[0043] 在多种实施方案中,纳米纤维的形态在化学处理后改变。例如,平均纤维直径根据化学处理类型减小或增加。在一些实例中,用钙和银溶液依次处理得到抗菌纳米纤维,其平均纤维直径比衍生出它们的纳米纤维更小。在一些实施方案中,化学处理得到具有平均纤维直径减小1%和50%之间的纳米纤维。在一些实施方案中,平均纤维直径减小在约1%和约20%之间、在约1%和约10%之间、在约1%和约9%之间、在约1%和约8%之间、在约2%和约10%之间、在约2%和约9%之间、在约2%和约8%之间或在约3%和约8%之间。在一些实施方案中,平均纤维直径减小小于约10%、小于约9%、小于约8%、小于约7%、小于约6%、小于约5%、小于约4%、小于约3%、小于约2%或小于约1%。在一些实施方案中,平均纤维直径在化学处理后不显著减小。在一些实施方案中,平均纤维直径在化学处理后增加。在一些实施方案中,经化学处理抗菌纳米纤维的平均纤维直径为约30nm至约500nm、约60nm至约440nm、约80nm至约200nm、约100nm至约160nm、约110nm至约150、约120nm至约150nm、约125nm至约145nm或约125nm至约140nm。在一些实施方案中,从钠-藻酸盐纳米纤维得到抗菌纳米纤维,其中钠-藻酸盐纳米纤维任选通过电纺包含藻酸钠和PEO的溶液来制备。

[0044] 在一些情况下,用抗菌剂处理纳米纤维得到具有比处理前纳米纤维更宽纤维直径分布的抗菌纳米纤维。在一些实施方案中,依次用钙和银溶液处理纳米纤维。在一些实施方案中,至少约75%抗菌纳米纤维具有约80nm和约200nm之间或约80nm和约160nm之间的纤维直径。在一些实施方案中,至少约50%抗菌纳米纤维具有约80nm和160nm之间或约100nm和约140nm之间的纤维直径。

[0045] 在一些情况下,用抗菌剂处理纳米纤维导致纳米纤维结构中的一根或多根纳米纤维断裂。在一些实施方案中,依次用钙和银溶液处理纳米纤维。在一些实施方案中,纳米纤维断裂至少部分与钙处理溶液中钙(II)离子的浓度相关。例如,用5% CaCl_2 溶液处理的纳米纤维结构具有比用1-4% CaCl_2 溶液处理的纳米纤维结构更多的断裂纳米纤维,例如1% CaCl_2 溶液。

[0046] 在一些情况下,用抗菌剂处理纳米纤维结构中的纳米纤维得到包含许多个球形颗粒的抗菌纳米纤维结构。在一些实施方案中,依次用钙和银溶液处理纳米纤维。在一些实施

方案中,球形颗粒包含单质银和/或银(I)离子,其中在处理过程期间任选例如用氯化物或另一种阴离子盐沉淀银(I)离子。在一些实施方案中,球形颗粒具有约100nm至约350nm或约150nm至约300nm的直径。在另一个实施方案中,球形颗粒的平均直径为约180nm至约250nm、约190nm至约230nm或约200nm至约220nm,其中标准偏差为约10nm至约50nm。

[0047] 在一些情况下,用抗菌剂处理纳米纤维得到抗菌纳米纤维,其具有与衍生出它们的纳米纤维相比在水性环境中增加抗溶解性。在一些实施方案中,依次用钙和银溶液处理纳米纤维。例如,在根据BS EN 13726-1:2002第3.7节(水凝胶敷料在水中的分散和稳定性)进行溶解度检验后,抗菌纳米纤维保持完整。在一些实施方案中,在水或模拟检验溶液(STS)中浸泡的抗菌纳米纤维在室温(例如,在约20℃和25℃之间)保持不溶至少120分钟。在一些实施方案中,在水中浸泡的抗菌纳米纤维保持不溶至少2小时、至少3小时、至少4小时、至少5小时、至少6小时、至少7小时、至少8小时、至少9小时、至少10小时、至少11小时、至少12小时、至少24小时或至少48小时。经浸泡抗菌纳米纤维的不溶性可通过视觉检查评估。示例性STS为包含血清和一种或多种盐以模拟伤口渗出物的水溶液。在一个实例中,STS包含0.4M氯化钠、0.02M氯化钙和10%新生小牛血清。

[0048] 纳米纤维组成

在多个方面,本文提供适用于伤口敷料的抗菌纳米纤维,其中通过化学处理生物聚合物纳米纤维制备抗菌纳米纤维。在多种情况下,从包含生物聚合物和任选载体和/或表面活性剂的初纺纤维制备抗菌纳米纤维。在一些实施方案中,生物聚合物包括藻酸盐。在一些实施方案中,载体包括PEO。在一些实施方案中,表面活性剂为Triton™ X-100。用抗微生物离子处理纳米纤维,例如,初纺纳米纤维,例如,用银处理溶液,以产生抗菌纳米纤维。在一些实施方案中,用配置为给予纳米纤维在水溶液中不溶性的溶液处理纳米纤维。在一些实施方案中,在用抗微生物离子处理之前用钙处理溶液处理初纺纳米纤维。

[0049] 在多种实施方案中,本文提供的抗菌纳米纤维与伤口敷料的一种或多种成分结合,和/或进一步用伤口敷料中所用的一种或多种剂处理。在一些实施方案中,伤口敷料中可用的剂为恶臭吸收剂,例如环糊精。

[0050] 在一些实施方案中,纳米纤维与背衬结合成复合敷料结构或纳米纤维敷料结构。在一些实施方案中,纳米纤维为抗菌纳米纤维。在一些实施方案中,纳米纤维与背衬结合,然后经化学处理,以在纳米纤维敷料结构内产生抗菌纳米纤维。复合敷料结构适合作为伤口敷料或用作伤口敷料的组分。适合背衬为可用于构造伤口敷料的机械稳定材料。适合背衬不加限制地包括包含例如羧甲基纤维素(CMC)的非织造背衬。在一些实施方案中,纳米纤维电纺到背衬上。在一些实施方案中,使纳米纤维或纳米纤维结构附着到背衬。在一些实施方案中,纳米纤维布置在背衬和另一个伤口敷料组分或层之间。在多种情况下,纳米纤维为藻酸盐纳米纤维,例如初纺藻酸盐纳米纤维。在一些实施方案中,背衬可用于吸收伤口渗出物、提供防止细菌穿透和外来污染的屏障、允许伤口中的氧平衡、帮助细胞生长或其任何组合。

[0051] 在多种实施方案中,化学处理纳米纤维敷料结构,以产生不溶性纳米纤维(例如,钙处理)。在一些实施方案中,化学处理纳米纤维敷料结构,以产生抗菌纳米纤维(例如,银处理)。在一些实施方案中,依次用钙和银的溶液化学处理纳米纤维敷料结构。在一些实施方案中,依次用钙和银的溶液化学处理纳米纤维,然后沉积、附着或另外与背衬结合,以产

生抗菌纳米纤维敷料结构。在一些实例中,纳米纤维敷料结构包括纳米纤维和背衬。在一些实例中,纳米纤维为藻酸盐纳米纤维,例如初纺藻酸盐纳米纤维。

[0052] 在多种实施方案中,如下制备抗菌纳米纤维敷料结构:a)使生物聚合物溶液沉积到背衬上,以产生纳米纤维结构;b)使纳米纤维结构与钙溶液接触,以产生钙-生物聚合物纳米纤维;和c)使钙-生物聚合物纳米纤维与银溶液接触,以产生包含银-生物聚合物纳米纤维的抗菌纳米纤维敷料结构。在一些情况下,使生物聚合物溶液通过电纺沉积到背衬上。在一些情况下,使生物聚合物溶液电纺成初纺纳米纤维。在一些情况下,生物聚合物溶液包含生物聚合物和任选载体和/或表面活性剂。在一些实例中,生物聚合物包括藻酸盐。在一些情况下,载体为PEO。在一些情况下,表面活性剂为TritonTM X-100。在一些实施方案中,在与钙溶液接触之前用有机溶剂洗涤纳米纤维结构。在一些实施方案中,钙溶液包括溶于有机溶剂(例如,乙醇)的钙(II)离子。在一些实施方案中,银溶液包括溶于有机溶剂(例如,乙醇)的银(I)离子。在多种实施方案中,方法进一步包括使抗菌纳米纤维敷料结构与有机溶剂接触,以去除经沉淀和未反应的盐。在一些实施方案中,方法进一步包括干燥抗菌纳米纤维敷料结构。在一些实施方案中,背衬包括CMC。在多种实施方案中,使抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0053] 在一些实施方案中,如下制备抗菌纳米纤维敷料结构:a)使纳米纤维与背衬结合,以产生纳米纤维结构;b)使纳米纤维结构与钙溶液接触,以产生钙-络合纳米纤维;和c)使钙-络合纳米纤维与银溶液接触,以产生包含银-络合纳米纤维的抗菌纳米纤维敷料结构。在一些实施方案中,纳米纤维为初纺纳米纤维。在一些实施方案中,纳米纤维包含生物聚合物和任选载体和/或表面活性剂。在一些实施方案中,纳米纤维从包含生物聚合物和任选载体和/或表面活性剂的溶液初纺。在一些实例中,生物聚合物包括藻酸盐。在一些情况下,载体为PEO。在一些情况下,表面活性剂为TritonTM X-100。在一些实施方案中,在与钙溶液接触之前用有机溶剂洗涤纳米纤维结构。在一些实施方案中,钙溶液包括溶于有机溶剂(例如,乙醇)的钙(II)离子。在一些实施方案中,银溶液包括溶于有机溶剂(例如,乙醇)的银(I)离子。在多种实施方案中,方法进一步包括使抗菌纳米纤维敷料结构与有机溶剂接触,以去除经沉淀和未反应的盐。在一些实施方案中,方法进一步包括干燥抗菌纳米纤维敷料结构。在一些实施方案中,背衬包括CMC。在多种实施方案中,使抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0054] 在一些实施方案中,如下制备抗菌纳米纤维敷料结构:a)用抗菌剂化学处理纳米纤维,以产生抗菌纳米纤维;和b)使抗菌纳米纤维与背衬结合。在一些情况下,通过i)施加使纳米纤维呈不溶性的溶液和ii)施加包含抗菌剂的溶液,化学处理纳米纤维。在一些实施方案中,抗菌剂为银。在一些实施方案中,背衬包括CMC。在多种实施方案中,使抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0055] 在一些实施方案中,用钙溶液处理本文所述纳米纤维结构。在一些实施方案中,纳米纤维结构包括包含CMC的背衬。在一些实例中,用钙溶液处理包含CMC的纳米纤维结构,得到钙-CMC络合物。在一些实施方案中,纳米纤维结构包含藻酸盐纳米纤维,其中用钙溶液处理纳米纤维(在与背衬结合之前或之后)产生钙-藻酸盐络合物。在一些情况下,钙-CMC络合物和/或钙-藻酸盐络合物通过离子交换产生。这些离子交换反应可以为具有恒定离子交换

通量的平衡反应。

[0056] 在一些实施方案中,用银溶液处理本文所述纳米纤维结构。在一些实施方案中,纳米纤维结构包括包含CMC的背衬。在一些实例中,用银溶液处理包含CMC的纳米纤维结构,得到银-CMC络合物。在一些实施方案中,纳米纤维结构包含藻酸盐纳米纤维,其中用银溶液处理纳米纤维(在与背衬结合之前或之后)产生银-藻酸盐络合物。在一些情况下,银-CMC络合物和/或银-藻酸盐络合物通过离子交换产生。这些离子交换反应可以为具有恒定离子交换通量的平衡反应。

[0057] 在多种实施方案中,用恶臭吸收剂结合或涂覆纳米纤维(包括纳米纤维垫、纳米纤维结构中的纳米纤维、伤口敷料或伤口敷料组分中的纳米纤维),以产生具有恶臭吸收性质的纳米纤维。在一些情况下,纳米纤维为抗菌纳米纤维。在一些情况下,用恶臭吸收剂结合或涂覆纳米纤维,然后处理,以产生具有恶臭吸收性质的抗菌纳米纤维。恶臭吸收剂纳米纤维可用作纳米纤维伤口敷料中的组分。示例性恶臭吸收剂包括环糊精。在一些实施方案中,恶臭吸收剂电纺到纳米纤维上。在一些实施方案中,恶臭吸收剂电喷到纳米纤维上。在一些实施方案中,恶臭吸收剂附着到纳米纤维或放置在旁边,例如,作为伤口敷料中的层。

[0058] 示例性恶臭吸收剂包括环糊精。环糊精包括 α -、 β -、 γ -环糊精及其组合。在一些实施方案中,恶臭吸收剂为羟丙基- β -环糊精(HP- β -CD)。

[0059] 在多种实施方案中,如下制备防臭抗菌纳米纤维敷料结构:a)使生物聚合物溶液沉积到背衬上,以产生纳米纤维结构;b)使纳米纤维结构与钙溶液接触,以产生钙-生物聚合物纳米纤维;c)使钙-生物聚合物纳米纤维与银溶液接触,以产生包含银-生物聚合物纳米纤维的抗菌纳米纤维结构;和d)使恶臭吸收剂沉积到抗菌纳米纤维结构的表面上,以产生防臭抗菌纳米纤维敷料结构。在一些情况下,使生物聚合物溶液通过电纺沉积到背衬上。在一些情况下,使生物聚合物溶液电纺成初纺纳米纤维。在一些情况下,生物聚合物溶液包含生物聚合物和任选载体和/或表面活性剂。在一些实例中,生物聚合物包括藻酸盐。在一些情况下,载体为PEO。在一些情况下,表面活性剂为TritonTM X-100。在一些实施方案中,在与钙溶液接触之前用有机溶剂洗涤纳米纤维结构。在一些实施方案中,钙溶液包括溶于有机溶剂(例如,乙醇)的钙(II)离子。在一些实施方案中,银溶液包括溶于有机溶剂(例如,乙醇)的银(I)离子。在多种实施方案中,方法进一步包括使抗菌纳米纤维敷料结构与有机溶剂接触,以去除经沉淀和未反应的盐。在一些实施方案中,方法进一步包括干燥抗菌纳米纤维敷料结构。在一些实施方案中,背衬包括CMC。在一些情况下,恶臭吸收剂通过电纺沉积到抗菌纳米纤维结构上。在一些情况下,恶臭吸收剂通过电喷沉积到抗菌纳米纤维结构上。在一些实例中,恶臭吸收剂为环糊精,例如HP- β -CD。在多种实施方案中,使防臭抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0060] 在一些实施方案中,如下制备防臭抗菌纳米纤维敷料结构:a)使纳米纤维与背衬结合,以产生纳米纤维结构;b)使纳米纤维结构与钙溶液接触,以产生钙-络合纳米纤维;c)使钙-络合纳米纤维与银溶液接触,以产生包含银-络合纳米纤维的抗菌纳米纤维结构;和d)使恶臭吸收剂沉积到抗菌纳米纤维结构的表面上,以产生防臭抗菌纳米纤维敷料结构。在一些实施方案中,纳米纤维为初纺纳米纤维。在一些实施方案中,纳米纤维包含生物聚合物和任选载体和/或表面活性剂。在一些实施方案中,纳米纤维从包含生物聚合物和任选载体和/或表面活性剂的溶液初纺。在一些实例中,生物聚合物包括藻酸盐。在一些情况下,载

体为PEO。在一些情况下,表面活性剂为TritonTM X-100。在一些实施方案中,在与钙溶液接触之前用有机溶剂洗涤纳米纤维结构。在一些实施方案中,钙溶液包括溶于有机溶剂(例如,乙醇)的钙(II)离子。在一些实施方案中,银溶液包括溶于有机溶剂(例如,乙醇)的银(I)离子。在多种实施方案中,方法进一步包括使抗菌纳米纤维敷料结构与有机溶剂接触,以去除经沉淀和未反应的盐。在一些实施方案中,方法进一步包括干燥抗菌纳米纤维敷料结构。在一些实施方案中,背衬包括CMC。在一些情况下,恶臭吸收剂通过电纺沉积到抗菌纳米纤维结构上。在一些情况下,恶臭吸收剂通过电喷沉积到抗菌纳米纤维结构上。在一些实例中,恶臭吸收剂为环糊精,例如HP- β -CD。在多种实施方案中,使防臭抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0061] 在一些实施方案中,如下制备防臭抗菌纳米纤维敷料结构:a)用抗菌剂化学处理纳米纤维,以产生抗菌纳米纤维;b)使抗菌纳米纤维与背衬结合,以产生抗菌纳米纤维结构;和c)使恶臭吸收剂沉积到抗菌纳米纤维结构的表面上,以产生防臭抗菌纳米纤维敷料结构。在一些情况下,通过i)施加使纳米纤维呈不溶性的溶液和ii)施加包含抗菌剂的溶液,化学处理纳米纤维。在一些实施方案中,抗菌剂为银。在一些实施方案中,背衬包括CMC。在一些情况下,恶臭吸收剂通过电纺沉积到抗菌纳米纤维结构上。在一些情况下,恶臭吸收剂通过电喷沉积到抗菌纳米纤维结构上。在一些实例中,恶臭吸收剂为环糊精,例如HP- β -CD。在多种实施方案中,使防臭抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0062] 在一些实施方案中,如下制备防臭抗菌纳米纤维敷料结构:a)用抗菌剂化学处理纳米纤维,以产生抗菌纳米纤维;b)使恶臭吸收剂沉积到抗菌纳米纤维的表面上,以产生防臭抗菌纳米纤维;和c)使防臭抗菌纳米纤维与背衬结合,以产生防臭抗菌纳米纤维敷料结构。在一些情况下,通过i)施加使纳米纤维呈不溶性的溶液和ii)施加包含抗菌剂的溶液,化学处理纳米纤维。在一些实施方案中,抗菌剂为银。在一些实施方案中,背衬包括CMC。在一些情况下,恶臭吸收剂通过电纺沉积到抗菌纳米纤维上。在一些情况下,恶臭吸收剂通过电喷沉积到抗菌纳米纤维上。在一些实例中,恶臭吸收剂为环糊精,例如HP- β -CD。在多种实施方案中,使防臭抗菌纳米纤维敷料结构与一种或多种另外的伤口敷料组分和或伤口敷料添加剂结合,以产生伤口敷料。

[0063] 在一些实施方案中,用包含恶臭吸收剂的溶液电喷纳米纤维。这些纳米纤维不加以限制地包括纳米纤维垫、纳米纤维结构中的纳米纤维和伤口敷料或伤口敷料组分中的纳米纤维。纳米纤维结构不加以限制地包括包含纳米纤维和背衬(例如,包含CMC的背衬)的纳米纤维结构。这些纳米纤维也包括本文所述抗菌纳米纤维(例如,银处理的纳米纤维)。在一些实施方案中,纳米纤维包含藻酸盐。在一些实施方案中,恶臭吸收剂为HP- β -CD。包含恶臭吸收剂(例如,HP- β -CD)的溶液可包含以重量计在约1%和约90%之间、约5%和约80%之间、约10%和约80%之间、约20%和约80%之间、约20%和约70%之间、约30%和80%之间、约30%和70%之间、约20%和约60%之间、约20%和约50%之间、约30%和约60%之间、约30%和约50%之间或约35%至约45%之间的恶臭吸收剂。在一个实例中,包含恶臭吸收剂(例如,HP- β -CD)的溶液包含40%重量恶臭吸收剂。至少在一些实施方案中,包含恶臭吸收剂(例如,HP- β -CD)的溶液电喷到纳米纤维上的溶液进料速率包括在约0.1ml/小时至约5ml/小时之间、约0.2ml/小时至约5ml/小时之间、约0.3ml/小时至约5ml/小时之间、约0.2ml/小时至约4ml/小时之间、约0.3ml/小

时至约4ml/小时之间、约0.3ml/小时至约3ml/小时之间、约0.3ml/小时至约2ml/小时之间、约0.4ml/小时至约5ml/小时之间、约0.4ml/小时至约4ml/小时之间、约0.4ml/小时至约3ml/小时之间、约0.4ml/小时至约2ml/小时之间、约0.5ml/小时至约5ml/小时之间、约0.5ml/小时至约4ml/小时之间、约0.5ml/小时至约3ml/小时之间、约0.5ml/小时至约2ml/小时之间、约0.8ml/小时至约1.5ml/小时之间或约0.8ml/小时至约1.2ml/小时之间的进料速率。在一个实例中,进料速率为约1.0ml/小时。至少在一些实施方案中,包含恶臭吸收剂(例如,HP- β -CD)的溶液电喷到纳米纤维上的工作距离包括在约10cm和约30cm之间、约10cm和约25cm之间、约10cm和约20cm之间、约12cm和约20cm之间、约10cm和约18cm之间或约12cm和约18 cm之间的距离。在一个实例中,从电喷装置的注射器到纳米纤维的工作距离为约16cm。在一些实施方案中,包含恶臭吸收剂(例如,HP- β -CD)的溶液用在2kV和30kV之间、4kV和25kV之间、4kV和20kV之间、5kV和25kV之间、5kV和20kV之间、7kV和20kV之间或7kV和15kV之间的施加电压电喷。在一个实例中,包含恶臭吸收剂(例如,HP- β -CD)的溶液用约12kV施加电压电喷。在一些实施方案中,电喷到具有小于约500cm²、小于约400cm²、小于约300cm²、小于约200cm²、小于约100cm²或小于约50cm²尺寸的抗菌纳米纤维结构上的包含恶臭吸收剂(例如,HP- β -CD)的溶液的量约为约0.5ml至约30ml、约0.5ml至约25ml、约0.5ml至约20ml、约0.5ml至约15ml、约0.5ml至约10ml、约0.5ml至约8ml、约0.5ml至约5ml或约1ml至约5ml包含恶臭吸收剂的溶液。电喷包含恶臭吸收剂(例如,HP- β -CD)的溶液到纳米纤维上的时间可以为约30分钟至约6小时、约1小时至约4小时。在一些实施方案中,电喷时间为1小时、2小时或4小时。在一些实施方案中,电喷的恶臭吸收剂(例如,HP- β -CD)产生纤维。在一些实施方案中,通过电喷沉积到纳米纤维上的平均恶臭吸收剂纤维直径为约300nm至约1,800nm、约400nm至约1,600nm、约500nm至约1,500nm、约500nm至约1,200nm、约500nm至约1,000nm、约600nm至约1,000nm、约600nm至约900nm或约700nm至约900nm。在一个实例中,平均电喷恶臭吸收剂纤维直径为约850nm。

[0064] 在一些实施方案中,用包含恶臭吸收剂的电纺溶液沉积纳米纤维。这些纳米纤维不加限制地包括纳米纤维垫、纳米纤维结构中的纳米纤维和伤口敷料或伤口敷料组分中的纳米纤维。纳米纤维结构不加限制地包括包含纳米纤维和背衬(例如,包含CMC的背衬)的纳米纤维结构。这些纳米纤维也包括本文所述抗菌纳米纤维(例如,银处理的纳米纤维)。在一些实施方案中,纳米纤维包含藻酸盐。在一些实施方案中,恶臭吸收剂为HP- β -CD。在一些实施方案中,包含恶臭吸收剂(例如,HP- β -CD)的溶液进一步包含载体,例如PEO。包含恶臭吸收剂的溶液可包含以重量计在约1%和约70%之间、约1%和约60%之间、约1%和约50%之间、约1%和约40%之间、约1%和约30%之间、约1%和20%之间、约1%和15%之间、约2%和约15%之间或约4%和约12%之间的恶臭吸收剂。在一些实例中,包含恶臭吸收剂的溶液包含40%重量恶臭吸收剂。在一些实施方案中,包含恶臭吸收剂的溶液包含恶臭吸收剂和载体。在一些实施方案中,包含恶臭吸收剂的溶液具有以下恶臭吸收剂:载体比:30-95剂:70-5载体、40-90剂:60-10载体、50-90剂:50-1载体。在一些实施方案中,剂:载体比为50:50、60:40、70:30、80:20或90:10。至少在一些实施方案中,包含恶臭吸收剂的溶液电纺到纳米纤维上的溶液进料速率包括在约0.1ml/小时至约5ml/小时之间、约0.2ml/小时至约5ml/小时之间、约0.3ml/小时至约5ml/小时之间、约0.2ml/小时至约4ml/小时之间、约0.3ml/小时至约4ml/小时之间、约0.3ml/小时至约3ml/小时之间、约0.3ml/小时至约2ml/小时之间、约0.4ml/小时至约5ml/

小时之间、约0.4ml/小时至约4ml/小时之间、约0.4ml/小时至约3ml/小时之间、约0.4ml/小时至约2ml/小时之间、约0.5ml/小时至约5ml/小时之间、约0.5ml/小时至约4ml/小时之间、约0.5ml/小时至约3ml/小时之间、约0.5ml/小时至约2ml/小时之间、约0.8ml/小时至约1.5ml/小时之间或约0.8ml/小时至约1.2ml/小时之间的进料速率。在一个实例中,进料速率为约1.0ml/小时。至少在一些实施方案中,包含恶臭吸收剂的溶液电纺到纳米纤维上的工作距离包括在约10cm和约30cm之间、约10cm和约25cm之间、约10cm和约20cm之间、约12cm和约20cm之间、约10cm和约18cm之间或约12cm和约18cm之间的距离。在一个实例中,从电纺装置的注射器到纳米纤维的工作距离为约12cm。在一些实施方案中,包含恶臭吸收剂的溶液用在2kV和30kV之间、4kV和25kV之间、4kV和20kV之间、5kV和25kV之间、5kV和20kV之间、7kV和20kV之间或7kV和15kV之间的施加电压电纺。在一个实例中,包含恶臭吸收剂的溶液用约12kV施加电压电纺。在一些实施方案中,电纺到具有小于约500cm²、小于约400cm²、小于约300cm²、小于约200cm²、小于约100cm²或小于约50cm²尺寸的纳米纤维结构上的包含恶臭吸收剂的溶液的量为约0.5ml至约30ml、约0.5ml至约25ml、约0.5ml至约20ml、约0.5ml至约15ml、约0.5ml至约10ml、约0.5ml至约8ml、约0.5ml至约5ml或约1ml至约5ml包含恶臭吸收剂的溶液。在一些实施方案中,包含恶臭吸收剂(HP-β-CD)的电纺溶液产生纤维。在一些实施方案中,通过电纺沉积到纳米纤维上的平均恶臭吸收剂纤维直径为约50nm至约1,800nm、约50nm至约1,500nm、约50nm至约1,000nm、约50nm至约800nm、约50nm至约700nm、约50nm至约600nm、约50nm至约500nm、约50nm至约400nm、约50nm至约300nm、约100nm至约300nm或约150nm至约300nm。在一个实例中,电纺的平均恶臭吸收剂纤维直径为约200nm、约210nm、约220nm、约230nm、约240nm、约250nm、约260nm、约270nm、约280nm、约290nm或约300nm。

[0065] 在整个本公开中,各种实施方案以范围形式提供。应了解,范围形式的描述只是为了方便和简洁,不应解释为对任何实施方案范围的硬性限制。因此,应认为范围的描述已明确公开了所有可能的子范围及和到下限单位十分之一的那个范围内的各单独数值,除非本文另外清楚地规定。

[0066] 本文所用专有名词只是为了描述具体实施方案,并不是要限制任何实施方案。除非本文另外清楚地指明,本文所用单数形式“一”和“所述”也旨在包括复数形式。应进一步了解,在本说明书中使用时,词语“包括”和/或“包含”说明所述特征、整体、步骤、操作、元素和/或组分的存在,但不排除一个或多个其它特征、整体、步骤、操作、元素、组分和/或其组的存在或加入。本文所用词语“和/或”包括一个或多个相关所列项目的任何和所有组合。

[0067] 提出以下实施例对本领域的技术人员更清楚地说明本文公开实施方案的原理和实施,而不应解释为限制任何提出实施方案的范围。除非另外说明,所有份数和百分数均以重量计。

实施例

[0068] 实施例1:制备和表征从藻酸盐纳米纤维得到的抗菌纳米纤维

制备抗菌纳米纤维的方法:通过化学改性初纺的钠-藻酸盐/PEO纳米纤维垫制备抗菌纳米纤维垫。通过电纺包含4%重量比例为70:30的钠-藻酸盐和PEO的水溶液产生初纺纳米纤维。如场枪发射扫描电子显微法(SEM)在图1图框A1所示,所得初纺纳米纤维没有珠粒。在包含约25mL无水乙醇的培养皿中浸泡初纺钠-藻酸盐/PEO纳米纤维。轻轻摇动培养皿10分

钟,同时使PEO从纳米纤维溶解。将经浸泡的初纺纳米纤维转移到在无水乙醇中包含 CaCl_2 的第二培养皿进行第二次10分钟浸泡。该第二次浸泡使钠和钙离子交换产生钙-藻酸盐纳米纤维。将钙-藻酸盐纳米纤维转移到在无水乙醇中包含 AgNO_3 的第三培养皿进行第三次10分钟浸泡。该第三次浸泡提供另外的离子交换,以产生银-藻酸盐纳米纤维。在无水乙醇中洗涤银-藻酸盐纳米纤维,以去除经沉淀和未反应的盐,随后在室温(20℃)干燥。所用 CaCl_2 和 AgNO_3 的浓度显示于表1中。

[0069] 表1:用于四组化学处理的初纺钠-藻酸盐/PEO纳米纤维的反应条件

样品名称	用 CaCl_2 的无水乙醇溶液 处理		用 AgNO_3 的无水乙醇溶液 处理	
	CaCl_2 浓度	处理时间	AgNO_3 浓度	处理时间
T0.5/1.0Ag/Ca	1.0%	10 min	0.5%	10 min
T1.0/1.0Ag/Ca	1.0%	10 min	1.0%	10 min
T0.5/5.0Ag/Ca	5.0%	10 min	0.5%	10 min
T1.0/5.0Ag/Ca	5.0%	10 min	1.0%	10 min

抗菌纳米纤维的表征:通过场枪发射扫描电子显微法(SEM)和能量色散X-射线(EDX)(Philips XL30 FEG-SEM)和傅里叶变换红外光谱(FTIR)(NICOLET5700 FT-IR, Thermo Electron Corporation)研究抗菌纳米纤维的形态和表征。

[0070] 通过专用于SEM的碳胶带使抗菌纳米纤维垫(0.5cm x 0.5cm)粘着到样品托上。使用gatan精确浸蚀涂布系统(Precision Etching Coating System)(682型),用碳涂覆粘着的垫。在2,000x, 10,000x, 20,000x放大率捕获SEM图像。SEM操作参数设定在6kV加速电压和束斑尺寸3。在ImageJ(ImageJ 2004)软件使用划线特征,从在10,000x和20,000x放大图像中在3个不同焦点下50根随机选择的纤维手工测量纤维直径。对于EDX分析,在2,000x放大率用10kV加速电压和束斑尺寸3进行扫描。

[0071] 在图1(图框A1-E1)提供显示化学处理之前和之后初纺纳米纤维形态的SEM图像。各纳米纤维垫的相应纤维尺寸分布显示于图1(图框A2-E2)中。图1图框A1为化学改性前初纺钠-藻酸盐/PEO的图像。图1图框B1为用1.0% CaCl_2 和0.5% AgNO_3 处理后银-藻酸盐纳米纤维垫的图像。图1图框C1为用1.0% CaCl_2 和1.0% AgNO_3 处理后银-藻酸盐纳米纤维垫的图像。图1图框D1为用5.0% CaCl_2 和0.5% AgNO_3 处理后银-藻酸盐纳米纤维垫的图像。图1图框E1为用5.0% CaCl_2 和1.0% AgNO_3 处理后银-藻酸盐纳米纤维垫的图像。化学处理前的纳米纤维比化学处理后的纳米纤维尺寸更均匀。T0.5/1.0/Ag/Ca和T1.0/1.0/Ag/Ca纳米纤维的结构在处理保持,而T0.05/5.0/Ag/Ca和T1.0/5.0/Ag/Ca有断裂纳米纤维。

[0072] 如图1(图框A2-E2)中所示,纳米纤维的平均直径在化学处理后减小,纤维尺寸分布在化学处理后增加。在化学处理前初纺钠-藻酸盐/PEO纳米纤维垫的平均纳米纤维直径为141nm,标准偏差为29nm。经处理T0.5/1.0Ag/Ca纳米纤维垫的平均纳米纤维直径为131nm,标准偏差为56nm。经处理T1.0/1.0Ag/Ca纳米纤维垫的平均纳米纤维直径为130nm,标准偏差为68nm。经处理T0.5/5.0Ag/Ca纳米纤维垫的平均纳米纤维直径为136nm,标准偏差为71nm。经处理T1.0/5.0Ag/Ca纳米纤维垫的平均纳米纤维直径为134nm,标准偏差为76nm。

[0073] 在这个实施例中构造的经处理和未处理纳米纤维垫的SEM图像显示在处理后的整个垫中颗粒的出现。见图1(图框A1-E1)。如这些图像中所示,随着银处理溶液中银浓度从0.5%增加到1.0%,粒径也增加。同样,随着钙处理溶液中钙浓度从1%增加到5%,粒径也增加。在ImageJ (ImageJ 2004) 软件使用划线特征,从在化学处理样品的10,000x和20,000x放大图像中的50个随机选择颗粒手工测量纳米纤维粒径。图2为图示说明在四个化学处理纳米纤维垫中粒径分布的图解。测量的银颗粒的平均直径为210nm,标准偏差为32nm。

[0074] 进行EDX分析,以测定四组化学处理纳米纤维垫中非碳元素的组成,其结果显示于表2中。纳米纤维中银的百分数与钙处理溶液中钙(II) 离子百分数增加成比例减小。

[0075] 表2:通过EDX测定的四组银-藻酸盐纳米纤维中的元素组成

样品	银(Ag)	钙(Ca)	钠(Na)	氯(Cl)	氧(O)
T0.5/1.0Ag/Ca	61.42%重量	5.80%重量	4.47%重量	5.24%重量	23.06%重量
T1.0/1.0Ag/Ca	59.81%重量	11.7%重量	3.93%重量	8.51%重量	16.04%重量
T0.5/5.0Ag/Ca	51.63%重量	11.44%重量	9.03%重量	8.58%重量	19.31%重量
T1.0/5.0Ag/Ca	50.56%重量	17.71%重量	2.59%重量	16.98%重量	12.16%重量

进行傅里叶变换红外光谱 (FTIR),以观察钠-藻酸盐/PEO纳米纤维和经处理藻酸盐纳米纤维(样品T0.5/1.0Ag/Ca、T1.0/1.0Ag/Ca、T0.5/5.0Ag/Ca和T1.0/5.0Ag/Ca) 之间的光谱峰变化。

[0076] 对化学处理之前和之后初纺纳米纤维垫得到的4,000至400 cm^{-1} 的FTIR光谱显示于3A中。从3,500至2,000 cm^{-1} 的光谱显示于图3B中。光谱包括在4 cm^{-1} 分辨率32次扫描。

[0077] 如图3B中所示,在处理前样品(钠-藻酸盐/PEO纳米纤维,310) 中在2883 cm^{-1} 的峰代表来自PEO的-CH₂基团。该峰在经处理样品(320, 330, 340, 350) 中减小或不可检测到,表明成功从经处理纳米纤维去除PEO。

[0078] 在3346和3336 cm^{-1} 之间的峰对应于-OH基团的氢键。在经处理样品中-OH峰偏移。在处理前样品310中-OH峰出现在3346 cm^{-1} 。在T0.5/1.0Ag/Ca样品320中-OH峰出现在3336 cm^{-1} 。在T1.0/1.0Ag/Ca样品330中-OH峰出现在3340 cm^{-1} 。在T0.5/5.0Ag/Ca样品340中-OH峰出现在3340 cm^{-1} 。在T1.0/5.0Ag/Ca样品350中-OH峰出现在3336 cm^{-1} 。

[0079] 根据BS EN 13726-1:2002第3.7节(水凝胶敷料的分散和稳定性) 检验经化学改性纳米纤维垫的溶解度。将纳米纤维垫(0.2cm x 0.2cm) 放入培养皿在20mL水中在37℃经历24小时。在24小时后目视评价垫。类似地将纳米纤维垫(0.2cm x 0.2cm) 放入培养皿,在20mL包含0.4M NaCl、0.02M CaCl₂和10%新生小牛血清的STS中。将纳米纤维垫在室温浸入STS经历24小时。视觉观察纤维内容物,以评价纳米纤维溶解度。在水或STS中浸泡24小时后纳米纤维保持完整。

[0080] 实施例2:制备藻酸盐纳米纤维

制备纺丝溶液:通过在23.875g蒸馏水中溶解0.7g钠-藻酸盐和0.3g PEO,制备用于电纺的4%重量70:30钠-藻酸盐/PEO溶液。为了改善纺丝溶液的均匀性,加入0.5%重量Triton™ X-100。类似地制备4%重量80:20钠-藻酸盐/PEO溶液。

[0081] 将纺丝溶液在暗处在室温储存20天,并用BROOKFIELD粘度计在第1、5、10和20天测定其粘度。钠-藻酸盐/PEO溶液的粘度经储存时间减小,由此,钠-藻酸盐/PEO纺丝溶液在制

备5天内电纺。粘度在第1天为2284cP,在第5天为2184cP,在第10天为1579cP,在第20天为202cP。

[0082] 电纺:用水平电纺装置制备钠-藻酸盐纳米纤维。过程参数设定到12-20cm工作距离、1.0-0.3ml/h进料速率和9-12kV施加电压。电纺纤维收集在铝箔上。在电纺1小时后,收集箔和沉积的纤维,并在室温干燥24小时,以去除残余溶剂。如表3中所示改变过程参数。用于产生初纺钠-藻酸盐/PEO纳米纤维的最终过程参数为16cm工作距离、0.4ml/小时流速和10.5kV施加电压。

[0083] 表3:产生钠-藻酸盐/PEO纳米纤维的电纺过程参数

观察编号	工作距离	进料速率	施加电压	观察结果
1	16 cm	0.5 ml/h	9 kV	稳定喷射, 均匀沉积, 但缓慢形成微滴
2	16 cm	0.5 ml/h	10 kV	稳定喷射, 均匀沉积, 但缓慢形成微滴
3	16 cm	0.5 ml/h	11 kV	稳定喷射, 均匀沉积, 但缓慢产生微滴
4	16 cm	0.4 ml/h	9 kV	稳定喷射和均匀沉积, 但缓慢形成微滴
5	16 cm	0.4ml/h	10 kV	稳定喷射和均匀沉积
6	16 cm	0.4 ml/h	11 kV	稳定喷射和均匀沉积
7	16 cm	0.3 ml/h	9 kV	稳定喷射和均匀沉积, 但缓慢形成微滴
8	16 cm	0.3 ml/h	10 kV	稳定喷射和均匀沉积
9	16 cm	0.3 ml/h	11 kV	稳定喷射, 均匀沉积
10	16 cm	0.4 ml/h	10.5 kV	稳定喷射, 均匀沉积 (优化过程参数)

初纺钠-藻酸盐/PEO纳米纤维的表征:通过SEM观察电纺或初纺钠-藻酸盐/PEO纳米纤维的形态和结构。通过FTIR分析初纺钠-藻酸盐/PEO纳米纤维的元素分析。根据BS EN 13726-1:2002第3.7节(水凝胶敷料的分散和稳定性)检验初纺钠-藻酸盐/PEO纳米纤维的溶解度。这些步骤基本如实施例1中所述进行。

[0084] 图4A显示来自4%重量70:30钠-藻酸盐:PEO溶液(400)和4%重量80:20钠-藻酸盐:PEO溶液(401)的初纺纳米纤维的SEM图像。来自4%重量70:30钠-藻酸盐:PEO溶液的初纺纳米纤维的平均直径为124nm,标准偏差为35nm,如图4B中所示。来自4%重量70:30钠-藻酸盐:PEO溶液的初纺纳米纤维均匀,且没有珠粒。

[0085] 图5显示在4000-400cm⁻¹和2000-1000cm⁻¹光谱范围内纯PEO(图框A)、钠-藻酸盐(图框B)和钠-藻酸盐/PEO(图框C)纳米纤维的FTIR光谱。PEO的光谱(图框A)具有在1100cm⁻¹和843cm⁻¹的峰,对应于醚基不对称伸缩和弯曲振动。钠-藻酸盐的光谱(图框B)具有在

3336 cm^{-1} 的峰,对应于羟基伸缩,在1593 cm^{-1} 的峰(对于羧酸根对称伸缩),在1410 cm^{-1} 的峰(对于羧酸根对称伸缩)。在钠-藻酸盐/PEO纳米纤维中,关于PEO醚基的不对称吸收带从1100 cm^{-1} 偏移到1095 cm^{-1} 。在钠-藻酸盐/PEO纳米纤维中,关于钠-藻酸盐羧酸根的不对称吸收带从1593 cm^{-1} 偏移到1612 cm^{-1} 。

[0086] 在水和STS中初纺钠-藻酸盐/PEO纳米纤维的溶解度如实施例1中评价。纳米纤维溶在浸泡2至3分钟内于水或STS。

[0087] 实施例3:构造包含初纺藻酸盐纳米纤维的复合敷料结构

在Na-CMC非织造基底表面上沉积如实施例2中所述制备的电纺纳米纤维。

[0088] 在电纺装置将Na-CMC非织造织物施加到收集器,并如实施例2中所述电纺4%重量70:30钠-藻酸盐/PEO溶液。用钠-藻酸盐/PEO纳米纤维沉积Na-CMC织物,以产生复合敷料结构。通过SEM目视在箔上和Na-CMC上沉积的初纺纳米纤维的形态,如图6(图框A-D)中所示。图6图框A显示Na-CMC基础织物的相片,图框B显示Na-CMC基础织物的SEM图像,图框C显示用初纺钠-藻酸盐/PEO纳米纤维沉积的Na-CMC基础织物的相片,图框D显示用初纺钠-藻酸盐/PEO纳米纤维沉积的Na-CMC基础织物的SEM图像。这些图像指示在初纺纳米纤维沉积到表面之前和之后,Na-CMC织物之间没有形态差异。

[0089] 实施例4:抗菌纳米纤维敷料结构

化学处理实施例3的复合敷料结构,以产生抗菌纳米纤维敷料结构。

[0090] 在轻轻摇动下,将10cm x 10cm实施例3的复合敷料结构浸入包含无水乙醇的培养皿10分钟,以溶解PEO。将乙醇洗涤的样品转移到包含钙溶液(在无水乙醇中1.0%重量或5%重量 CaCl_2)的培养皿,并浸泡10分钟。在此钙处理步骤期间,在来自钠-藻酸盐纳米纤维的钠(I)离子和来自钙溶液的钙(II)离子之间发生离子交换反应,以产生不溶性钙-藻酸盐纳米纤维。类似地,来自Na-CMC织物的钠(I)离子可与来自钙溶液的钙(II)离子交换。然后将样品转移到包含银溶液(在无水乙醇中0.5%重量或1%重量 AgNO_3)的培养皿,并浸泡10分钟。在此银处理步骤期间,在来自钠-藻酸盐纳米纤维的钠(I)离子、来自钙-藻酸盐的钙(II)离子和来自银溶液的银(I)离子之间发生离子交换反应,以产生具有钠-藻酸盐、钙-藻酸盐和银-藻酸盐的纳米纤维。类似地,来自Na-CMC织物的钠(I)离子和来自Ca-CMC织物的钙(II)离子可与来自银溶液的银(I)离子交换。然后在无水乙醇中洗涤样品,以去除经沉淀和未反应的盐。在室温(约20 $^{\circ}\text{C}$)干燥样品。

[0091] 用表1中所示不同 CaCl_2 和 AgNO_3 浓度重复该过程。图1(图框B1-E1)示出显示用钙和银处理溶液处理后在Na-CMC背衬上沉积的纳米纤维形态的SEM图像。

[0092] 实施例5:用恶臭吸收剂通过电喷沉积的抗菌纳米纤维敷料结构

用恶臭吸收剂羟丙基- β -环糊精(HP- β -CD)电喷在实施例4中制备的抗菌纳米纤维敷料结构。图7显示用1.0% CaCl_2 溶液和0.5% AgNO_3 溶液制备的纳米纤维敷料结构的图像。

[0093] 电喷过程参数调节到0.5-2ml/h进料速率、7-15kV施加电压和12-20cm工作距离,以在包括铝箔的收集器上得到HP- β -CD颗粒的均匀分散体。干燥和表征在铝箔上收集的电喷HP- β -CD颗粒,以优化过程参数。电喷过程优化在1.0ml/h进料速率、12kV施加电压和16cm工作距离。

[0094] 使用优化过程参数,在实施例4中制备的抗菌纳米纤维敷料结构上沉积HP- β -CD颗粒。图7(图框A-C)示出显示实施例4的电喷纳米纤维敷料的表面形态的SEM图像。图7图框A

中所示的敷料电喷1小时,图框B中所示的敷料电喷2小时,图框C中所示的敷料电喷4小时。

[0095] 实施例6:用恶臭吸收剂通过电纺沉积的抗菌纳米纤维敷料结构

通过在敷料结构的纳米纤维表面上电纺HP- β -CD溶液,使在实施例4中制备的抗菌纳米纤维敷料结构与恶臭吸收剂羟丙基- β -环糊精(HP- β -CD)结合。HP- β -CD溶液包含载体聚合物PEO。

[0096] 在水中制备具有4-12%重量50:50 HP- β -CD:PEO的一系列纺丝溶液。在水中制备具有8%重量50:50至90:10 HP- β -CD:PEO的另一系列纺丝溶液。

[0097] 电纺过程参数调节到0.5-2.5ml/h进料速率、5-11kV施加电压和8-16cm工作距离,以得到光滑纤维。在铝箔上收集电纺HP- β -CD颗粒,干燥24小时,并表征,以优化过程参数。电喷过程优化在1.0ml/h进料速率、12kV施加电压和16cm工作距离。

[0098] 用不同质量比和浓度在1ml/h进料速率、12cm工作距离和7kV施加电压进行HP- β -CD/PEO电纺,以得到光滑纳米纤维。表4提供在箔上沉积的HP- β -CD/PEO电纺纳米纤维的纺丝溶液组成和性质。

[0099] 表4:电纺HP- β -CD/PEO纤维特性的汇总

聚合物浓度(%重量)	HP- β -CD/PEO 比	纤维直径范围(nm)	平均直径(nm)	纤维形态	纳米纤维网的直径(cm)
8	50:50	240-289	264	光滑纤维	9.2
8	60:40	189-301	244	光滑纤维	10.5
8	70:30	128-390	236	很少珠粒	15.5
8	80:20	80-1628	208	大部分珠粒	-
8	90:10	-	-	大部分珠粒	-
4	50:50	60-972	268	大部分珠粒	-
6	50:50	177-362	248	光滑纤维	12.5
8	50:50	240-289	264	光滑纤维	9.2
10	50:50	194-302	254	光滑纤维	7.4
12	50:50	128-328	281	支化纤维	5.7

电纺HP- β -CD/PEO纤维的形态显示于图8(图框A-D)的SEM图像(2,000x,插图10,000x)中。图8中纤维从8%具有50:50(图框A)、60:40(图框B)、70:30(图框C)和80:20(图框D) HP- β -CD/PEO混合比的溶液电纺。

[0100] 使用优化过程参数,在实施例4的纳米纤维敷料结构上收集电纺HP- β -CD颗粒。

[0101] 实施例7:包含抗菌纳米纤维的敷料结构

所提出敷料结构的方案显示于图9中。使用实施例3中所述的方法,在背衬表面上沉积如实施例2中所述制备的电纺纳米纤维,以产生纳米纤维敷料结构。如实施例4化学处理敷料结构,以产生抗菌纳米纤维敷料结构。如实施例5中所述用HP- β -CD电喷抗菌纳米纤维敷料结构,以产生最终敷料。最终敷料结构包括钠-CMC基础织物、包含抗菌银-藻酸盐的纳米纤维网和HP- β -CD涂层。

[0102] 实施例8:制备包含抗菌纳米纤维的敷料结构的方法

汇总实施例1至实施例7所述方法的示意提供于图10中。

[0103] 实施例9:评价敷料结构和敷料结构组分

通过实施例1至实施例7中所述方法制备的组合物汇总于表5中。

[0104] 表5:伤口敷料组合物的汇总

检验	组	样品组
质量/单位面积 厚度 流体吸收和保留 侧向芯吸 收缩	组-1	基础织物
		化学处理(T0.5/1.0Ag/Ca)样品
		最终(F0.5/1.0Ag/Ca(2h))样品
	组-2	基础织物
		化学处理(T0.5/5.0Ag/Ca)样品
		最终(F0.5/5.0Ag/Ca(2h))样品
	组-3	基础织物
		化学处理(T1.0/1.0Ag/Ca)样品
		最终(F1.0/1.0Ag/Ca(2h))样品
	组-4	基础织物
		化学处理(T1.0/5.0Ag/Ca)样品
		最终(F1.0/5.0Ag/Ca(2h))样品

敷料组合物的平均质量/单位面积根据BS EN 12127:1998检验方法评价。表6提供不同组合物的平均质量/100cm²。与基础织物比较,在化学处理组合物中质量/单位面积增加。

[0105] 表6. 伤口敷料组合物的质量/单位面积

样品	质量/单位面积 (g/100cm ²)	%+/-, 关于基础织物
基础织物	1.043	-
T0.5/1.0Ag/Ca	1.096	+5.08%
F0.5/1.0Ag/Ca(2h)	1.320	+26.55%
T0.5/5.0Ag/Ca	1.384	+32.69%
F0.5/5.0Ag/Ca(2h)	1.429	+37%
T1.0/1.0Ag/Ca	1.111	+6.51%
F1.0/1.0Ag/Ca(2h)	1.398	+34.03%
T1.0/5.0Ag/Ca	1.856	+77.94%
F1.0/5.0Ag/Ca(2h)	1.906	+82.74%

根据BS EN ISO 9073-2:1997评估敷料组合物的厚度。用0.0重量(没有附加重量,即,正常检验仪器状态)和100g重量(具有100g已知重量)进行检验。表7提供不同组合物的平均厚度和相对厚度变化。加HP-β-CD涂层到敷料组合物增加总敷料组合物厚度。钙对组合物厚度有影响。

[0106] 表7:伤口敷料组合物的平均厚度

样品	厚度 (mm), 在 0.0 重量	% +/-, 相对于 基础敷料	厚度 (mm), 在 100g 重量	% +/-, 相对于 基础织物	0.0 重量和 100g 重量 之间的差
基础敷料	1.550	-	1.083	-	-30%
T0.5/1.0Ag/Ca	1.633	+ 5.35%	1.167	+7.75%	-29%
F0.5/1.0Ag/Ca(2h)	1.967	+26.9%	1.383	+27.7%	-30%
T0.5/5.0Ag/Ca	1.883	+21.48%	1.667	+53.92%	-12%
F0.5/5.0Ag/Ca(2h)	2.133	+37.6%	1.700	+56.97%	-20%
T1.0/1.0Ag/Ca	1.650	+6.45%	1.233	+13.85%	-25%
F1.0/1.0Ag/Ca(2h)	1.800	+16.1%	1.417	+30.84%	-21%
T1.0/5.0Ag/Ca	1.883	+21.48%	1.583	+46.16%	-16%
F1.0/5.0Ag/Ca(2h)	2.133	+37.6%	1.750	+61.58%	-18%

根据BS EN 13726-1:2002第3.2节自由溶胀吸收容量(free swell absorptive capacity)测定伤口敷料组合物的平均吸收和保留性质。吸收指各组合物吸收多少流体。保留指在一定压力下组合物中保留多少流体。表8提供伤口敷料组合物的流体处理性质的汇总。已发现基础织物的平均吸收和保留高于经化学处理的组合物和最终敷料。化学处理期间银和钙离子的浓度负面影响组合物的吸收和保留能力。

[0107] 表8:伤口敷料组合物中流体的吸收和保留

样品	吸收 (g/g)	保留 (g/g)	% 保留*	吸收 (g/100cm ²)	保留 (g/100cm ²)
基础织物	17.50	11.85	67.72	18.01	12.2
T0.5/1.0Ag/Ca	14.58	10.03	68.8	15.97	10.98
F0.5/1.0Ag/Ca(2h)	14.37	8.10	56.37	18.97	10.7
T0.5/5.0Ag/Ca	13.77	7.95	57.74	19.06	11
F0.5/5.0Ag/Ca(2h)	12.23	6.79	55.52	17.47	9.7
T1.0/1.0Ag/Ca	14.84	8.36	56.34	16.48	9.28
F1.0/1.0Ag/Ca(2h)	13.24	7.47	56.42	18.5	10.45
T1.0/5.0Ag/Ca	8.73	5.42	62.09	16.21	10.07
F1.0/5.0Ag/Ca(2h)	11.03	6.30	57.12	20.97	11.97

*%保留=[保留(g/g)/吸收(g/g)×100]

根据BS 3424-18:1986标准检验方法检验伤口敷料组合物的垂直芯吸。表9提供伤口敷料组合物的芯吸性质的汇总。用钙和银溶液处理的组合物的平均芯吸高度高于基础织物的平均芯吸高度。加入HP-β-CD对组合物的平均芯吸高度有很小或可忽略的影响。

[0108] 表9:伤口敷料组合物的纵向和横向芯吸检验

样品	纵向(mm)	横向(mm)	平均(mm)
基础织物	18.67	18.00	18.34
T0.5/1.0AgCa	25.67	28.67	27.17
F0.5/1.0AgCa(2h)	27.67	28.67	28.17
T0.5/5.0AgCa	38.67	45.33	42
F0.5/5.0AgCa(2h)	39.67	47.00	43.33
T1.0/1.0AgCa	26.33	27.67	27
F1.0/1.0AgCa(2h)	25.67	27.67	26.67
T1.0/5.0AgCa	45.00	46.00	45.5
F1.0/5.0AgCa(2h)	46.00	51.33	48.66

评价伤口敷料组合物的收缩性质。表10提供伤口敷料组合物的面积收缩。在组合物上电喷HP-β-CD对该组合物的尺寸稳定性有积极作用。化学处理过程中钙的浓度负面影响伤口敷料组合物的尺寸稳定性。

[0109] 表10:水合和经干燥伤口敷料组合物的面积收缩

样品	水合(%)	经干燥(%)
基础织物	31.27	46.83
T0.5/1.0Ag/Ca	31.27	62.54
F0.5/1.0Ag/Ca(2h)	33.27	36.08
T0.5/5.0Ag/Ca	20.50	43.85
F0.5/5.0Ag/Ca(2h)	24.92	38.66
T1.0/1.0Ag/Ca	27.75	55.16
F1.0/1.0Ag/Ca(2h)	28.45	35.33
T1.0/5.0Ag/Ca	15.98	24.16
F1.0/5.0Ag/Ca(2h)	25.58	29.23

实施例10:从抗菌敷料结构的银释放

检验从实施例5用HP-β-CD电喷的抗菌纳米纤维敷料结构的银释放性质。将各敷料结构的2cm x 2cm样品在玻璃瓶中浸入20mL溶液A (0.4M NaCl, 0.02M CaCl₂, 蒸馏水), 并在37℃培养7天。在培养期间以24个间隔抽取10mL溶液样品。每次抽取样品, 将新鲜的10mL溶液A等分试样补加到培养样品。用电感耦合等离子发射光谱(ICP-OES)测定经抽取样品中的银含量。从各敷料结构释放的银的量显示于表11中。

[0110] 表11. 从抗菌敷料结构的银释放

样品 编号	样品 大小	银释放量(ppm)						
		1-天	2-天	3-天	4-天	5-天	6-天	7-天
F0.5/1.0AG/Ca(2h)	2cm x 2cm	1.4	1.6	1.1	1.1	1.0	1.0	1.0
F0.5/5.0AG/Ca(2h)	2cm x 2cm	1.5	1.5	1.4	1.3	1.4	1.3	1.4
F1.0/1.0AG/Ca(2h)		1.4	1.4	1.4	1.4	1.4	1.4	1.4
F1.0/5.0AG/Ca(2h)		1.4	1.5	1.5	1.5	1.5	1.5	1.5

实施例11: 抗菌敷料结构的恶臭吸收

检验从实施例5用HP-β-CD电喷的抗菌纳米纤维敷料结构的吸收恶臭能力。使敷料结构样品 (2cm x 2cm) 暴露于包含0.5ml刺激检验溶液 (0.4M NaCl, 0.02M CaCl₂, 10%新生小牛血清, 2%二乙胺) 的恶臭环境。类似地检验市售产品样品 (CarboFLEX[®], ConvaTec)。10个随机选择的个人通过评定0至10气味评价各样品的气味强度。得分0表示“没有气味”, 得分10表示“最大气味”。敷料结构的气味评价结果显示于表12中。用HP-β-CD较长时间 (4小时相对于1或2小时) 电喷的样品具有较低气味评级。

[0111] 表11: 用HP-β-CD电喷的抗菌敷料结构的恶臭吸收能力

敷料样品	评级 (1 天培养时间)	评级 (7 天培养时间)	规格 (恶臭水平)	等级
F0.5/1.0Ag/Ca(1h)	6.9	7.5	中等	一般
F0.5/1.0Ag/Ca(2h)	6.1	6.6	中等	一般
F0.5/1.0Ag/Ca(4h)	5.1	4.7	最小	好
CarboFlex	4.3	4.9	最小	好

虽然本文已显示和描述本发明的优选实施方案, 但对本领域的技术人员显而易见, 这些实施方案只作为实例。本领域的技术人员现在会不脱离本发明想到很多变动、变化和替代。应了解, 本文所述本发明实施方案的替代可用于实施本发明。以下权利要求旨在限定本发明的范围, 并由其覆盖这些权利要求范围内的方法和结构及其相当。

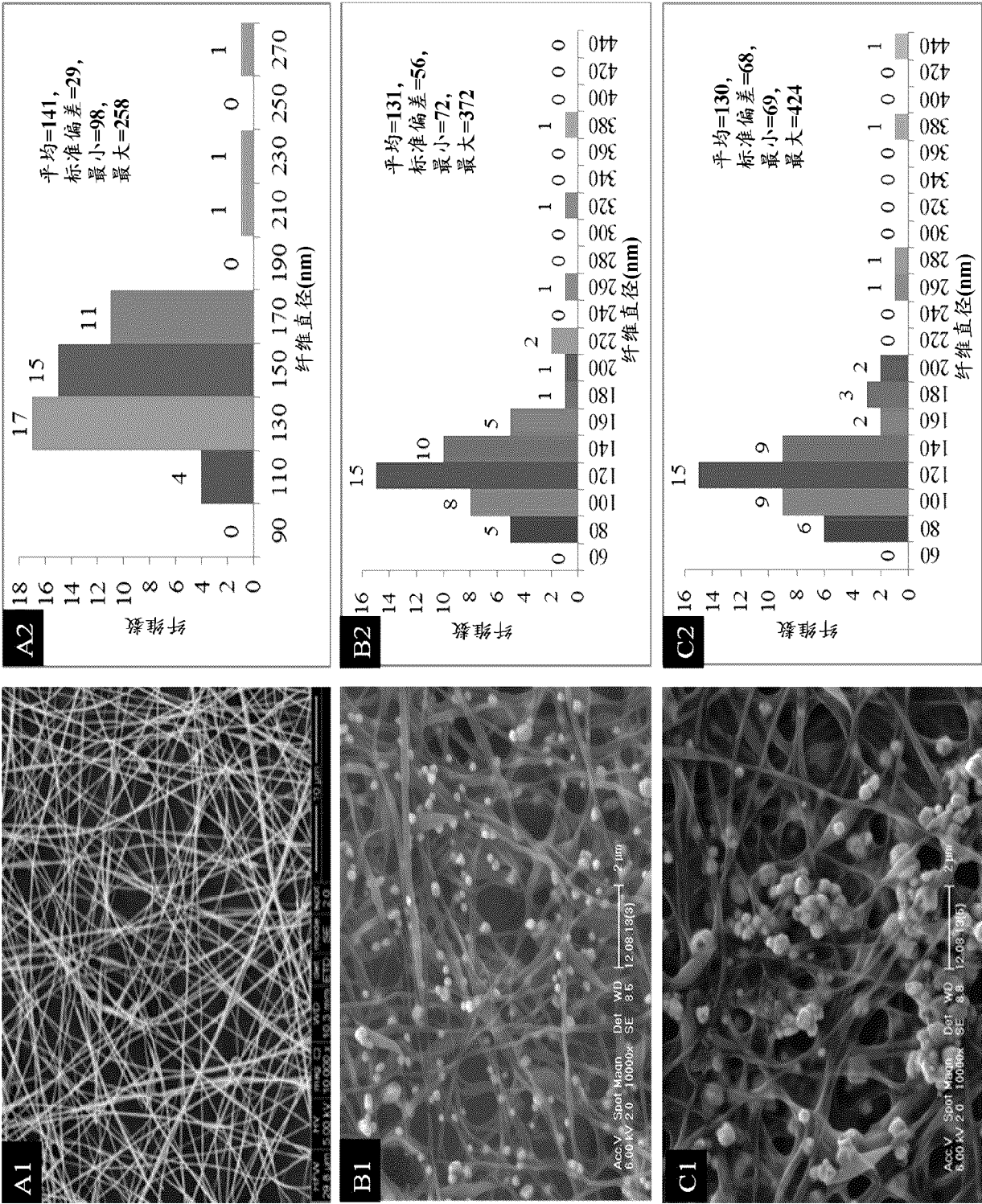


图 1

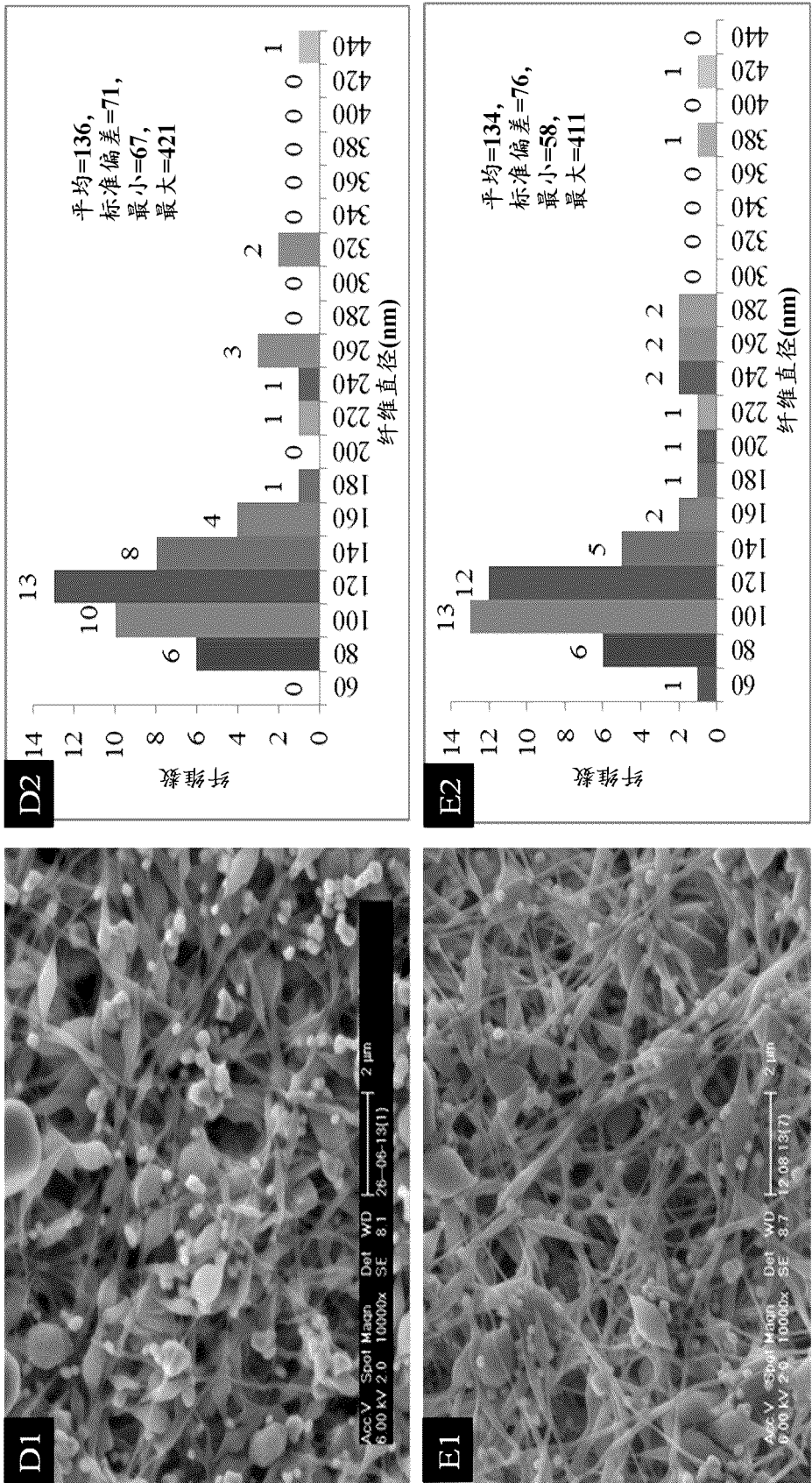


图 1 续

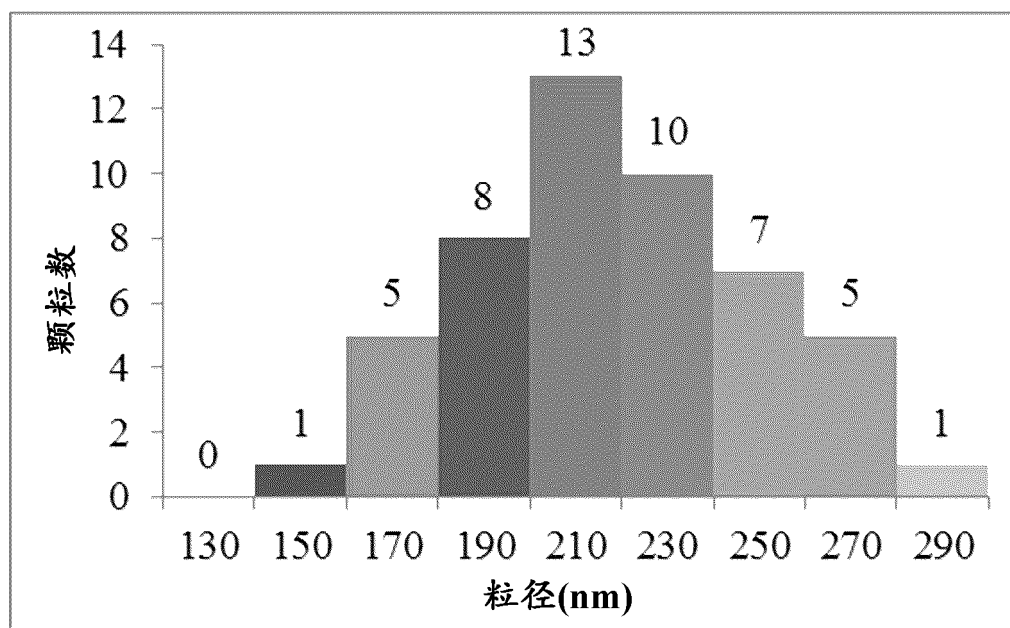


图 2

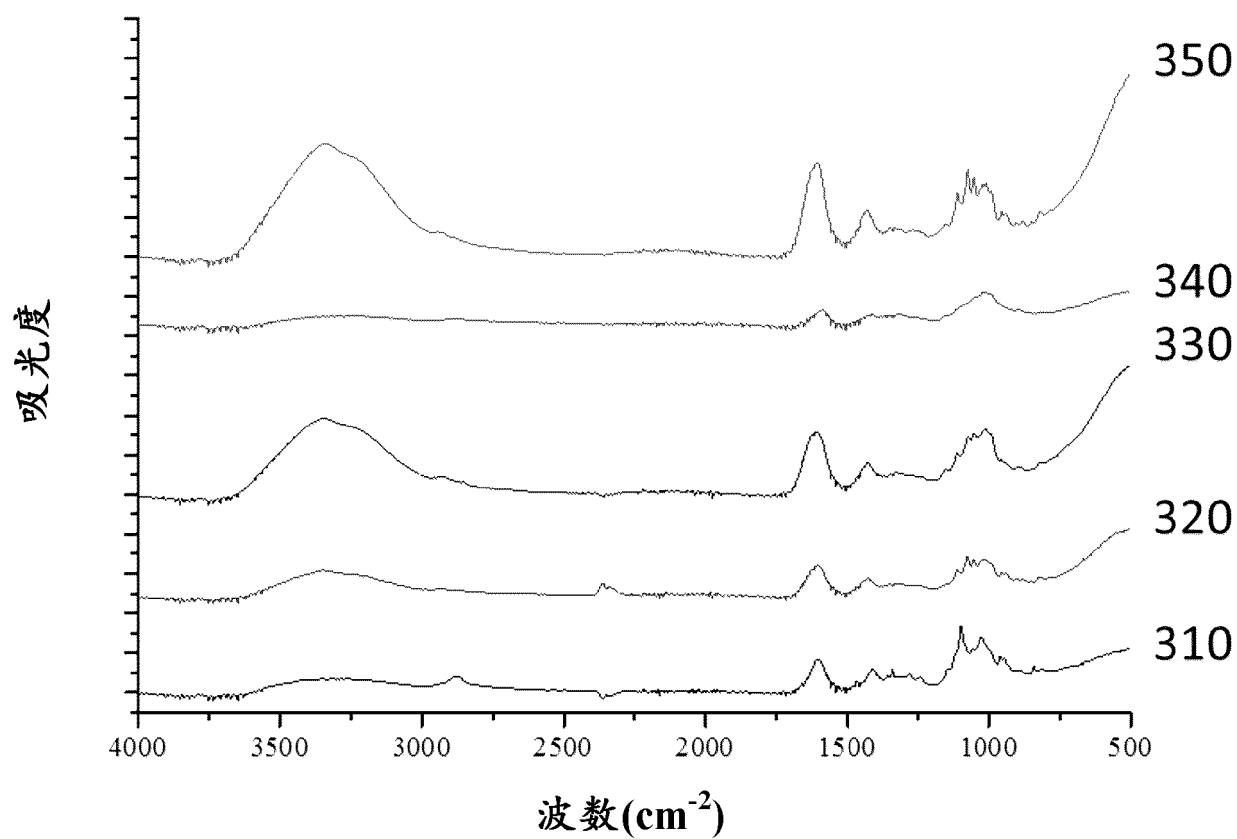


图 3A

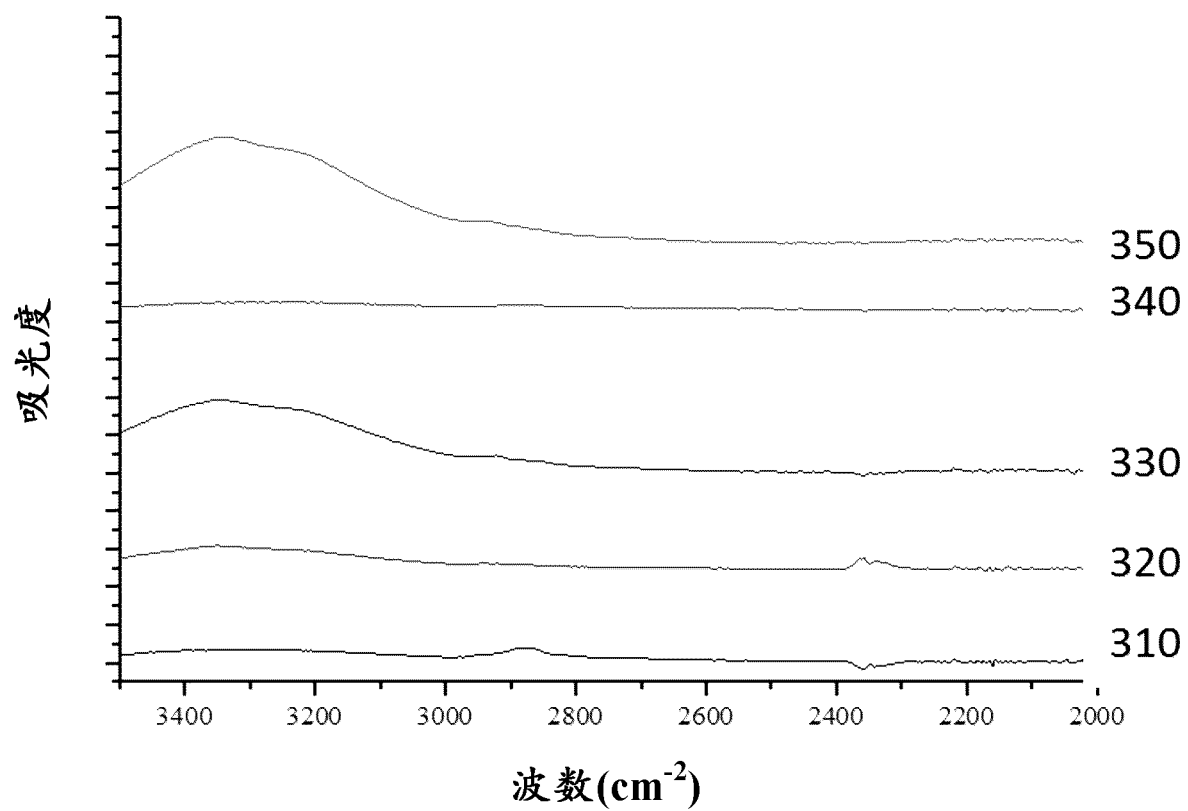


图 3B

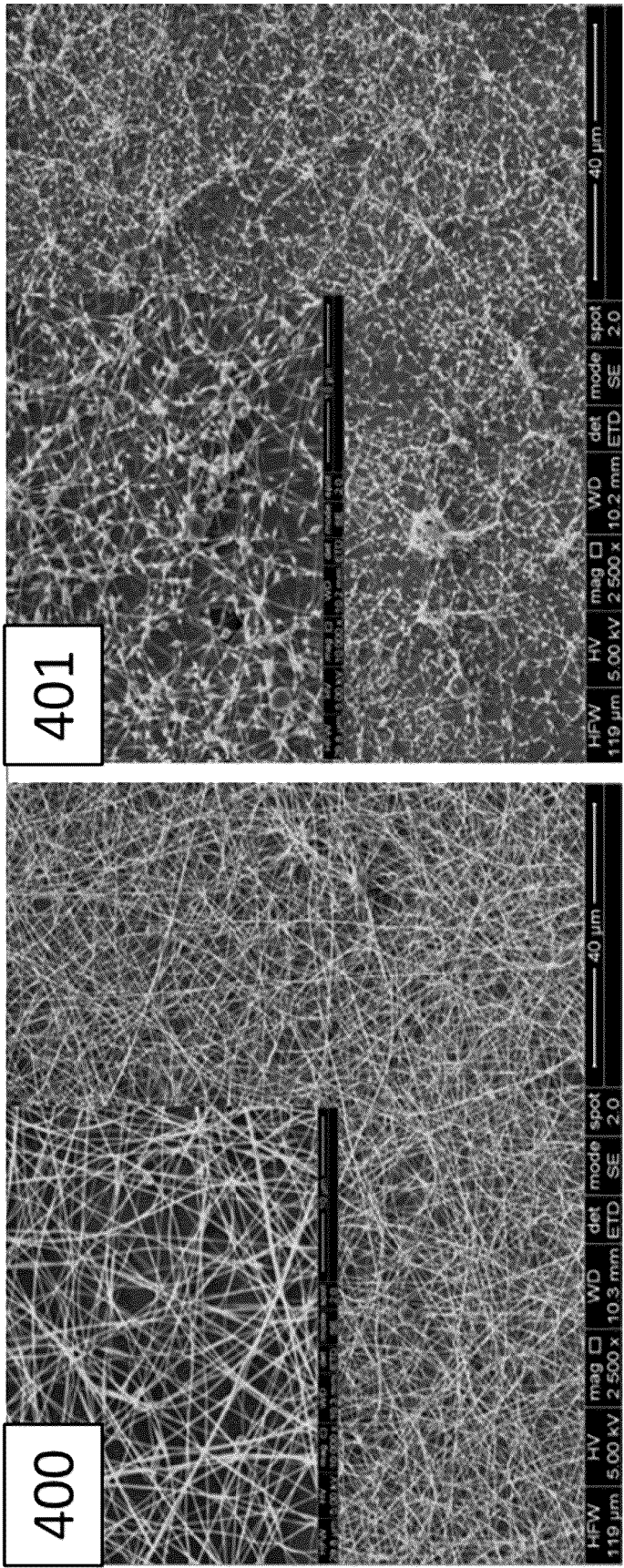


图 4A

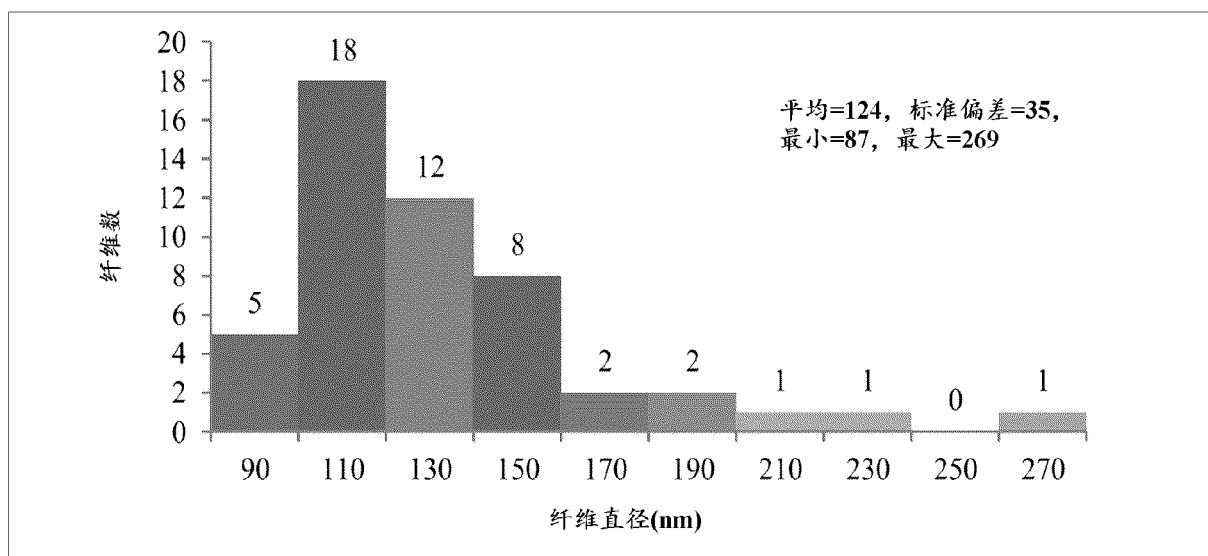


图 4B

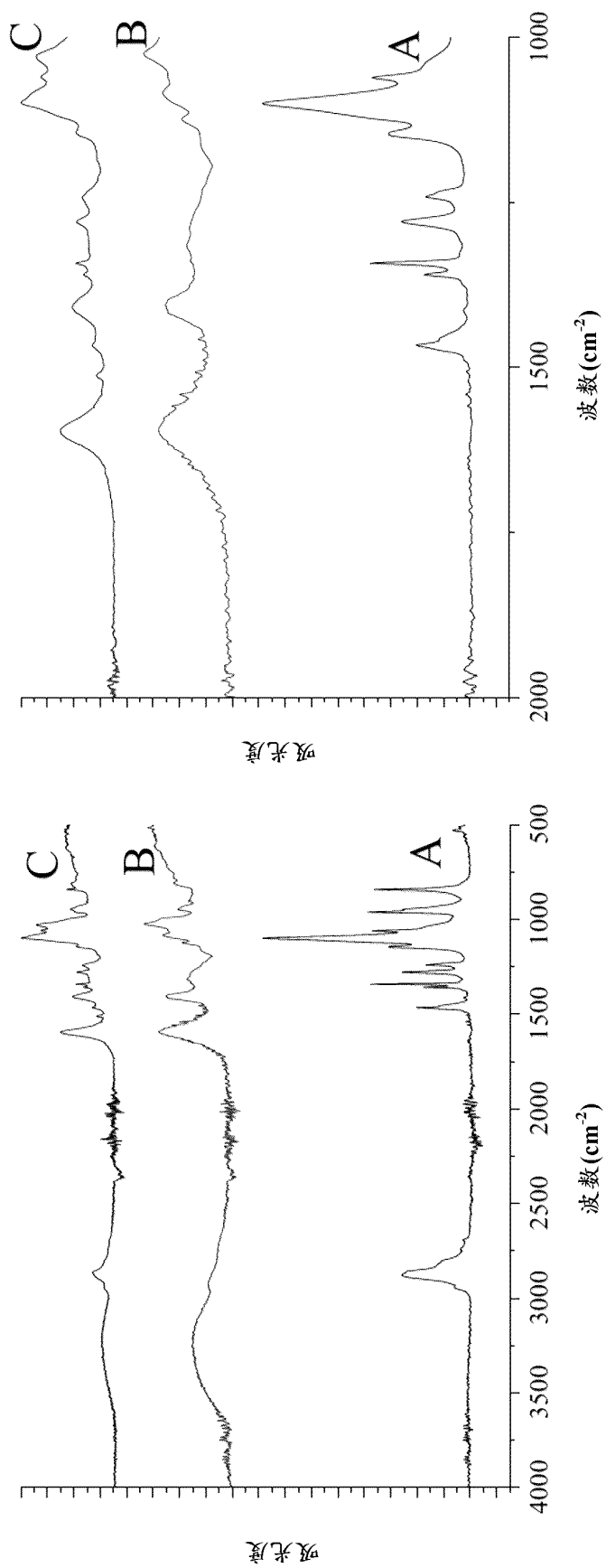


图 5

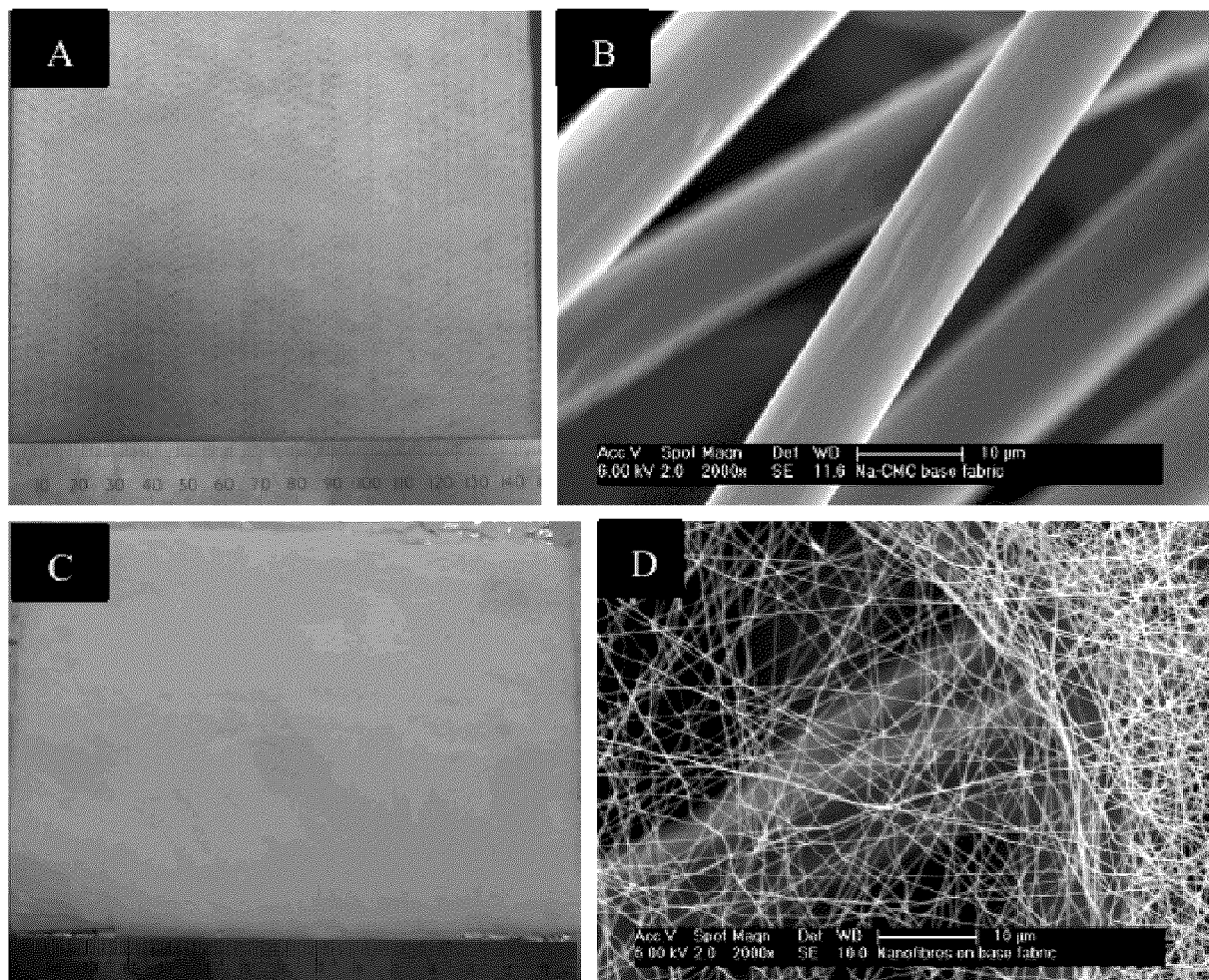


图 6

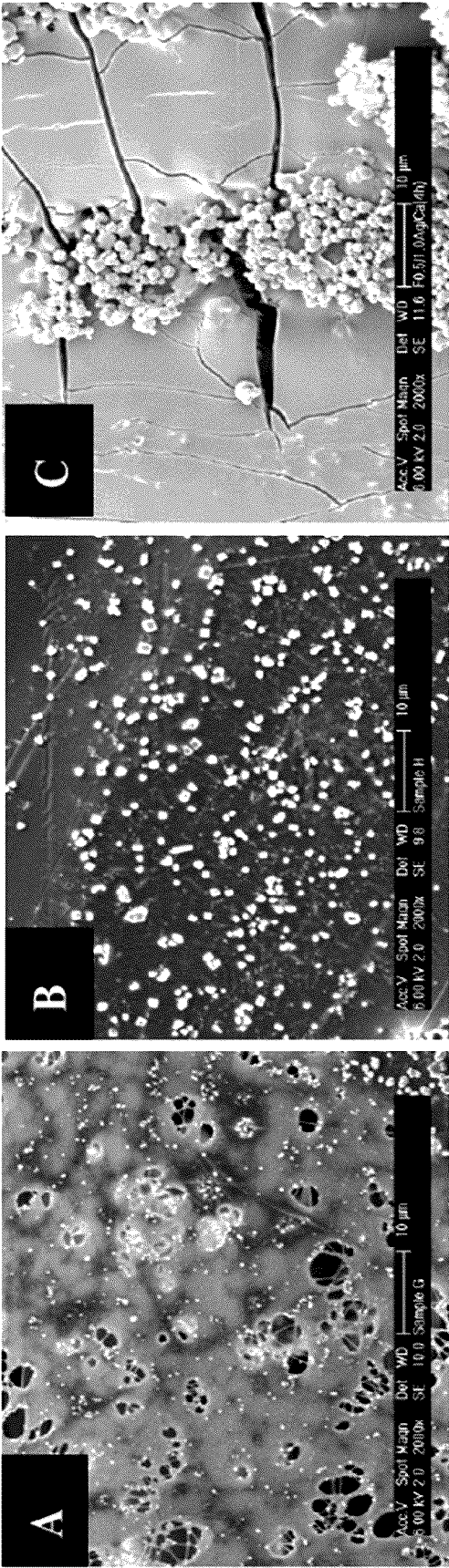


图 7

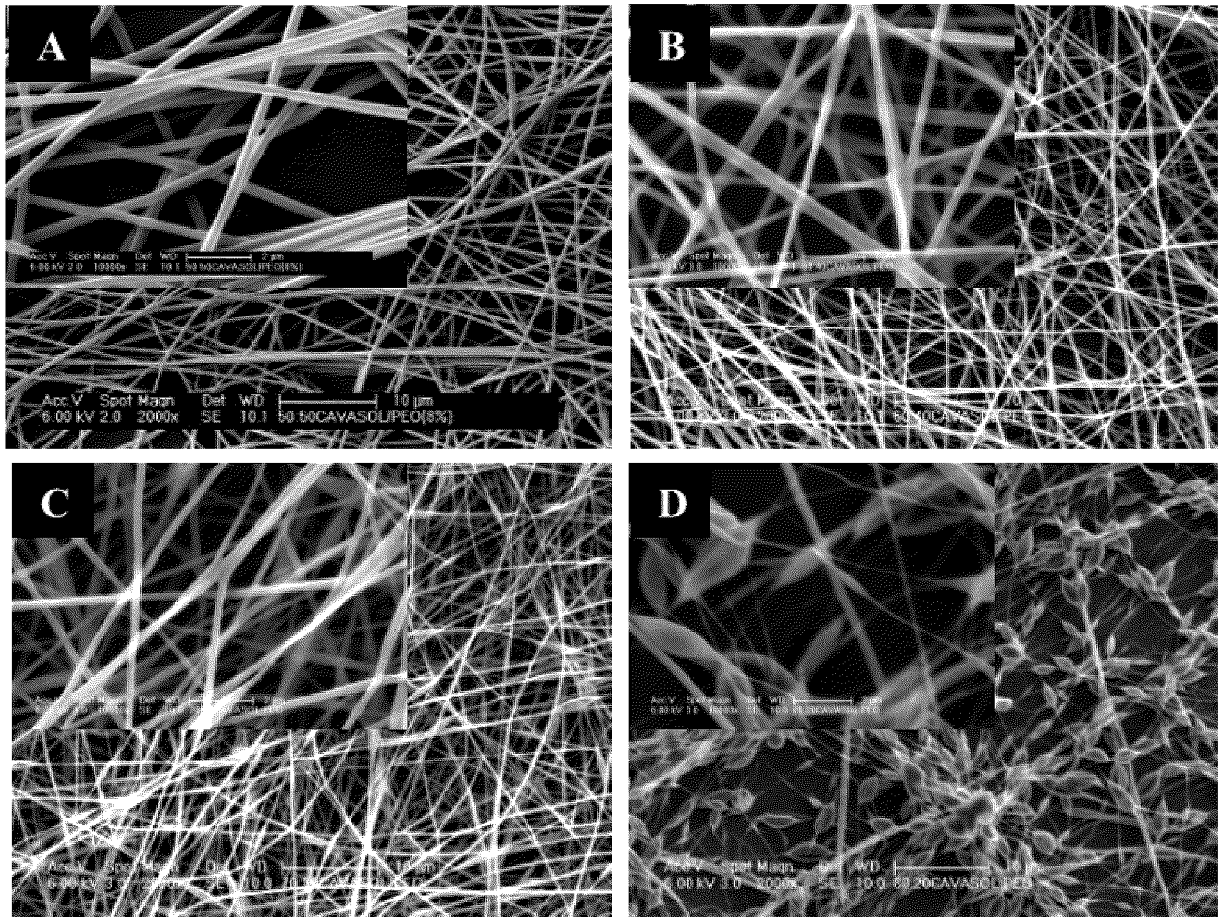


图 8

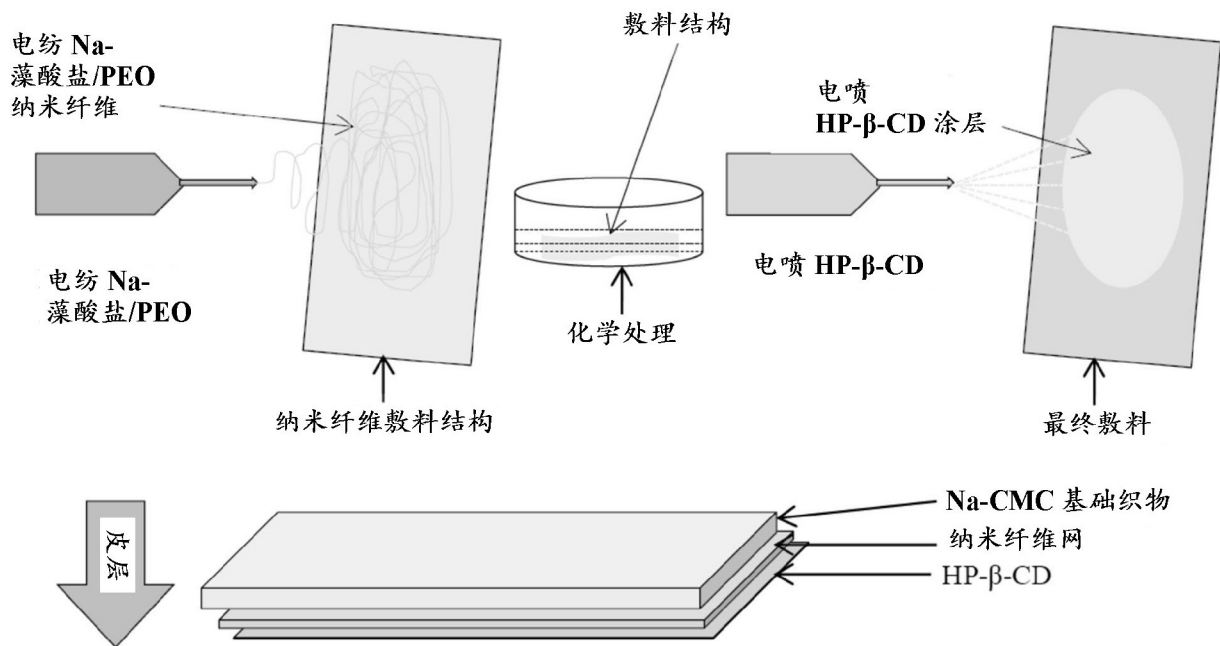
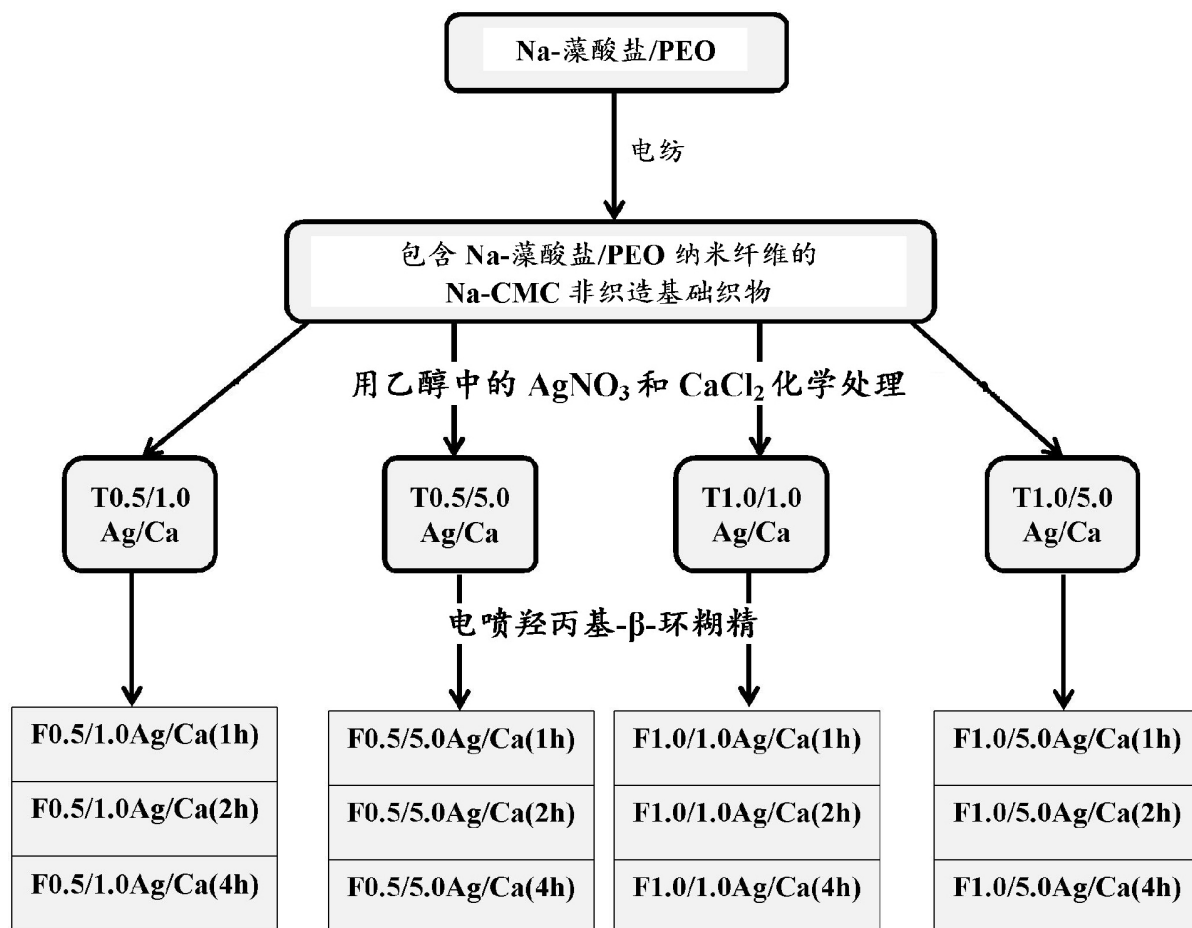


图 9



相应的检验和评价

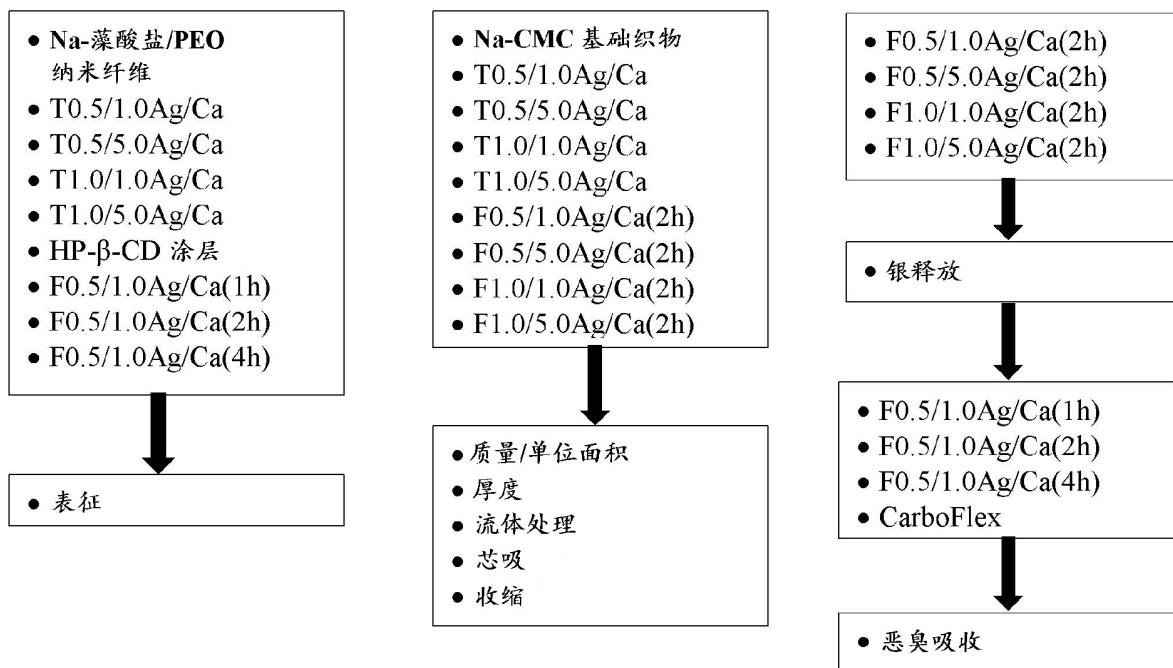


图 10