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(54) **Title**: NANOFIBER MATRICES FORMED FROM ELECTROSPUN HYPERBRANCHED POLYMERS

(57) **Abstract**: A nanofiber matrix comprising an active agent suspended or enmeshed in fibers formed by the electrospinning of one or more hyperbranched polymers can be used in cosmetics, drug delivery and for the growth of cells. The process of electrospinning the hyperbranched polymer solution is carried out without an added solvent or with a solvent and a compressed gas.

Nanofiber Matrices Formed from Electrospun Hyperbranched Polymers

Field of the Invention

The present invention is directed to nanofiber matrices formed by electrospinning hyperbranched polymers in the presence of active agents. The matrices may be used for the controlled release of agents such as cosmetics or drugs. The matrices may also be used as a scaffold for growing eukaryotic cells.

Background of the Invention

Electrospinning is a technique for forming fibers by creating an electric field at the surface of a polymeric solution. Typically, the solution is fed into a nozzle or syringe and a voltage is applied at the tip. If the viscosity of the solution is in an appropriate range, the solution is drawn out in a liquid jet toward a grounded collector and, as the jet elongates, solvent rapidly evaporates. This results in the formation of uniform fibers that are deposited on the collector and that typically have a diameter in the micrometer or nanometer range.

The electrospinning process was originally patented in 1934 (US 1,975,504) and numerous patents describing variations in the technique have appeared since. Examples of recent patents directed to methods and devices for electrospinning include: US 7,297,305; 7,264,762; 7,332,050; 7,326,043; 7,134,857; 6,991,702; 6,753,454 and 6,713,011. Electrospun fibers have

been used as a support matrix for cell growth (US 7,323,190; US 6,790,455); for immobilizing catalysts during chemical reactions (US 7,229,944; US 6,916,758); in fabrics (US 6,110,590; US 7,070,836); as wound dressings (US 4,043,331; US 6,753,454); and as prostheses in the repair of blood vessels (US 4,878,908) and breast replacement (US 5,376,117).

Recently, methods for producing fibers using gas assisted electrospinning have been described (US 2008/0018015). These methods allow fibers to be produced that are highly porous and that are essentially free of organic solvents, characteristics well suited to biological uses. The further development of these methods and their adaptation to unique types of polymers may lead to new products in areas such as cosmetics and medicine.

Summary of the Invention

General Summary

The present invention is based, in part, upon a recognition that hyperbranched polymers have characteristics that make them especially well suited to the controlled delivery of cosmetics, pharmaceuticals and other active agents. Due to their highly branched structure, these polymers have a lower melt and solution viscosity than their unbranched counterparts and they can therefore be electrospun with little or no gas or organic solvent. The need for solvent can also be reduced by modifying the number and type of functional groups present on the polymers. In addition, by adjusting the polarity of the functional groups within a hyperbranched polymer, its glass transition temperature

and/or its melting temperature can be modified to ensure that the polymers are not solid under the process conditions of the electrospinning procedure.

Nanofiber matrices formed by the electrospinning of hyperbranched polymers may be used to suspend or enmesh a variety of active agents and, depending upon the particular agent chosen, can be used, *inter alia*, for cosmetic or therapeutic purposes. In addition, the matrices can be used as a support scaffold for the growth of eukaryotic cells. Electrospinning can be performed under mild conditions that do not destroy labile compounds and a fiber matrix can be made that releases agents in a predictable manner. As noted above, the process can also be performed with little or no potentially harmful organic solvent.

Specific Aspects of the Invention

In its first aspect, the invention is directed to a nanofiber matrix comprising an active agent suspended or enmeshed in fibers formed by the electrospinning of one or more hyperbranched polymers. The matrix has less that 0.1 wt % organic solvent, which makes it suitable for use in pharmaceuticals and cosmetics and may be produced at a temperature (10-200 °C, and preferably 10-120 °C) suitable for many heat sensitive active agents. The hyperbranched polymers preferably have a molecular weight of 1,000 to 100,000 g/mol and preferably have a melting temperature of 30°C or higher. In the context of the invention, the term melting temperature encompasses a melting temperature of a crystalline polymer and a glass transition point of an amorphous polymer, above which the polymer shows a viscous

flow upon shear. The fibers in the matrix should have an average width of between 50 nanometers and 100 microns and preferably of between 50 nanometers and 10 micrometers. Especially preferred are matrices formed from polymers that are enzymatically degradable and that can be used to release active agents in a controlled manner over time. Active agents that may be used include compounds that are typically used in cosmetic preparations such as: colorants; emollients; sunscreens; exfoliants; antioxidants; humectants; and nutrients. Specific examples of such compounds include: aloe vera; zinc oxide; titanium oxide; an alpha, beta or poly hydroxy acid; vitamins; retinol; retinal; retinoic acid; coenzyme Q; glycerine; diprobase; propylene glycol; glyceryl triacetate; sorbitol; xylitol; malitol; polydextrose; tocopherol and derivatives of tocopherol; ascorbic acid and derivatives of ascorbic acid; deoxyribonucleic acids; retinol and derivatives of retinol; alpha fatty acids; niacinamide; ubichinon; bisabolol; alantoin; phytantriol; panthenol; alpha hydroxy acid; amino acids; hyaluronic acid; polyglutamic acid; beta-glucan; creatine and derivatives of creatine; guanidine and derivatives of guanidine; ceramide; sphingolipid; phytosphingosine and derivatives of phytosphingosine; sphingosine and derivatives of sphingosine; sphinganine and derivatives of sphinganine; pseudoceramide; essential oils; peptides; proteins; protein hydrolysates; plant extracts; or vitamin complexes.

Active agents may also be pharmaceuticals for the treatment of wounds or skin conditions such as acne; psoriasis; eczema; contact dermatitis; and rosacea. Examples of specific pharmaceuticals useful in treating skin conditions include: benzoyl peroxide; triclorosan; chlorhexidine gluconate; erythromycin; clindamycin; tetracycline; a topical retinoid;

coal tar; dithranol; corticosteroids; calcipotriol; and argan oil. Examples of agents useful in the treatment of wounds include: epidermal growth factor; plasminogen activator inhibitor-1; plasminogen activator inhibitor-2; and alpha-1 antitrypsin. Matrices having these active agents or cosmetic compounds would typically be used in lotions, creams, emulsions or gels applied topically.

In addition, matrices that release active agent at a predictable rate or that degrade slowly over time can be implanted in a patient's body for the sustained release of therapeutic agents. Drugs that may be used in such matrices include: COX-2 inhibitors, anticancer agents, NSAIDS, anti-obesity drugs, nutraceuticals, corticosteroids, elastase inhibitors, analgesics, anti-fungals, anti-emetics, analgesics, cardiovascular agents, anti-inflammatory agents, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytics, sedatives, astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiac inotropic agents, cough suppressants, diuretics, antiparkinsonian agents, haemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, sex hormones, anti-allergic agents, stimulants and anoretics, sympathomimetics, thyroid agents, vasodilators, xanthines, therapeutics for asthma, emphysema drugs, respiratory distress syndrome drugs, chronic bronchitis drugs, chronic obstructive pulmonary disease drugs, organ-transplant rejection drugs, drugs for

tuberculosis and other infections of the lung, and respiratory illness drugs.

In another aspect, the invention is directed to processes for preparing a nanofiber matrix suitable for pharmaceutical or cosmetic use or for the sustained release of nutritionally beneficial agents. In one embodiment, a polymeric solution is first prepared by mixing a solvent, an active agent and a hyperbranched polymer and this is then electrospun. Electrospinning is performed under conditions in which the polymeric solution is exposed to a first pressurized gas and nanofibers are collected in a collection vessel containing a second pressurized gas that may, or may not, be the same as the first. Preferably, the solvent itself is a pressurized gas or a supercritical fluid such as carbon dioxide; nitrous oxide; an alkane; an alkene; ammonia; or water vapor. In order to maintain the integrity of heat sensitive active agents, the process may be carried out at a temperature of 0-200°C and preferably at 10-60°C. The gas pressure on the polymeric solution and the pressure in the collection vessel should be in the range of 10-20,000 psig and preferably in the range of 50-10,000 psig or 50-5,000 psig. Due to their highly branched structure, hyperbranched polymers have a lower melt and solution viscosity (no chain entanglements as for linear polymers) and therefore they allow for electrospinning with less gas or solvent or without using any gas or solvent at all. The active agents used in the process are the same as those described above. In addition to the process for producing matrices, the invention includes the nanofiber matrices themselves and topical pads or compositions such as lotions, creams, emulsions, and gels containing the matrices.

In another embodiment, the process of electospinning is carried out using hyperbranched polymers that have a low enough viscosity and melt temperature to be used in the absence of any added organic solvent, preferably in the absence of any added solvent. Any of the active agents described above can be included in this process.

In another aspect, the invention is directed to a nanofiber cell matrix which is the same as that described above but which includes eukaryotic cells rather than active agents. The matrix provides a support for the growth of the cells either *in vitro* or *in vivo* after the implantation of the matrix/cell combination. Examples of cells that may be grown include: progenitor cells; embryonic stem cells; embryonic germ cells; mesenchymal stem cells; bone marrow stromal cells; cardiomyocytes; endothelial cells; and neuronal cells. In addition, factors that support the growth or survival of cells may be included in the matrix. Examples of such factors include: insulin-like growth factors I or II; transforming growth factors; fibroblast derived growth factor; platelet derived growth factor; epidermal growth factor; and vascular endothelial growth factor.

Detailed Description of the Invention

I. Electrospinning in General

In general, electrospinning is carried out by having a polymer solution flow through a nozzle, capillary tube, or needle that is charged by connection to a high voltage source. An electron flux from the charged nozzle to an

electrically grounded target draws the polymer solution as a thin liquid jet through the open space between the nozzle and target. During this process, solvent in the liquid jet is evaporated or vaporized to form dry polymer fibers on the target.

Adequate Removal of Solvent

Dry fiber will not be created in the electrospinning process if the liquid jet arrives at the target as a droplet or a spray due to inadequate removal of solvent. Most failures to create dry fiber occur when low volatility solvents are used. This problem may be corrected by either using mixtures containing a low volatile solvent, such as DMF, with a highly volatile solvent, such as acetone, to adjust the vapor pressure of the "mixed" solvent or by using longer nozzle-to-target distances. As discussed further herein, an alternative approach, is to add a compressed gas to the receiver vessel to rapidly extract solvent during fiber formation.

Viscosity and Processing Parameters

McKee and coworkers determined how electrospun fiber morphology is controlled by processing variables including applied voltage, nozzle to target distance, and feed rate of the solution to the nozzle as well as solution properties such as solvent type, viscosity, polymer concentration, solution conductivity, and solution surface tension (*Macromolecules 37*:1760-1767 (2004), incorporated herein by reference in its entirety). They report that branched polymers possess a smaller hydrodynamic volume than linear

polymers of equivalent molecular weight and consequently a higher concentration of branched polymers can be electrospun, relative to linear polymers, since the concentration for chain entanglement is larger with branched polymers.

It is only possible to electrospin polymeric fibers if the viscosity of the polymer solution is within a certain range. If the solution viscosity is too low, the jet will break up into droplets rather than form a coherent fiber and if the solution viscosity is too high it will not be possible to force the solution through a small diameter nozzle. Often, an increase in solution viscosity results in the production of fibers with a larger diameter (Kim, *et al.*, *Fibers and Polymers 5*:122-127 (2004)). However, the properties of the fibers made by electrospinning depend on many variables. For example, changing the solvent used can sometimes have a greater affect on fiber diameter than changing the viscosity.

Effect of Added Electrolytes

In order to process highly concentrated polymer solutions, it may be necessary to increase charge density by increasing electrolyte concentration. Electrolyte appears to have its greatest effect at concentrations of up to about 1 or 2 wt% in solution (Zhong, *et al.*, *Polymer 43*:4403-4412 (2002); see also Lin, *et al.*, *Polymer 48*:6384-6394 (2007)). The addition of salts results in higher charges of the liquid jet which, in turn, results in higher elongation forces imposed on the jet under the electrical field. It may also be possible to decrease the fiber diameter with the addition of salts.

Use of Compressed Gas

In a variation of the electrospinning process, the solvent for the polymer can be totally replaced with a compressed gas (McHugh, *et al.*, (US 2008/0018015). This reduces viscosity and thereby allows for the electrospinning of viscous, refractory polymers without the use of a liquid solvent (see Lee, *et al.*, US 4,923,720). The receiver vessel for the electrospinning process typically also contains the same compressed gas at a slightly lower pressure relative to the pressure of the solution in the nozzle. Besides lowering the solution viscosity, another advantage of a gas such as CO_2 added to the polymer solution, is that the "effective" glass temperature, T_g, of the polymer is reduced significantly (see, Chow, *Macromolecules 13*:362-364 (1980); Pantoula, *et al.*, *J. Supercritical Fluids 37*:254-262 (2006)).

Applying pressurized gas to the polymer solution being expelled from the electrospinning nozzle affects the morphology of the fibers formed. Assuming that the pressure in the receiving vessel is lower, gas will be removed from the jet as it travels from the nozzle to the target. This will cause the polymer T_g to increase and a "dry" skin to be produced on the exterior of the jet while still maintaining a molten interior. Eventually all of the compressed gas will escape from the jet leaving behind "solvent-free" fibers with a porous interior. In addition, a porous fiber skin will result from the evolving gas leaving behind holes. The pressurized gas in the spinning vessel can extract residual solvent from the solution jet leaving behind a "dry" solvent-free polymer fiber.

Because highly branched polymers exhibit less chain entanglement than linear polymers with a comparable molecular

weight, their solubility will be increased. As a result, the amount of gas or solvent needed to carry out electrospinning will be reduced. In addition, by adjusting the number and polarity of functional groups, the solubility of the hyperbranched polymers can be increased, thereby reducing the need for solvent further or, preferably, eliminating it altogether. Solvents that may be used include water, alcohols such as methanol, ethanol or isopropanol, compressed CO_2, compressed propane, tetrahydrofuran, dimethyl formamide, dimethyl acetamide, toluene, acetone, aqueous HCl solutions, hexane, acetic acid, ethanediol, dichloromethane, dichloroethane and ionic liquids.

Preferred Temperatures and Pressures

The preferred operating temperature can be as high as 200°C using compressed gas in the electrospinning process. However, for most applications, it is preferred to maintain an operating temperature of from sub-ambient temperatures to 60°C. A preferred operating pressure range is 50 to 3,000 psia (and more preferably 50-1500 psia).

II. Hyperbranched Polymers and Polymer Compositions

Hyperbranched polymers and methods for producing hyperbranched polymers have been described in numerous publications, including: EP 0630389;EP 1034839; US 5,041,516; US 5,136,014; US 5,183,862; US 5,196,502; US 5,225,522; US 5,227,462; US 5,266,106; US 3,306,561; US 5,362,843; US 5,418,301; US 6,379,683; WO 97/06825; WO 98/30604; WO 2004/072153; WO 00/065024; WO 03/037383; WO 00/06267 and

WO 03/033027, all of which are incorporated by reference herein in their entirety.

The most preferred hyperbranched polymers and methods for making these polymers are described in WO 2007/048672, also incorporated by reference herein in its entirety. These hyperbranched polymers comprise a hydrophilic core having polyester units and hydrophobic end groups. The hyperbranched polymers have a molecular weight greater than or equal to 6000 g/mol and a hydroxyl number in the range from 0 to 200 mg KOH/g. The degree of branching of the polymers should be in the range of from 20 to 70%, and the polymers should have a melting point of at least 30°C. The polymers are designed to release a low molecular weight substance, such as the active agents described herein, at a steady rate that can be controlled by varying the number and type of hydrophobic groups present. Roughly 20-30 wt% of low molecular weight substance may be used based on the binary system consisting of polymer and low molecular weight substance.

As mentioned above the hyperbranched polymers have a hydrophilic core. In a preferred aspect of the invention, the core has a solubility in water at 90°C that is at least 10% by mass, and more preferably at least 20% by mass. This parameter is measured on the basis of the hyperbranched polymer before hydrophobization, *i.e.* on the hydrophilic core as such. The measurement can be effected by the so-called flask method, which measures the water solubility of the pure substance.

The hydrophilic core preferably has a hydroxyl number measured before hydrophobization in the range of from 400 to 600 mg KOH/g, and more preferably in the range of from 450 to 550 mg KOH/g. This property is measured to ASTM E222. In this

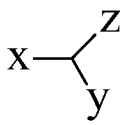
method, the polymer is reacted with a defined amount of acetic anhydride, unconverted acetic anhydride is hydrolyzed with water and the mixture is titrated with NaOH. The hydroxyl number corresponds to the difference between a comparative sample and the value measured for the polymer.

The core comprises polyester units (described, *e.g.*, in EP 0 630 389). In general, the hydrophilic core is usually derived from an initiator molecule having at least two, and preferably at least three, hydroxyl groups and repeat units. The repeat units are made up of monomers having at least one carbonyl group and at least two hydroxyl groups. The terms "initiator molecule" and "repeat unit" are well known in the art.

Highly branched globular polymers are also referred to in the technical literature as "dendritic polymers." These dendritic polymers are synthesized from polyfunctional monomers and can be divided into two different categories, the "dendrimers" and the "hyperbranched polymers." Dendrimers have a very regular, radially symmetric generation structure. They are monodisperse globular polymers which - compared to hyperbranched polymers - are prepared in multistep syntheses with a high level of synthesis complexity. The structure is characterized by three different areas: - the polyfunctional core which constitutes the center of symmetry, - various well-defined radially symmetric layers of a repeat unit (generation) and - the terminal groups. In contrast to the dendrimers, the hyperbranched polymers are polydisperse and irregular with regard to their branching and structure. In addition to dendritic and linear units (in contrast to dendrimers) linear units also occur in hyperbranched polymers.

It is preferred that the hyperbranched polymers have at least three repeat units per molecule, preferably at least 10, 100, 200 or 400 repeat units, each of which have at least three, and preferably at least four bonding mean. At least 3 of these repeat units, and more preferably at least 10 or 20, are each bonded via at least three, preferably via at least four bonding means to at least three, and preferably at least four, further repeat units. The hyperbranched polymers should not have more than 10,000, and preferably not more than 5000 or 2500 repeat units.

In this context, the term "repeat unit" means a constantly repeating structure within the hyperbranched molecule. The term "bonding means" is understood to mean the functional structure within a repeat unit which allows bonding to another repeat unit. Based on the examples detailed above of a dendrimer and of a hyperbranched polymer, the repeat unit is a structure with three bonding means (X,Y,Z) as follows:



Bonding can be accomplished by condensation polymerization, by free-radical polymerization, by anionic polymerization, by cationic polymerization, by group transfer polymerization, by coordinative polymerization or by ring-opening polymerization.

For example, it is possible to obtain the hyperbranched polymers to be used in accordance with the invention by polycondensation, in which a polyhydric alcohol is used to convert the carboxylic acid groups of the monomers to ester

groups. Since the monomers comprise at least 2 hydroxyl groups, the macromolecule after each reaction has more hydroxyl groups than before the reaction. The initiator molecule is preferably an aliphatic polyol with preferably 3, 4, 5, 6, 7 or 8, and more preferably 3-5 hydroxyl groups. The initiator molecule is may be selected from: ditrimethylolpropane, ditrimethylolethane, dipentaerythritol, pentaerythritol, alkoxylated pentaerythritol, trimethylolethane, trimethylolpropane, alkoxylated trimethylolpropane, glycerol, neopentyl alcohol, dimethylolpropane and/or 1,3-dioxane-5,5-dimethanol.

In general, the repeat units in the hyperbranched polymers are derived from monomers having one carboxyl group and at least two hydroxyl groups. The preferred monomers include dimethylpropionic acid, α,α-bis(hydroxymethyl)butyric acid, α,α,α-tris(hydroxymethyl)acetic acid, α,α-bis(hydroxymethyl)-valeric acid, α,α-bis(hydroxy) propionic acid and/or 3,5-dihydroxybenzoic acid. The hydrophilic core may be obtained by polymerization of dimethylolpropionic acid, in which case the initiator molecule used is preferably ditrimethylolpropane, trimethylolpropane, ethoxylated pentaerythritol, pentaerythritol or glycerol.

In a preferred embodiment, the hydrophilic core has a molecular weight of at least 1500 g/mol, and more preferably at least 2500 g/mol. This parameter is based on the weight-average molecular weight (Mw), which can be measured by means of gel permeation chromatography. The hydrophilic core preferably has a glass transition temperature which is in the range of from -40 to 60°C, more preferably 0 to 50°C and most preferably 10 to 40°C. The glass transition temperature can be determined by DSC processes using a heating rate of

3°C/min (DMA Tan δ peak; Netzch DMA 242 3-point bending 1Hz 3°C/min).

In addition to the hydrophilic core, at least some of the chain ends of the hyperbranched polymers have hydrophobic groups. The degree of functionalization of the hyperbranched molecules with hydrophobic end groups, preferably fatty acid-containing units, is in the range of from 30 to 100%, preferably in the range of from 35 to 95%, more preferably in the range of from 40 to 90% and most preferably in the range of from 45 to 85%. The degree of functionalization is based on the proportion of hydroxyl groups which are converted in the hydrophobization. Accordingly, the degree of functionalization or the degree of esterification with fatty acids can be determined by the measurement of the hydroxyl number for the hyperbranched core molecule both before and after the hydrophobization reaction.

Carboxylic acids used as hydrophobic groups should be at least 6, and preferably at least 12, carbon atoms in length. They should be no more than 40, and preferably no more than 32, 28, and most preferably no more than 24, carbon atoms in length. The groups may be derived from saturated and/or unsaturated fatty acids. The proportion of the carboxylic acids having 12 to 24 carbon atoms is preferably at least 30% by weight, more preferably at least 50% by weight and most preferably at least 60% by weight, based on the weight of the carboxylic acids used for the hydrophobization. These include especially fatty acids which are present in linseeds, soybeans and/or tall oil. Particularly suitable fatty acids are those which have a low proportion of double bonds, for example hexadecenoic acid, and especially palmitoleic acid, octadecenoic acid, or oleic acid. Preferred carboxylic acids

in this context have a melting point of at least 35°C, and preferably at least 40°C or 60°C. Accordingly, preference is given to using linear, saturated carboxylic acids. These include especially octanoic acid, decanoic acid, dodecanoic acid, tetradecanoic acid, hexadecanoic acid, heptadecanoic acid, octadecanoic acid, eicosanoic acid, docosanoic acid and tetracosanoic acid. Particular preference is given to saturated fatty acids having 16 to 28 carbon atoms, and most preferably 16 to 24 carbon atoms.

The hyperbranched polymer (after hydrophobization) has a molecular weight of at least 6000 g/mol, and preferably at least 7500 g/mol. The molecular weight is preferably at most 30 000 g/mol, and more preferably at most 25 000 g/mol. This parameter is based on the weight-average molecular weight (Mw), which can be measured by means of gel permeation chromatography (cf., *inter alia*, Burgath, *et al. Macromol. Chem. Phys.*, *201*:782-791 (2000)).

The polydispersity Mw/Mn of preferred hyperbranched polymers is in the range of from 1.1 to 5.0, more preferably in the range of from 1.10 to 5.0 and most preferably in the range of from 1.2 to 3.0, where the number-average molecular weight (Mn) can likewise be obtained by gel permeation chromatography.

The weight ratio of hydrophilic core to hydrophobic end groups should generally be in the range of from 10:1 to 1:10, preferably of from 1:1 to 1:2.5. This ratio is based upon the weight average of the hydrophilic core and the weight average of the hyperbranched polymer.

The viscosity of the hyperbranched polymers is preferably in the range of from 50 mPas to 5.00 Pas, and more preferably in

the range of from 70 mPas to 3.00 Pas, where this parameter can be determined by means of rotational viscometry at 110°C and 30 s^{-1} between two 20 mm plates.

The acid number of the hyperbranched polymer should generally be in the range of from 0 to 20 mg KOH/g, preferably in the range of from 1 to 15 mg KOH/g and most preferably in the range of from 6 to 10 mg KOH/g. This property can be measured by titration with NaOH (cf. DIN 53402).

In addition, the hyperbranched polymer, after hydrophobization, should have a hydroxyl number in the range of from 0 to 200 mg KOH/g, preferably in the range of from 1 to 150 mg KOH/g and most preferably in the range of from 10 to 140 mg KOH/g. This property is measured to ASTM E222. In this case, the polymer is reacted with a defined amount of acetic anhydride, unconverted acetic anhydride is hydrolyzed with water and the mixture is then titrated with NaOH. The hydroxyl number is calculated from the difference between a comparative sample and the value measured for the polymer. In this case, it is the number of acid groups of the polymer that should be taken into account.

The degree of branching of the hyperbranched polymer is in the range of from 20 to 70%, and preferably 25 to 60%. The degree of branching depends on the components used to prepare the polymer, especially the hydrophilic core, and the reaction conditions. The degree of branching can be determined according to Frey *et al.*, (see Hölter, *et al.*, *Acta Polymer 48*:30 (1997) and Magnusson, *et al.*, *Polymer 43*:301 (2002)).

The hyperbranched polymer should have a melting point of at least 30°C, preferably of at least 35°C and more preferably

of at least 40°C. In a particular aspect of the present invention, the melting point of the hyperbranched polymer may be at most 65°C, and preferably at most 60°C, 57°C or 55°C. The melting point can be determined by means of differential scanning calorimetry (DSC), for example with the Mettler DSC 27 HP apparatus and a heating rate of 10°C/min.

The water solubility of the hyperbranched polymer after hydrophobization is preferably at most 10% by mass, and more preferably at most 7% or 5% by mass, measured by the flask method detailed above at 40°C.

In addition, particularly preferred hyperbranched polymers, when mixed with water at a temperature of 60°C or less, preferably of 50°C or less and more preferably approx. 48°C, exhibit only liquid-liquid equilibria, but no solid-liquid equilibria or solid-liquid-liquid equilibria, this property being determined by using a mixture of 50% by weight of water and 50% by weight of hyperbranched polymer. The measurement can be effected by means of filter experiments, the mixture being filtered through a filter with a suitable pore size, which is preferably 20 µm or less. In the presence of solid-liquid equilibria or solid-liquid-liquid equilibria, the solid constituents of the equilibria remain in the filter, whereas no residue is observed in the case of liquid-liquid equilibria. This property can be controlled, inter alia, through the degree of functionalization and the carboxylic acids used for hydrophobization. When the hyperbranched polymers have a low degree of functionalization and/or short-chain carboxylic acids, these polymers generally exhibit only liquid-liquid equilibria under the conditions detailed above, but no solid-liquid equilibria.

The hyperbranched polymer preferably consists essentially of hydrogen, oxygen and carbon. The term "essentially" means that further elements are present in the hyperbranched polymer up to, at most, 10% by weight, and preferably at most 5% by weight. In a particular aspect of the present invention, the hyperbranched polymer can be degraded enzymatically. This can be achieved, for example, by virtue of the hydrophilic core and/or the hydrophobic shell comprising enzymatically degradable organic ester groups.

Preferred hyperbranched polymers or preparations of hyperbranched polymers according to the present invention exhibit enzymatic degradation over a chosen period of time, *e.g.*, a year, 6 months, 3 months, 1 month, 10 days, 3 days, 2 days or 1 day. To analyze enzyme controlled release, preparations may be degraded with a lipase such as, for example, Lipomod 34P (Biocatalyst Lmt., UK) and time until 50% by weight of the active ingredient has been released may be determined . For example, preparations with a loading of from 10 to 20% by weight can be analyzed by suspending 0.22 g of active ingredient-laden polymer particles in 15 ml of phosphate buffer (pH 5.01) or in a 15 ml solution of the enzyme Lipomod 34P (Biocatalyst Lmt., UK) in the same buffer (concentration of the Lipomod 34P is 0.5 mg/ml). The samples may be kept in a water bath at 37°C without mixing. At regular time intervals, for example 5 hours, samples of approx. 2 ml can be taken, and the concentration of the active ingredient can be analyzed by a suitable process, such as HPLC (High- Pressure Liquid Chromatography).

The preparation of these hyperbranched polymers is described, *inter alia*, in EP 630 389. In general, an initiator molecule may be reacted with at least one compound having at least two

hydroxyl groups and at least one carboxylic acid group. This results in a hydrophilic core which can be reacted with at least one hydrophobic compound, for example a long-chain carboxylic acid. In general, the reaction is performed at a temperature in the range of from 0°C to 300°C, and preferably of from 100°C to 250°C, and the reaction can be accelerated by known esterification catalysts. These catalysts include, for example, Lewis and Brønsted acids, especially p-toluenesulfonic acid, methanesulfonic acid, trifluoroacetic acid, BF_3, $AlCl_3$ and $SnCl_4$; titanium compounds, especially tetrabutyl titanate; zinc powder and/or tin powder.

The active agent comprised in the nanofiber matrix should preferably have a molar mass in the range of from 15 g/mol to 1000 g/mol, more preferably of 30 g/mol to 800 g/mol and most preferably of from 60 g/mol to 500 g/mol. The low molecular weight substance is preferably bound to the hyperbranched polymer by a noncovalent method, *e.g.* by ionic or polar interactions or by van der Waals forces. The nanofiber matrix can be designed for delayed release of the low molecular weight substance into a medium. Delayed release can be measured according to the method described by Smirnova, et al. (*J. Non-Crystalline Solids 54-60* (2004).

The repeating units that may be used in the hyperbranched polymers include especially: olefins such as 1-butene, 1-hexene, and norbornene; vinyl halides such as vinyl chloride, vinyl fluoride, vinylidene chloride and vinylidene fluoride; vinyl esters such as vinyl acetate; heterocyclic vinyl compounds such as 2-vinylpyridine, 3-vinylpyridine, 2-methyl-5-vinylpyridine, 3-ethyl-4-vinylpyridine, 2,3-dimethyl-5-vinylpyridine, vinylpyrimidine, vinylpiperidine, 9-vinylcarbazole, 3-vinylcarbazole, 4-vinylcarbazole,

1-vinylimidazole, 2-methyl-1-vinylimidazole, N-vinylpyrrolidone, 2-vinylpyrrolidone, N-vinylpyrrolidine, 3-vinylpyrrolidine, N-vinylcaprolactam, N-vinylbutyrolactam, vinyloxolane, vinylfuran, vinylthiophene, vinylthiolane, vinylthiazoles and hydrogenated vinylthiazoles, vinyloxazoles and hydrogenated vinyloxazoles; vinyl and isoprenyl ethers; maleic acid and maleic acid derivatives such as mono- and diesters of maleic acid, maleic anhydride, methylmaleic anhydride, maleimide, methylmaleimide; fumaric acid and fumaric acid derivatives such as mono- and diesters of fumaric acid; dienes such as divinylbenzene; acrylates and methacrylates, which are referred to hereinafter as (meth)acrylates and include (meth)acrylates which derive from saturated alcohols such as methyl (meth)acrylate, ethyl (meth)acrylate, n-propyl (meth)acrylate, isopropyl (meth)acrylate, n-butyl (meth)acrylate, tert-butyl (meth)acrylate, pentyl (meth)acrylate, hexyl (meth)acrylate, 2-ethylhexyl (meth)acrylate, heptyl (meth)acrylate, 2-tert-butylheptyl (meth)acrylate, octyl (meth)acrylate, 3-isopropylheptyl (meth)acrylate, nonyl (meth)acrylate, decyl (meth)acrylate, undecyl (meth)acrylate, 5-methylundecyl (meth)acrylate, dodecyl (meth)acrylate, 2-methyldodecyl (meth)acrylate, tridecyl (meth)acrylate, 5-methyltridecyl (meth)acrylate, tetradecyl (meth)acrylate, pentadecyl (meth)-acrylate, hexadecyl (meth)acrylate, 2-methylhexadecyl (meth)acrylate, heptadecyl (meth)acrylate, 5-isopropyl-heptadecyl (meth)acrylate, 4-tert-butyloctadecyl (meth)acrylate, 5-ethyloctadecyl (meth)acrylate, 3-isopropyloctadecyl (meth)acrylate, octadecyl (meth)acrylate, nonadecyl (meth)acrylate, eicosyl (meth)-acrylate, cetyleicosyl (meth)acrylate, stearyleicosyl (meth)acrylate, docosyl (meth)acrylate and/or

eicosyltetratriacontyl (meth)acrylate; cycloalkyl (meth)acrylates such as cyclopentyl (meth)acrylate, 3-vinylcyclohexyl (meth)acrylate, cyclohexyl (meth)acrylate, bornyl (meth)acrylate; (meth)acrylates which derive from unsaturated alcohols such as 2-propynyl (meth)acrylate, allyl (meth)acrylate, vinyl (meth)acrylate and/or oleyl (meth)-acrylate; aryl (meth)acrylates such as benzyl methacrylate or phenyl methacrylate, where the aryl radicals may each be unsubstituted or up to tetrasubstituted; methacrylates of halogenated alcohols, such as 2,3-dibromopropyl methacrylate, 4-bromophenyl methacrylate, 1,3-dichloro-2-propyl methacrylate, 2-bromoethyl methacrylate, 2-iodoethyl methacrylate, and chloromethyl methacrylate. Examples of hyperbranched polymers that are not enzymatically degradable include: styrene; substituted styrenes with an alkyl substituent in the side chain such as α-methylstyrene and α-ethylstyrene; substituted styrenes with an alkyl substituent on the ring such as vinyltoluene and p-methylstyrene; halogenated styrenes such as mono-chlorostyrenes, dichlorostyrenes, tribromostyrenes and tetrabromostyrenes;

III. Electrospinning Using Hyperbranched Polymers

The present invention is based, in part, upon the discovery that hyperbranched polymers can be electrospun to form a mesh of small diameter fibers suitable for use in applications such as cosmetics, drug delivery and cell growth. The polymers have a high solubility which allows solvent to be avoided and can be electrospun at a low enough temperature to avoid the destruction of most active agents. In one

embodiment, the polymers are electrospun in the presence of a pressurized gas at about ambient temperature, and in another embodiment, electrospinning takes place in the absence of added organic solvent, preferably in the absence of any added solvent. The polymer solution is spun into fibers that are collected on a target plate in a collection vessel that may, or may not, contain a pressurized gas or supercritical fluid.

Process Parameters

When present, the gas, supercritical fluid or solvent in the collection vessel may be or may not be the same as that used for the polymer solution. Any gas may be used as long as it has solvating properties that are sufficient to remove solvent present in the fibers. Solvents that may be used include: water, alcohols such as ethanol or isopropanol, compressed CO_2, compressed propane, tetrahydrofuran, toluene, acetone, benzoyl peroxide, aqueous HCl solutions, hexane, acetic acid, ethanediol, dichloromethane, dichloroethane or ionic liquids. Because organic solvent can be essentially totally eliminated, and the process can be performed under mild conditions, it is possible to entrap low molecular weight substances such as cosmetic compounds, drugs and cells in the spun fiber matrix. An apparatus suitable for this process, along with a general description of suitable parameters has been provided by McHugh *et al.* (US 2008/0018015), hereby incorporated by reference in its entirety.

The morphology and physical characteristics of the fibers made from the hyperbranched polymers can be varied by adjusting the parameters used during electrospinning or by

including chemical additives during the process. As discussed above, parameters that may be adjusted include: the viscosity of the spinning solution, temperature, applied voltage, nozzle-to-target distance; amount of compressed gas in the spinning solution, the temperature and pressure in the receiver vessel, the pressure difference between the spinning solution and the compressed gas in the receiver vessel. In the embodiment where a polymeric solution exposed to a pressurized gas is subjected to electrospinning, the polymeric solution subjected to electrospinning preferably has a viscosity of from 100 to 20 000 mPas. In the embodiment where a polymeric composition containing no added organic solvent is subjected to electrospinning, the polymeric composition subjected to electrospinning preferably has a viscosity of from 400 to 170 000 mPas. Active agents in polymer solutions should constitute 1-80 wt% of the final formulation. Preferably, the pressures used to make fibers should be less than 700 psi and the operating temperature should be about room temperature. Gases that may be used include, for example, carbon dioxide, ethane, propane, halofluorocarbons and ammonia.

Porous, semi-hollow fibers are particularly preferred and may be formed as the result of large amounts of gas in the polymer solution and a low interfacial tension of the polymer-gas phase. The compressed gas acts essentially as a porogen that helps create the interior porous structure and potentially can cause nanopores to develop along the exterior skin of the jet. Compressed gas is easily removed from the fiber when the pressure is released at the end of processing to give a solvent-free, "dry" fiber. In addition, it may be possible to align the nanofibers during electrospinning using methods reported by others. The alignment of nanotubes or

nanofibers allows for applications that need materials with anisotropic properties.

Preferably, formulations used for electrospinning contain 3 to 95 wt % hyperbranched polymer, more preferably about 5 to 85 wt %, and most preferably 10 to 80 wt %. The pressure on the polymer solution should generally be at least 5 psi and preferably at least 10 psi higher than the pressure inside the collection vessel. The collection vessel is preferably at a pressure of at least twice atmospheric pressure, more preferably at least 10 times atmospheric pressure, most preferably at least 20, 40 or 50 times atmospheric pressure, *e.g.*, 50 to 300 times atmospheric pressure.

As mentioned previously, the stream of fiber from the polymeric solution is delivered to a target at which fibers collect. Examples of targets include: a wire mesh, a polymeric mesh, a rotating cylinder, a metal grid, metal foil, paper, a syringe needle, a decomposable substrate such as a decomposable polymer fiber, an electrospun substrate, and the like. The target can be an electrically charged or grounded electrode which attracts the fibers or the target can be located between a suitably charged or grounded electrode and the flow tube. The electric field needed to produce the electrospun fibers can be established by electrically charging or grounding the flow tube.

In an alternative embodiment, active agents can be entrapped by electrospinning hyperbranched polymers in the absence of added solvent. This procedure can be performed at elevated pressures as described above or at ambient pressure.

Advantages

Overall, the advantages of the present procedure may be summarized as follows:

1) Fibers can be produced at low temperatures thereby permitting the use of thermally sensitive active agents. The hyperbranched polymers provide a matrix that is dense enough to trap active agents and release them at a controlled rate.

2) Due to their lower melt and solution viscosity, hyperbranched polymers are much more soluble than unbranched polymers and, as a result, little or no organic solvent is needed during electrospinning. This means that the fibers formed will be nontoxic to organisms and cells.

3) The small dimensions of the fibers produced allows for active agents to be rapidly released at low fiber density or released slowly at high fiber density. Thus, a release profile can be tailored to a particular need.

4) When the polymer + active agent + gas solution is electrospun into a receiver vessel with pure gas at a lower pressure, the gas in the polymer liquid jet rapidly escapes, resulting in fibers that are highly porous and well suited to skin care, drug delivery or cell growth.

All references cited herein are fully incorporated by reference. Having now fully described the invention, it will be understood by those of skill in the art that the invention may be practiced within a wide and equivalent range of

conditions, parameters and the like, without affecting the spirit or scope of the invention or any embodiment thereof.

The following examples illustrate the invention without being meant to limit the scope of the invention.

Examples

Example 1

A hyperbranched polymer solution was prepared by placing 83.9 g water in a 100 ml flask, adding 10 g creatine monohydrate, 0.1 g sodium dodecylsulfate, 10 g hyperbranched polyester Boltorn® H20 (molecular weight 2100 g/mol) supplied by Perstorp and 6.0 g polyethylene oxide 900.000 while stirring with a magnetic stirrer and stirring the resulting solution for 14 h at 37°C. The obtained solution was electrospun with an apparatus similar to the apparatus of Fig. 1 of US 2008/0018015, using a syringe canula with an inner diameter of 0.8 mm cut off at a right angle as the flow tube and a silicon wafer mounted at a distance of 12 cm as the counter electrode. The hyperbranched polymer solution was exposed to CO_2 at a pressure of 50 bar and a temperature of 25°C in the mixing vessel. The collection vessel contained CO_2 at a pressure of 40 bar and a temperature of 20°C. During electrospinning, the flow tube was held at a potential of 20 kV, the counter electrode was held at a potential of 5 kV and the hyperbranched polymer solution was charged from the flow tube at a flow rate of 2 ml/h. The nanofibers collected at the counter electrode were analyzed for fiber diameter by electron microscopy, for concentration of creatine, for solvent content by measuring the partial solvent pressure at

25°C as described in Journal of Chemical Engineering Data, 20 (1975) 316-319 and for release of creatine by exposing the nanofibers to an aqueous phosphate buffer solution of pH 5.0 at 37°C as described in examples 2 and 4 of WO 2007/048464. The properties of the obtained nanofibers are summarized in table 1.

Example 2

Example 1 was repeated with the difference that the collection vessel contained nitrogen at a pressure of 10 bar and a temperature of 20°C.

Example 3

Example 1 was repeated with the difference that the hyperbranched polymer solution was prepared without the addition of water by adding the creatine monohydrate, the sodium dodecylsulfate and the polyethylene oxide 900.000 to molten hyperbranched polyester Boltorn® H20 at a temperature of 80°C. The resulting dispersion was exposed to CO_2 at a pressure of 200 bar and a temperature of 25°C in the mixing vessel and the collection vessel contained CO_2 at a pressure of 10 bar and a temperature of 20°C.

Example 4

Example 1 was repeated with the difference that the hyperbranched polymer solution was not exposed to pressurized

CO_2 before feeding it to the flow tube and the collection vessel contained air at ambient pressure and temperature.

Table 1: Properties of the obtained nanofibers

Example	1	2	3	4
Fiber diameter in nm	860	710	7000	920
Creatine concentration in the fiber in wt%	45	47	48	42
Solvent content of fiber in wt%	0.08 water no CO_2	0.07 water no CO_2	none	0.09 water
Release of creatine after 5 min in %	12	13	15	4
Release of creatine after 1 h in %	85	93	94	75

What is Claimed is:

1. A nanofiber matrix comprising an active agent suspended or enmeshed in fibers formed by the electrospinning of one or more hyperbranched polymers and wherein said nanofiber matrix comprises less that 0.1 wt % organic solvent and wherein said hyperbranched polymers have a molecular weight of 1,000 to 100,000 g/mol and a melting temperature of 30°C or higher.

2. The nanofiber matrix of claim 1, wherein said fibers have an average width of 50 nm to 10 µm.

3. The nanofiber matrix of claim 1, wherein said active agent is a cosmetic compound selected from the group consisting of: a colorant; emollient; sunscreen; exfoliant; antioxidant; humectant; and nutrient.

4. The nanofiber matrix of claim 1, wherein said active agent is selected from the group consisting of: aloe vera; zinc oxide; titanium oxide; an alpha, beta or poly hydroxy acid; a vitamin; retinol; retinal; retinoic acid; coenzyme Q; glycerine; diprobase; propylene glycol; glyceryl triacetate; sorbitol; xylitol; malitol; polydextrose; tocopherol and derivatives of tocopherol; ascorbic acid and derivatives of ascorbic acid; deoxyribonucleic acids; retinol and derivatives of retinol; alpha fatty acids; niacinamide; ubichinon; bisabolol; alantoin; phytantriol; panthenol; alpha hydroxy acid; amino acids; hyaluronic acid; polyglutamic acid; beta-glucan; creatine and derivatives of creatine; guanidine and derivatives of guanidine; ceramide; sphingolipid; phytosphingosine and derivatives of phytosphingosine; sphingosine and derivatives of

sphingosine; sphinganine and derivatives of sphinganine; pseudoceramide; essential oils; peptides; proteins; protein hydrolysates; plant extracts; and vitamin complexes.

5. The nanofiber matrix of claim 1, wherein said active agent is a pharmaceutical used for the treatment of wounds or a skin condition selected from the group consisting of: acne; psoriasis; eczema; contact dermatitis; and rosacea.

6. The nanofiber matrix of claim 5, wherein said active agent is selected from the group consisting of: benzoyl peroxide; triclorosan; chlorhexidine gluconate; erythromycin; clindamycin; tetracycline; a topical retinoid; coal tar; dithranol; a corticosteroid; calcipotriol and argan oil.

7. The nanofiber matrix of claim 5, wherein said active agent is selected from the group consisting of: epidermal growth factor; plasminogen activator inhibitor-1; plasminogen activator inhibitor-2; and alpha-1 antitrypsin.

8. The nanofiber matrix of claim 1, wherein said nanofiber matrix releases active agent over time when implanted in a patient's body.

9. The nanofiber matrix of claim 8, wherein said active agent is a drug selected from the group consisting of: COX-2 inhibitors, anticancer agents, NSAIDS, anti-obesity drugs, nutraceuticals, corticosteroids, elastase inhibitors, analgesics, anti-fungals, anti-emetics, analgesics, cardiovascular agents, anti-inflammatory

agents, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytics, sedatives, astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiac inotropic agents, cough suppressants, diuretics, antiparkinsonian agents, haemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, sex hormones, anti-allergic agents, stimulants and anoretics, sympathomimetics, thyroid agents, vasodilators, xanthines, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, and respiratory illness therapies.

10. A process for preparing a nanofiber matrix suitable for pharmaceutical or cosmetic use, comprising:

    a) preparing a polymeric composition comprising an active agent and a hyperbranched polymer, wherein said polymeric composition does not contain an added organic solvent;

    b) electrospinning the polymeric composition prepared in step a) into nanofibers.

11. A process for preparing a nanofiber matrix, comprising:

a) preparing a polymeric solution by mixing a solvent, an active agent and a hyperbranched polymer;

b) electrospinning the polymeric solution prepared in step a) into nanofibers, wherein said polymeric solution is exposed to a first pressurized gas and said nanofibers are collected in a collection vessel comprising a second pressurized gas.

12. The process of claim 10 or 11, wherein said process is carried out at a temperature of 200°C or less and preferably at a temperature of 10 to 180°C.

13. The process of claim 10 or 11, wherein said active agent is a cosmetic compound selected from the group consisting of: a colorant; emollient; sunscreen; exfoliant; antioxidant; humectant; and nutrient.

14. The process of claim 10 or 11, wherein said active agent is selected from the group consisting of: aloe vera; zinc oxide; titanium oxide; an alpha, beta or poly hydroxy acid; a vitamin; retinol; retinal; retinoic acid; coenzyme Q; glycerine; diprobase; propylene glycol; glyceryl triacetate; sorbitol; xylitol; malitol; polydextrose; tocopherol and derivatives of tocopherol; ascorbic acid and derivatives of ascorbic acid; deoxyribonucleic acids; retinol and derivatives of retinol; alpha fatty acids; niacinamide; ubichinon; bisabolol; alantoin; phytantriol; panthenol; alpha hydroxy acid; amino acids; hyaluronic acid; polyglutamic acid; beta-glucan; creatine and derivatives of creatine; guanidine and derivatives of guanidine; ceramide; sphingolipid; phytosphingosine and derivatives of phytosphingosine; sphingosine and derivatives of

sphingosine; sphinganine and derivatives of sphinganine; pseudoceramide; essential oils; peptides; proteins; protein hydrolysates; plant extracts; and vitamin complexes.

15. The process of claim 10 or 11, wherein said active agent is a pharmaceutical used for the treatment of wounds or a skin condition selected from the group consisting of: acne; psoriasis; eczema; contact dermatitis; and rosacea.

16. The process of claim 15, wherein said active agent is selected from the group consisting of: benzoyl peroxide; triclorosan; chlorhexidine gluconate; erythromycin; clindamycin; tetracycline; a topical retinoid; coal tar; dithranol; a corticosteroid; calcipotriol and argan oil.

17. The process of claim 15, wherein said active agent is selected from the group consisting of: epidermal growth factor; plasminogen activator inhibitor-1; plasminogen activator inhibitor-2; and alpha-1 antitrypsin.

18. The process of claim 10 or 11, wherein said nanofiber matrix releases active agent over time when implanted in a patient's body.

19. The process of claim 18, wherein said active agent is a drug selected from the group consisting of: COX-2 inhibitors, anticancer agents, NSAIDS, anti-obesity drugs, nutraceuticals, corticosteroids, elastase inhibitors, analgesics, anti-fungals, anti-emetics, analgesics, cardiovascular agents, anti-inflammatory agents, anti-arrhythmic agents, antibiotics,

anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytics, sedatives, astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiac inotropic agents, cough suppressants, diuretics, antiparkinsonian agents, haemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, sex hormones, anti-allergic agents, stimulants and anoretics, sympathomimetics, thyroid agents, vasodilators, xanthines, asthma therapies, emphysema therapies, respiratory distress syndrome therapies, chronic bronchitis therapies, chronic obstructive pulmonary disease therapies, organ-transplant rejection therapies, therapies for tuberculosis and other infections of the lung, and respiratory illness therapies.

20. The process of claim 10, wherein said polymeric composition does not contain an added solvent.

21. The process of claim 10, wherein said polymeric composition subjected to electrospinning has a viscosity of from 400 to 170 000 mPas.

22. The process of claim 11, wherein said solvent is a pressurized gas or a supercritical fluid.

23. The process of claim 11, wherein said solvent is selected from the group consisting of: water; methanol; ethanol; isopropanol; tetrahydrofuran; dimethyl

formamide; dimethyl acetamide; toluene; acetone; aqueous HCl; hexane; acetic acid; ethanediol; dichloromethane; dichloroethane; and ionic liquids

24. The process of claim 11, wherein said first pressurized gas and said second pressurized gas are each independently selected from the group consisting of: carbon dioxide; nitrous oxide; an alkane; an alkene; ammonia; propane and water vapor.

25. The process of claim 11, wherein said first pressurized gas and said second pressurized gas are propane.

26. The process of claim 11, wherein the gas pressure on the polymeric solution and the pressure in the collection vessel is in the range of 10-20,000 psig and preferably in the range of 50-10,000 psig.

27. The process of claim 11, wherein said polymeric solution subjected to electrospinning has a viscosity of from 100 to 20 000 mPas.

28. The nanofiber matrix produced by the process of any one of claims 10-27.

29. A topical lotion cream, emulsion, or gel comprising the nanofiber matrix of claim 28.

30. A pad, sponge or cloth used for skin cleansing or application of make-up to skin comprising nanofiber matrix of claim 28.

31. A nanofiber cell matrix comprising eukaryotic cells attached to fibers formed by the electrospinning of one

or more hyperbranched polymers, wherein said nanofiber matrix comprises less that 0.1 wt % organic solvent.

32. The nanofiber cell matrix of claim 31, wherein said fibers have an average width of 50 nm to 10 µm.

33. The nanofiber cell matrix of claim 31, wherein said eukaryotic cells are selected from the group consisting of: progenitor cells, embryonic stem cells; embryonic germ cells; mesenchymal stem cells; bone marrow stromal cells; cardiomyocytes; endothelial cells; and neuronal cells.

34. The nanofiber cell matrix of claim 33, further comprising one or more compounds promoting cell growth or survival selected from the group consisting of insulin-like growth factors I or II; transforming growth factors; fibroblast derived growth factor; platelet derived growth factor; epidermal growth factor; and vascular endothelial growth factors.