HU000032364T2

(19) **HU**

(11) Lajstromszám: **E 032 364**

(13) **T2**

MAGYARORSZÁG
Szellemi Tulajdon Nemzeti Hivatala

EURÓPAI SZABADALOM
SZÖVEGÉNEK FORDÍTÁSA

(21) Magyar ügyszám: **E 10 195654**
(22) A bejelentés napja: **2007. 01. 30.**

(51) Int. Cl.: ***A61L 29/08*** *(2006.01)*
A61L 29/14 *(2006.01)*

(96) Az európai bejelentés bejelentési száma:
EP 20070195654
(97) Az európai bejelentés közzétételi adatai:
EP 2289573 A2 **2011. 03. 02.**
(97) Az európai szabadalom megadásának meghirdetési adatai:
EP 2289573 B1 **2016. 10. 26.**

(30) Elsőbbségi adatok:
764151 P **2006. 02. 01.** **US**

(72) Feltaláló(k):
Gilman, Thomas H., Spring Grove, IL 60081 (US)

(73) Jogosult(ak):
Hollister Incorporated, Libertyville, IL 60048-3781 (US)

(74) Képviselő:
Danubia Szabadalmi és Jogi Iroda Kft., Budapest

(54) **Eljárások hidrofil bevonat szubsztrátumra történő felvitelére és hidrofil bevonattal ellátott szubsztrátok**

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 2 289 573 B1

(12) **EUROPEAN PATENT SPECIFICATION**

(45) Date of publication and mention of the grant of the patent:
26.10.2016 Bulletin 2016/43

(51) Int Cl.:
A61L 29/08 *(2006.01)* ***A61L 29/14*** *(2006.01)*

(21) Application number: **10195654.8**

(22) Date of filing: **30.01.2007**

(54) **Methods of applying a hydrophilic coating to a substrate, and substrates having a hydrophilic coating**

Verfahren zur Anbringung einer hydrophilen Beschichtung auf einem Substrat und Substrat mit der hydrophilen Beschichtung

Procédés d'application d'un revêtement hydrophile sur un substrat, et substrats disposant d'un revêtement hydrophile

(84) Designated Contracting States:
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT LI LT LU LV MC NL PL PT RO SE SI SK TR

(30) Priority: **01.02.2006 US 764151 P**

(43) Date of publication of application:
02.03.2011 Bulletin 2011/09

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
07762800.6 / 1 979 016

(73) Proprietor: **Hollister Incorporated**
Libertyville, IL 60048-3781 (US)

(72) Inventor: **Gilman, Thomas H.**
Spring Grove, IL 60081 (US)

(74) Representative: **Høiberg A/S**
Adelgade 12
1304 Copenhagen K (DK)

(56) References cited:
WO-A-98/58990
US-A- 4 589 873
US-A- 4 840 851
US-A- 4 876 126
US-A- 5 331 027
US-A- 5 670 558
US-A- 6 048 620

EP 2 289 573 B1

Description

FIELD OF THE INVENTION

[0001] This invention relates to methods of applying to a substrate a hydrophilic coating that becomes lubricious when activated with water or water vapor, and to substrates having such a hydrophilic coating.

BACKGROUND

[0002] In the medical field, and in other fields as well, there has developed a need for substrates with surfaces that become lubricious upon contact with water. A main use of lubricious materials involves catheters, catheter guide wires, and other medical devices that are meant to be inserted into the body. The lubricious nature of such materials allows the insertion (and subsequent removal) of a catheter or other medical device to be accomplished with minimum resistance, thereby reducing discomfort and possible injury.

[0003] In many cases, it is easy to prepare a functional lubricious coating for a substrate surface. However, it is more difficult to prepare a lubricious coating that is securely anchored to the substrate surface. Secure anchoring of a lubricious coating to a substrate surface is generally desirable, and particularly useful in the medical field, where secure anchorage of the coating is often an important requirement.

[0004] U.S. Patent 4,642,267 to Creasy et al. discloses a hydrophilic polymer blend comprising a thermoplastic polyurethane and a poly(N-vinyl lactam). When used as a coating material, the polymer blend components are co-dissolved in an organic solvent capable of solubilizing both polymers, a substrate is dip coated in the solution, and the solvent is then driven off by a drying process so as to form a hydrophilic coating on the substrate surface. However, the coating attachment to the substrate is considered to lack the security desired. Another disadvantage of the '267 patent is that high boiling point and potentially toxic solvents are used to deliver the coating formulation, and thus significant costs must be incurred to drive off the solvent residuals from the coated product so as to obtain the desired biocompatibility.

[0005] U.S. Patent 5,702,754 to Zhong discloses coating a substrate surface with a polymer having reactive functional groups and an excess of cross-linking agent. The polymer is cured to form a coating. Then, a second coating comprising a hydrophilic polymer having the same type of reactive functional groups is applied thereover. When the hydrophilic polymer is then cured, the second coating becomes covalently bonded to the first coating because the first coating includes an excess of cross-linking agent thereby permitting covalent bonding between the first coating and the hydrophilic polymer. Disadvantages of this approach include the fact that multiple steps are required and multiple polymer solutions are involved. There are also significant limitations in the selection of lubricious polymers and cross-linking agents.

[0006] US5670558 discloses a process for producing a medical instrument (e.g. catheter) with surface lubricity comprising coating the matrix surface of the medical instrument with a solution containing a water-soluble or water-swellable polymer having a reactive functional group in the molecule (e.g. a block or graft copolymer comprising vinyl pyrrolidone, (meth)acrylic acid) and insolubilizing (crosslinking) said water-soluble or water-swellable polymer to form a layer on the surface of the medical instrument that will form a hydrogel when wetted. After coating the water-soluble or water-swellable polymer of the matrix and increasing the temperature, the water-soluble or water-swellable polymers will react either with themselves or with the matrix surface. In order to form a tenacious hydrogel layer on the matrix surface, it is important that an intermolecular reaction be carried out with the matrix being thoroughly impregnated with the water-soluble or water-swellable polymer, so as to achieve an interpenetrating network.

SUMMARY OF THE INVENTION

[0007] In one aspect, the invention provides a method of applying a lubricious hydrophilic coating to a surface of a medical device having a surface comprised at least in part of a water-swellable material, and contacting the surface of the medical device with a solution comprising at least one of(i) a water-soluble polymer capable of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a water-soluble monomer capable of being polymerized to form a cross-linked, lubricious, hydrophilic coating. The water-soluble polymer can be cross-linked in the presence of the swollen medical device surface to provide a cross-linked coating that is entangled with and securely anchored to the medical device surface. Similarly, the monomer can either form a crosslinked hydrogel network as it is polymerized, or can be polymerized and then subsequently cross-linked, in the presence of the swollen medical device surface, to provide a cross-linked coating that is entangled with and securely anchored to the surface of the medical device. The medical device includes a first or outer layer comprising a water-swellable material. The medical device may further include an optional second or support layer, which comprises non-water-swellable materials and/or water-swellable materials.

[0008] In another aspect, the invention provides a medical device having a hydrophilic coating, such medical device, prior to coating, having a surface comprised at least in part of a water-swellable material having swollen and non-swollen states, and the coating comprises an interpenetrating polymer network disposed on at least a part of the surface, the interpenetrating polymer network formed by at least one of (i) a water-soluble polymer capable of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a water-soluble monomer capable of being polymerized to form a cross-linked

lubricious, hydrophilic coating, in the presence of the swollen state of the surface of the medical device, so as to secure the hydrophilic coating to the surface.

DETAILED DESCRIPTION

[0009] One aspect of the invention relates to methods of applying a lubricious, hydrophilic coating to a substrate, which is a medical device. An additional aspect of the invention relates to medical devices having such a lubricious, hydrophilic coating.

[0010] As used herein, the term "lubricious coating" refers to a coating that provides a substrate surface having a coefficient of friction value less than about 0.3, less than about 0.1, and/or less than about 0.05, for example, 0.03, or even 0.01.

[0011] The invention involves creating an interpenetrating polymer network *in situ* on a substrate surface. For example, a substrate surface comprising a water-swellable material is contacted with a solution comprising a water-soluble hydrophilic polymer capable of being cross-linked to form a cross-linked, lubricious hydrophilic coating. Alternatively, a water-soluble monomer, either capable of being polymerized to form a cross-linked, lubricious, hydrophilic coating, or of being polymerized and then cross-linked to form a cross-linked, lubricious, hydrophilic coating, may be used in place of, or in addition to, the water-soluble hydrophilic polymer. The coating is typically then cured, for example, by exposure to UV light, in order to cross-link the water-soluble polymer and/or polymer formed from the water-soluble monomer.

[0012] The use of one or more water-soluble polymers is typically preferred relative to the use of one or more water-soluble monomers, however, particularly for medical applications, because residual unpolymerized monomer can present biocompatibility issues for medical device applications.

[0013] Because the water-swellable material of the substrate swells in the presence of water and/or alcohol, it is believed to become physically entangled with the water-soluble hydrophilic polymer before cross-linking, and those entanglements are locked in during cross-linking. Thus, a coating comprising the interpenetrating polymer network is formed by polymerizing the water-soluble polymer in the presence of the water-swellable substrate surface when the water-swellable substrate surface is in a swollen state, and results in the lubricious coating being securely anchored to the substrate (after cross-linking thereof). Essentially, the method allows two hydrogels to be linked together mechanically on a molecular scale.

[0014] Advantageously, the hydrophilic coating can be secured to the surface without the need for covalent interactions between the hydrophilic coating and the first layer. Another advantage is that the coating formulation can be carried using solvents such as water and lower alcohols, which are inexpensive, biocompatible, and relatively easy to drive off from the coated product. Still another advantage is the versatility of the invention; the invention will provide secure anchorage for any hydrophilic coating formed from a water-soluble polymer and/or water-soluble monomer, which can be coated from an aqueous or alcohol based solution, without the need for a primer layer or other polymer solution based anchorage means. This versatility allows a wide number of polymer / cross-linking agent systems and/or monomer / initiator / cross-linking systems to be utilized, and thus for an optimal system to be implemented for any given application.

[0015] In one embodiment, the terms "well-anchored" or "securely anchored" refers to a coating that, after an abrasion protocol is conducted on the substrate carrying the coating, results in a substrate having a final coefficient of friction value, when the coating is activated, for example, by water immersion, that is not more than ten times, not more than five times, and/or not more than two times the original coefficient of friction value prior to abrasion. A suitable abrasion protocol includes passing a coated tube through a hole which is about 10% smaller diameter than the outside diameter of the tubing 100 times, while keeping the coating wet during the abrasion cycles. After this abrasion protocol, the tube is immersed in deionized water for about 30 seconds so as to activate the coating, and the coefficient of friction can be determined using standard means.

[0016] A substrate, such as a catheter tube, to be coated by the methods of this invention, is formed in a way that provides it with a surface or surface layer comprised at least in part of a water-swellable material. That may be accomplished in a variety of ways including but not limited to coextruding a substrate having a first or outer layer comprising any suitable water-swellable material, and a second or inner support layer comprised of non-water-swellable materials and/or water-swellable materials.

[0017] Generally, any water swellable-materials or mixtures thereof could be used for the first or outer layer. Suitable water-swellable materials include but are not limited to water-swellable polyamide-based copolymers, water-swellable polyester-based copolymers, water-swellable urethane-based copolymers, and mixtures thereof. Any of a variety of thermoplastic polymers, thermoplastic elastomers, and/or thermoplastic alloys, which are capable of swelling in the presence of water (e.g., an aqueous solution) may be used. In general, such water swellable polymers will also swell in lower alcohols such as methanol, ethanol, propanol, isopropanol, butanol, and the like. Higher alcohols such as hexanol and octanol may also be used, but lower alcohols are typically preferred because of their increased volatility relative to water.

[0018] Preferably, the first layer is comprised of a water-swellable thermoplastic elastomer comprising a block copolymer having rigid and flexible blocks. Suitable rigid blocks include polyamide blocks, polyester blocks, and polyurethane blocks, but other rigid polymer blocks may

be used. The rigid block is preferably either glassy or crystalline at room temperature. Suitable flexible blocks include flexible polyether blocks such as flexible polyethylene oxide blocks, flexible poly-N-vinyl lactam blocks such as flexible polyvinylpyrrolidone blocks, flexible polyalcohol blocks, and flexible polyacid blocks. Of course, other flexible blocks could also be used.

[0019] Suitable water-swellable thermoplastic elastomers include but are not limited to polyether/polyamide block elastomers such as those sold under the PEBAX® trade name (Arkema, PA), for example, such as PEBAX® 1647, PEBAX® 1074, and PUBAX® MX1652, and polyester elastomers such as those sold under the HYTREL® trade name (Du Pont de Nemours, DE), for example, such as HYTREL® 8171 and HYTREL® 8206. Other suitable water-swellable thermoplastic elastomers include but are not limited to thermoplastic polyurethanes such as polyether thermoplastic polyurethanes sold under the ESTANE® and the TECOPHILIC® trade names (Noveon Inc., OH) and polyester thermoplastic polyurethanes such as those sold under the ESTANE® and CARBOTHANE® trade names (Noveon Inc., OH).

[0020] The substrate can be made entirely from a water-swellable material. Polymer blends including at least one water-swellable material can alternatively be used. Surprisingly, even polymer blends where a water-swellable material comprises only a minority of the polymer blend will provide securely anchored hydrophilic coatings. This allows flexibility in designing substrates, for example, as a homoextrusion that will have the mechanical properties needed for a given application. For example, tubing made of 40 weight percent (wt,%) PEBAX® 1074 (a water-swellable thermoplastic elastomer) and 60 wt.% PEBAX® 3533 (a non-water-swellable thermoplastic elastomer) has desirable properties for a urinary catheter application, and provides many or all of the advantages of this invention.

[0021] Alternatively, the substrate can have an outer layer made from a water-swellable material, or an outer layer made from a blend comprised of water-swellable and non-water-swellable materials. The substrate can then have an inner or support layer comprised of one or more non-water-swellable materials. Of course, the inner or support layer may be made from or further include one or more water-swellable materials.

[0022] As used herein, the term "water-swellable" generally refers to a material that swells in the presence of water or alcohol. In various embodiments, the term refers to a material that increases in at least one dimension by at least 0.5%, at least 1%, at least 2%, at least 5%, at least 10%, at least 25%, or even greater when immersed in water for a period of approximately 90 minutes. In accordance with the foregoing embodiments, a 25.4 mm (1 inch) by 25.4 mm (1 inch) by 0.0254 mm (1 mil) square of material can be immersed in water for a period of 90 minutes, and the increase in the height or length can be determined relative to the original height or length so as to ascertain whether a certain material swells sufficiently to be considered a water-swellable material in accordance with the invention. If so, the material can generally be considered suitable for use as a water-swellable material in the invention.

[0023] Generally, any material can be used in forming the optional second or support layer, but materials capable of being extruded or otherwise melt-processed are generally preferred. Suitable materials for use in the optional second or support layer include but are not limited to thermoplastic resins, such as, for example, olefin polymers, particularly, polyethylenes, polypropylenes, polyvinylchlorides, polytetrafluoroethylenes, polyvinylacetates, polystyrenes, polyesters, polyurethanes, polyamides, other suitable polymers, and mixtures thereof. Metals, ceramics, and other materials may also be used as the support layer, but then the outer layer needs to be affixed or coupled to the second layer by a mechanism different than co-extrusion, for example, by spin-casting, dip-coating, wire extrusion coating, or otherwise affixing, coupling, or adhering the water-swellable surface layer (or substrate comprising same) to the second layer.

[0024] The substrate can be a medical device. Exemplary medical devices that may be coated with the lubricious coatings in accordance with the invention include but are not limited to contact lenses, medical implants including but not limited to pacemakers and wire leads for same, intravascular implants including but not limited to arterial stents, and catheters including but not limited to urinary catheters, fecal catheters, catheters for administration of intravenous fluids, medications, and nutrition, and coronary catheters such as angioplasty catheters. Further still, in certain medical device applications it may be desirable to incorporate a drug into the coating solution, or to add a drug after formation of the coating on the medical device. For example, stents having a coating in accordance with the invention can comprise a drug, for example, taxol to prevent late stenosis, or heparin to prevent the formation of a thrombus.

[0025] Additionally, non-medical device applications of the invention can also be envisioned where surfaces having a low coefficient of friction in a wet environment are desired because the invention can provide a highly lubricious coating to any product that is used in a wet environment. Possible non-limiting examples include marine uses, for example, such as wet suits or boat hulls where the coating could be applied to reduce drag.

[0026] The untreated substrate is typically dipped or otherwise coated with a polymer solution in which the coating polymer is dissolved in water, alcohol, or a solution containing both water and alcohol. If a catheter is being coated, a mandrel can be inserted into the catheter structure in order to prevent any coating solution from contacting and/or coating the inside of the catheter when the coating solution is applied.

[0027] Any suitable hydrophilic polymer capable of being cross-linked and of swelling and becoming lubricious when exposed to water or water vapor may be used to provide the hydrophilic coating. Upon being cross-linked,

the network of the coating polymer forms an interpolymer with the swollen water-swellable material, for example, with the flexible (or soft) blocks of the substrate surface block polymer, resulting in a coating that is securely anchored to the substrate. Suitable water-soluble hydrophilic polymers include but are not limited to polyacrylic acids, acrylic acid copolymers such as acrylamide/acrylic acid copolymers, polyvinylpyrollidones, polyvinylalcohols, water-soluble polymers containing carboxylic acid functional groups, and mixtures thereof. Other water-soluble polymers that can be cross-linked to form a hydrophilic coating may also be used.

[0028] Similarly, any suitable hydrophilic monomer capable of being polymerized to form a cross-linked network and becoming lubricious when exposed to water or water vapor may be used to provide the hydrophilic coating. Suitable water-soluble hydrophilic monomers that can be used include but are not limited to vinyl monomers, for example, vinyl alcohols, vinylpyrollidones, acrylamides, methacrylates, acrylic acids, and mixtures thereof. Some of these can be copolymerized with multifunctional monomer to form a network *in situ,* others can be polymerized and subsequently cross-linked using methods well known in the art. Various initiators, for example, photoinitiators including but not limited to benzophenone can be used to polymerize the monomers.

[0029] An important advantage of this method is that it is relatively easy to prepare a substrate with a securely anchored hydrophilic coating. Since the outer layer of the substrate generally includes a thermoplastic polymer, known manufacturing methods that are uncomplicated, direct, and economical, such as extrusion, co-extrusion, or injection molding, may be used to produce a substrate having a water swellable surface. The coating method is applicable to any system of hydrophilic coating polymer and cross-linking method that can be achieved using a water- or alcohol-based solvent system. Similarly, the coating method is applicable to any system of hydrophilic monomer, initiator, and cross-linking method that can be achieved using a water- or alcohol-based solvent system.

[0030] Suitable cross-linking agents are well known in the art and include but are not limited to UV activatable cross-linking agents, carbodiimides, aziridines, melamine formaldehydes, and multifunctional carboxylic acid cross-linking agents. Exemplary UV activatable cross-linking agents include polymeric hydroxyl ketones sold under the ESACURE™ trade name (Sartomer Company, PA), for example, ESACURE™ KIP 150 and ESACURE™ ONE. Exemplary carbodiimide cross-linking agents are sold under the CARBODILTTE™ trade name (Nisshinbo Industries, Inc., JP), for example, CARBODILITE™ V-02-L2 and CARBODILITE™ E-02. Exemplary aziridine cross-linking agents are sold under the cross-linker CX-100 trade name (DSM NeoResins, DSM, NL). Heat and/or light can also be used to cross-link some water-soluble polymers.

[0031] The methods of applying a hydrophilic coating to a substrate and substrates having such a hydrophilic coating in accordance with the invention can be better understood in light of the following examples. However, the foregoing description and the following examples are merely illustrative, and therefore no unnecessary limitations should be understood therefrom as numerous modifications and variations are expected to occur to those skilled in the art.

EXAMPLE 1

[0032] A coating polymer solution was prepared in an approximately 70:30 weight/weight isopropyl alcohol/water solvent system, where the polymer was polyvinylpyrrolidone K-90 at about 9 wt./vol. Included in the solution was about 0.03 wt.% UV activatable cross-linking agent (ESACURE™ KIP 150, Sartomer).

[0033] A thermoplastic substrate was employed in the form of a coextruded tube having an outside diameter of about 4.57 mm (0.180 inches) and an inside diameter of about 3.12 mm (0.123 inches). The tube had an outer layer of about 0.076 mm (0.003 inches) thick that was a blend of a polyether/polyamide block elastomer (PEBAX® 1074, a water-swellable thermoplastic elastomer available from Arkema, PA) with an ethylene acid copolymer resin (NUCREL® 2806, a non-water-swellable thermoplastic elastomer available from Du Pont de Nemours, DE) at a weight ratio of about 40:60. The inner layer of the tube was a blend of thermoplastic, non-water-swellable resins designed to give the desired mechanical properties to the overall tube structure. The tube was dipped in the coating solution and held therein for about 10 minutes prior to withdrawal. After withdrawal, the tube was air dried for about 30 minutes. Thereafter, the coated tube was exposed to UV light for about 5 minutes.

[0034] The tube with its cured coating was immersed in deionized water for 30 seconds. At that point, the surface of the tube was found to be highly lubricious, and the lubricious coating was securely adhered to the tube.

EXAMPLE 2

[0035] Another approach is to use a separate, second solution that contains a cross-linking agent for the coating polymer. The second solution can be applied to the substrate having a water-swellable outer surface either before, or after, the coating polymer solution is applied. After both solutions have been applied, the coating is then cross-linked.

[0036] A coextruded tube was prepared having an outer layer of a polyether/polyamide block elastomer (PEBAX® 1074, Arkema, PA), and an inner layer of a polyether/polyamide block elastomer (PEBAX® 2533, a non-water-swellable thermoplastic elastomer available from Arkema, PA). The tube was first dipped in an approximately 70:30 weight/weight isopropyl alcohol/water solution containing about 12wt.% of a carbodiimide cross-linking agent (CARBODILITE® V-02-L2, Nisshinbo, Japan), and held therein for ten minutes prior to with-

drawal. The tube was then air dried for ten minutes, subsequently dipped in an approximately 70:30 weight/weight isopropyl alcohol/water solution containing about 7.5 wt.% of a water-soluble polymer containing carboxylic acid functional groups (GANTREZ™ S-97BF, ISP Technologies, Inc.), and then withdrawn immediately. After withdrawal, the tube was air dried for ten minutes.

[0037] The water-soluble polymer of this example is a methyl vinyl ether copolymer with maleic anhydride where the anhydride has been hydrolyzed into a diacid. The acid groups can be cross-linked by the carbodiimide cross-linking agent.

[0038] Curing was accomplished by heating the tubing to approximately 70° C for about 20 minutes in a conventional oven. The coating was neutralized by dipping it in a buffer solution. The resulting tube with its cured coating was then dipped in deionized water for 30 seconds. The surface of the wetted tube was slippery and the coating was securely adhered to the tube.

EXAMPLE 3

[0039] A thermoplastic substrate was employed in the form of a coextruded tube having an outside diameter of about 4.60 mm (0.181 inches) and an inside diameter of about 3.10 mm (0.122 inches) The tube had an outer layer of about 0.076 mm (0.003 inches) thick, with the inner layer accounting for the balance of the tube. The inner tube layer comprised a blend of an ethylene octene copolymer (EXACT™ 5371, ExxonMobil Chemical Company, ExxonMobil, TX) with an ethylene acid copolymer resin (NUCREL® 2806, Du Pont de Nemours, DE) at a weight ratio of approximately 20:80, and the outer tube layer comprised a blend of a polyether/polyamide block elastomer (PEBAX® 1074, Arkema, PA) with an ethylene acid copolymer resin (NUCREL® 2806, Du Pont de Nemours, DE) at a weight ratio of approximately 40:60.

[0040] The tubing was coated by dipping in an approximately 70:30 weight/weight isopropyl alcohol/water solution containing about 5.5 wt.% polyvinylpyrollidone K-90 (ICI Chemicals, England) and about 0.11 wt.% ESACURE™ One (Sartomer, PA). The tubing was held in the coating solution for about 5 minutes in this solution and then withdrawn. After withdrawal, the coated tubing was air dried for about 50 minutes (at room temperature). Thereafter, the coated tube was exposed to UVC light for approximately 2.5 minutes.

[0041] The resulting tube with its cured coating was then immersed in deionized water for about 30 seconds. At that point, the surface of the tube was found to be highly lubricious, having an average coefficient of friction (n = 12 samples tested) of about 0.02.

[0042] To test coating anchorage to the substrate tubing, an abrasion testing protocol was performed on the resulting coated tubing. The sample was passed through a hole in a 0.79 mm (1/32") thick silicone rubber sheet, with the hole being about 10% smaller diameter than the outside diameter of the tubing. This was done 100 times, keeping the coating wet during the abrasion testing. After this abrasion protocol, the tube was again immersed in deionized water for about 30 seconds and tested for coefficient of friction. Again, the average coefficient of friction for the samples was about 0.02.

[0043] Another group of samples was immersed for about 30 seconds in water to activate the coating, and then allowed to stand out in open air for about 10 minutes. Following this drying protocol, the average coefficient of friction (n = 12 samples tested) was about 0.02.

[0044] Still another group of samples (n = three samples) were subjected to a thermoforming process to create a bullet shaped closed tip on one end in order to make a tipped tube suitable for use as a urinary catheter. This tipped tubing was subjected to a coating process as described in this example above, except the cure was by accomplished by exposure to UVC light for a period of about 3 minutes. After immersion in deionized water for about 20 minutes, the surface of the coated tubing was very slippery and the slippery coating was well adhered to both the formed tip portion of the tubing and the straight wall portion of the tubing.

[0045] The foregoing examples demonstrate several advantages of the invention. For example, highly lubricious, highly adherent coatings have been achieved with two different water soluble polymer/cross-linker systems, and with three different substrate constructions. Example 3 further demonstrates that it is possible to thermoform a multi-layered tube while maintaining the water-swellable properties of the outer layer surface, which allows a securely anchored coating to be achieved, even in the formed portion of the substrate. Example 3 also demonstrates that coatings made per this invention are able to maintain their slippery nature even after an extended period of air exposure. It is theorized that the water-swellable nature of the substrate surface helps in this regard, as the substrate surface will hold water and thus perhaps contribute to the ability of the coating to maintain hydration and therefore lubricity. This attribute of the invention is particularly advantageous for intermittent urinary catheters.

Claims

1. A method of applying a lubricious hydrophilic coating to a surface of a medical device, comprising:

   providing a medical device for coating, having a surface prior to coating comprising at least in part a water-swellable material;

   contacting the surface of the medical device with a solution to swell the water swellable material, said solution comprising at least one of (i) a water-soluble polymer capable of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a water-soluble monomer capable of being polymerized to form a

cross-linked, lubricious, hydrophilic coating; and,
forming the cross-linked, lubricious, hydrophilic coating,

said coating being entangled with and securely anchored to the surface of the medical device.

2. The method of claim 1, wherein the solution comprises at least one solvent selected from the group consisting of water, alcohols, and mixtures thereof.

3. The method of claim 1, wherein the medical device comprises a first layer, and a second layer, wherein the first layer comprises the water-swellable material.

4. The method of claim 3, wherein the second layer comprises a non-water-swellable material.

5. The method of claim 1, wherein the medical device is selected from the group consisting of medical implants, intravascular implants, catheters, and contact lenses.

6. The method of claim 1, wherein the water-swellable material comprises a block copolymer.

7. The method of claim 6, wherein the block copolymer is selected from the group consisting of water-swellable polyamide-based copolymers, water-swellable polyester-based copolymers, water-swellable urethane-based copolymers, and mixtures thereof.

8. The method of claim 1, wherein the water-soluble polymer is selected from the group consisting of polyacrylic acids, acrylic acid copolymers, poly-N-vinyl lactams, polyvinylalcohols, polyvinylalcohol copolymers, and mixtures thereof.

9. The method of claim 8, wherein the poly-N-vinyl lactam comprises polyvinylpyrollidone.

10. The method of claim 1, wherein the water-soluble monomer is selected from the group consisting of vinyl alcohols, vinylpyrollidones, acrylamides, methacrylates, acrylic acids, and mixtures thereof.

11. The method of claim 1, wherein the solution further comprises a cross-linking agent.

12. The method of claim 1, wherein the hydrophilic coating is secured to the surface without covalent interactions between the hydrophilic coating and the surface.

13. The method of claim 11, wherein the cross-linking agent is selected from the group consisting of UV activatable cross-linking agents, carbodiimides, aziridines, melamine formaldehydes, and multifunctional carboxylic acid cross-linking agents.

14. The method of claim 1, further comprising contacting the medical device with a solution comprising a cross-linking agent.

15. A medical device having a hydrophilic coating made according to the method of claim 1, comprising:

a medical device having a surface comprising at least in part a water-swellable material having swollen and non-swollen states; and
an interpenetrating polymer network disposed on the surface, the interpenetrating polymer network formed by contacting the surface of the medical device with a solution to swell the water swellable material, said solution comprising at least one of (i) a water-soluble polymer capable of being cross-linked to form a cross-linked, lubricious, hydrophilic coating and (ii) a water-soluble monomer capable of being polymerized to form a cross-linked, lubricious, hydrophilic coating, in the presence of the swollen state of the water-swellable material, so as to secure the hydrophilic coating to the surface.

16. The medical device of claim 15, wherein the medical device comprises a first layer, and a second layer, wherein the first layer comprises the water-swellable material.

17. The medical device of claim 16, wherein the second layer comprises a non-water-swellable material.

18. The medical device of claim 15, wherein the medical device is selected from the group consisting of medical implants, intravascular implants, catheters, and contact lenses.

19. The medical device of claim 15, wherein the water-swellable material comprises a block copolymer selected from the group consisting of water-swellable polyamide-based copolymers, water-swellable polyester-based copolymers, water-swellable urethane-based copolymers, and mixtures thereof.

20. The medical device of claim 15, wherein the water-soluble polymer is selected from the group consisting of polyacrylic acids, acrylic acid copolymers, poly-N-vinyl lactams, polyvinylalcohols, polyvinylalcohol copolymers, and mixtures thereof.

Patentansprüche

1. Verfahren zum Aufbringen einer gleitfähigen hydro-

philen Beschichtung auf eine Oberfläche einer medizinischen Vorrichtung, umfassend:

Bereitstellen einer medizinischen Vorrichtung zum Beschichten, die vor dem Beschichten eine Oberfläche aufweist, die wenigstens zum Teil ein wasserquellfähiges Material umfasst;
Inkontaktbringen der Oberfläche der medizinischen Vorrichtung mit einer Lösung zum Quellen des wasserquellfähigen Materials, wobei die Lösung wenigstens eines von (i) einem wasserlöslichen Polymer, das im Stande ist, vernetzt zu werden unter Bildung einer vernetzten, gleitfähigen hydrophilen Beschichtung, und (ii) einem wasserlöslichen Monomer, das im Stande ist, polymerisiert zu werden unter Bildung einer vernetzten, gleitfähigen, hydrophilen Beschichtung, umfasst; und
Bilden der vernetzten, gleitfähigen, hydrophilen Beschichtung,

wobei die Beschichtung mit der Oberfläche der medizinischen Vorrichtung verhakt und an ihr sicher verankert ist.

2. Verfahren nach Anspruch 1, wobei die Lösung wenigstens ein Lösungsmittel, ausgewählt aus der Gruppe bestehend aus Wasser, Alkoholen und Mischungen davon, umfasst.

3. Verfahren nach Anspruch 1, wobei die medizinische Vorrichtung eine erste Schicht und eine zweite Schicht umfasst, wobei die erste Schicht das wasserquellfähige Material umfasst.

4. Verfahren nach Anspruch 3, wobei die zweite Schicht ein nicht wasserquellfähiges Material umfasst.

5. Verfahren nach Anspruch 1, wobei die medizinische Vorrichtung ausgewählt ist aus der Gruppe bestehend aus medizinischen Implantaten, intravaskulären Implantaten, Kathetern und Kontaktlinsen.

6. Verfahren nach Anspruch 1, wobei das wasserquellfähige Material ein Blockcopolymer umfasst.

7. Verfahren nach Anspruch 6, wobei das Blockcopolymer ausgewählt ist aus der Gruppe bestehend aus wasserquellfähigen Copolymeren auf Polyamidbasis, wasserquellfähigen Copolymeren auf Polyesterbasis, wasserquellfähigen Copolymeren auf Urethanbasis und Mischungen davon.

8. Verfahren nach Anspruch 1, wobei das wasserlösliche Polymer ausgewählt ist aus der Gruppe bestehend aus Polyacrylsäuren, Acrylsäure-Copolymeren, Poly-N-vinyllactamen, Polyvinylalkoholen, Polyvinylalkohol-Copolymeren und Mischungen davon.

9. Verfahren nach Anspruch 8, wobei das Poly-N-vinyllactam Polyvinylpyrrolidon umfasst.

10. Verfahren nach Anspruch 1, wobei das wasserlösliche Monomer ausgewählt ist aus der Gruppe bestehend aus Vinylalkoholen, Vinylpyrrolidonen, Acrylamiden, Methacrylaten, Acrylsäuren und Mischungen davon.

11. Verfahren nach Anspruch 1, wobei die Lösung außerdem ein Vernetzungsmittel umfasst.

12. Verfahren nach Anspruch 1, wobei die hydrophile Beschichtung ohne kovalente Wechselwirkungen zwischen der hydrophilen Beschichtung und der Oberfläche an der Oberfläche befestigt ist.

13. Verfahren nach Anspruch 11, wobei das Vernetzungsmittel ausgewählt ist aus der Gruppe bestehend aus UV-aktivierbaren Vernetzungsmitteln, Carbodiimide, Aziridinen, Melamin-Formaldehyden und multifunktionellen Carbonsäure-Vernetzungsmitteln.

14. Verfahren nach Anspruch 1, außerdem umfassend das Inkontaktbringen der medizinischen Vorrichtung mit einer Lösung, die ein Vernetzungsmittel umfasst.

15. Medizinische Vorrichtung mit einer hydrophilen Beschichtung, die gemäß dem Verfahren nach Anspruch 1 hergestellt ist, umfassend:

eine medizinische Vorrichtung mit einer Oberfläche, die wenigstens zum Teil ein wasserquellfähiges Material mit gequollenen und nicht-gequollenen Zuständen umfasst; und
ein interpenetrierendes Polymernetzwerk, das auf der Oberfläche angeordnet ist, wobei das interpenetrierende Polymernetzwerk gebildet wird durch Inkontaktbringen der Oberfläche der medizinischen Vorrichtung mit einer Lösung zum Quellen des wasserquellfähigen Materials, wobei die Lösung wenigstens eines von (i) einem wasserlöslichen Polymer, das im Stande ist, vernetzt zu werden unter Bildung einer vernetzten, gleitfähigen, hydrophilen Beschichtung, und (ii) einem wasserlöslichen Monomer, das im Stande ist, polymerisiert zu werden unter Bildung einer vernetzten, gleitfähigen, hydrophilen Beschichtung, umfasst, in Gegenwart des gequollenen Zustands des wasserquellfähigen Materials, um die hydrophile Beschichtung an der Oberfläche zu befestigen.

16. Medizinische Vorrichtung nach Anspruch 15, wobei

die medizinische Vorrichtung eine erste Schicht und eine zweite Schicht umfasst, wobei die erste Schicht das wasserquellfähige Material umfasst.

17. Medizinische Vorrichtung nach Anspruch 16, wobei die zweite Schicht ein nicht wasserquellfähiges Material umfasst.

18. Medizinische Vorrichtung nach Anspruch 15, wobei die medizinische Vorrichtung ausgewählt ist aus der Gruppe bestehend aus medizinischen Implantaten, intravaskulären Implantaten, Kathetern und Kontaktlinsen.

19. Medizinische Vorrichtung nach Anspruch 15, wobei das wasserquellfähige Material ein Blockcopolymer, ausgewählt aus der Gruppe bestehend aus wasserquellfähigen Copolymeren auf Polyamidbasis, wasserquellfähigen Copolymeren auf Polyesterbasis, wasserquellfähigen Copolymeren auf Urethanbasis und Mischungen davon, umfasst.

20. Medizinische Vorrichtung nach Anspruch 15, wobei das wasserlösliche Polymer ausgewählt ist aus der Gruppe bestehend aus Polyacrylsäuren, Acrylsäure-Copolymeren, Poly-N-vinyllactamen, Polyvinylalkoholen, Polyvinylalkohol-Copolymeren und Mischungen davon.

Revendications

1. Procédé d'application d'un revêtement hydrophile lubrifiant sur une surface d'un dispositif médical, comprenant :

la fourniture d'un dispositif médical à revêtir, ayant une surface avant le revêtement comprenant au moins en partie un matériau dilatable à l'eau ;
la mise en contact de la surface du dispositif médical avec une solution pour dilater le matériau dilatable à l'eau, ladite solution comprenant au moins un parmi (i) un polymère soluble dans l'eau capable d'être réticulé pour former un revêtement hydrophile lubrifiant, réticulé, et (ii) un monomère soluble dans l'eau capable d'être polymérisé pour former un revêtement hydrophile lubrifiant, réticulé ; et,
la formation du revêtement hydrophile lubrifiant, réticulé,

ledit revêtement étant entremêlé avec la surface du dispositif médical et ancré solidement à celle-ci.

2. Procédé selon la revendication 1, dans lequel la solution comprend au moins un solvant choisi dans le groupe constitué de l'eau, des alcools, et des mélanges de ceux-ci.

3. Procédé selon la revendication 1, dans lequel le dispositif médical comprend une première couche, et une seconde couche, dans lequel la première couche comprend le matériau dilatable à l'eau.

4. Procédé selon la revendication 3, dans lequel la seconde couche comprend un matériau non dilatable à l'eau.

5. Procédé selon la revendication 1, dans lequel le dispositif médical est choisi dans le groupe constitué des implants médicaux, des implants intravasculaires, des cathéters et des lentilles de contact.

6. Procédé selon la revendication 1, dans lequel le matériau dilatable à l'eau comprend un copolymère séquencé.

7. Procédé selon la revendication 6, dans lequel le copolymère séquencé est choisi dans le groupe constitué des copolymères à base de polyamide dilatables à l'eau, des copolymères à base de polyester dilatables à l'eau, des copolymères à base d'uréthane dilatables à l'eau, et des mélanges de ceux-ci.

8. Procédé selon la revendication 1, dans lequel le polymère soluble dans l'eau est choisi dans le groupe constitué des poly(acides acryliques), des copolymères d'acide acrylique, des poly-N-vinyl-lactames, des poly(alcools vinyliques), des copolymères de poly(alcool vinylique), et des mélanges de ceux-ci.

9. Procédé selon la revendication 8, dans lequel le poly-N-vinyl-lactame comprend la polyvinylpyrollidone.

10. Procédé selon la revendication 1, dans lequel le monomère soluble dans l'eau est choisi dans le groupe constitué des alcools vinyliques, des vinylpyrollidone, des acrylamides, des méthacrylates, des acides acryliques, et des mélanges de ceux-ci.

11. Procédé selon la revendication 1, dans lequel la solution comprend en outre un agent de réticulation.

12. Procédé selon la revendication 1, dans lequel le revêtement hydrophile est fixé sur la surface sans interactions covalentes entre le revêtement hydrophile et la surface.

13. Procédé selon la revendication 11, dans lequel l'agent de réticulation est choisi dans le groupe constitué des agents de réticulation activables par des UV, des carbodiimides, des aziridines, des mélamine formaldéhydes, et des agents de réticulation multifonctionnels à base d'acides carboxyliques.

14. Procédé selon la revendication 1, comprenant en outre la mise en contact du dispositif médical avec une solution comprenant un agent de réticulation.

15. Dispositif médical portant un revêtement hydrophile fabriqué selon le procédé de la revendication 1, comprenant :

un dispositif médical ayant une surface comprenant au moins en partie un matériau dilatable à l'eau ayant des états dilatés et non dilatés ; et
un réseau de polymère interpénétrant placé sur la surface, le réseau de polymère interpénétrant formé par mise en contact de la surface du dispositif médical avec une solution pour dilater le matériau dilatable à l'eau, ladite solution comprenant au moins un parmi (i) un polymère soluble dans l'eau pouvant être réticulé pour former un revêtement hydrophile lubrifiant, réticulé, et (ii) un monomère soluble dans l'eau pouvant être polymérisé pour former un revêtement hydrophile lubrifiant, réticulé, en présence de l'état dilaté du matériau dilatable à l'eau, de façon à fixer le revêtement hydrophile sur la surface.

16. Dispositif médical selon la revendication 15, dans lequel le dispositif médical comprend une première couche, et une seconde couche, dans lequel la première couche comprend le matériau dilatable à l'eau.

17. Dispositif médical selon la revendication 16, dans lequel la seconde couche comprend un matériau non dilatable à l'eau.

18. Dispositif médical selon la revendication 15, dans lequel le dispositif médical est choisi dans le groupe constitué des implants médicaux, des implants intravasculaires, des cathéters et des lentilles de contact.

19. Dispositif médical selon la revendication 15, dans lequel le matériau dilatable à l'eau comprend un copolymère séquencé choisi dans le groupe constitué des copolymères à base de polyamide dilatables à l'eau, des copolymères à base de polyester dilatables à l'eau, des copolymères à base d'uréthane dilatables à l'eau, et des mélanges de ceux-ci.

20. Dispositif médical selon la revendication 15, dans lequel le polymère soluble dans l'eau est choisi dans le groupe constitué des poly(acides acryliques), des copolymères d'acide acrylique, des poly-N-vinyl-lactames, des poly(alcools vinyliques), des copolymères de poly(alcool vinylique), et des mélanges de ceux-ci.

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 4642267 A, Creasy **[0004]**
- US 5702754 A, Zhong **[0005]**
- US 5670558 A **[0006]**

Szabadalmi igénypontok

1. Eljárás síkos hidrofil bevonatnak orvosi eszköz felszínére történő felvitelére, amely tartalmazza a következőket:

előállítunk egy bevonásra alkalmas orvosi eszközt, amelynek felszíne a bevonás előtt legalább részben vízben duzzasztható anyagot tartalmaz;

az orvosi eszköz felszínét egy oldattal érintkeztetjük, így a vízben duzzasztható anyag megduzzad, ahol az említett oldat a következők közül legalább egyet tartalmaz: (i) egy vízoldható polimer, amely térhálósodásra képes térhálósított síkos hidrofil bevonatot képezve, és (ii) egy vízoldható monomer, amely polimerizálni képes térhálósított síkos hidrofil bevonatot képezve; és

előállítjuk a térhálósított síkos hidrofil bevonatot,

az említett a bevonat az orvosi eszköz felszínébe behatol és a felszínen biztonságosan rögzül.

2. Az 1. igénypont szerinti eljárás, ahol az oldat legalább egy oldószert tartalmaz víz, alkoholok és ezek keverékei csoportjából kiválasztva.

3. Az 1. igénypont szerinti eljárás, ahol az orvosi eszköz tartalmaz egy első réteget és egy második réteget, ahol az első réteg tartalmazza a vízben duzzasztható anyagot.

4. A 3. igénypont szerinti eljárás, ahol a második réteg tartalmaz egy vízben nem duzzasztható anyagot.

5. Az 1. igénypont szerinti eljárás, ahol az orvosi eszköz orvosi implantámok, intravaszkuláris implantátumok, katéterek és kontaktlencsék csoportjából van kiválasztva.

6. Az 1. igénypont szerinti eljárás, ahol a vízben duzzasztható anyag tartalmaz egy blokk kopolimert.

7. A 6. igénypont szerinti eljárás, ahol a blokk kopolimer vízben duzzasztható poliamid-alapú kopolimerek vízben duzzasztható poliészter alapú kopolimerek, vízben duzzasztható uretán alapú kopolimerek és ezek keverékei csoportjából van kiválasztva.

8. Az 1. igénypont szerinti eljárás, ahol a vízoldható polimer poliakrilsavak, akrilsav-kopolimerek, poli-N-vinil-laktámok, polivinilalkoholok, polivinilalkohol-kopolimerek és ezek keverékei csoportjából van kiválasztva.

9. A 8. igénypont szerinti eljárás, ahol a polivinil-N-laktám polivinilpirrolidont tartarlmaz.

10. Az 1. igénypont szerinti eljárás, ahol a vízoldható monomer vinil-alkoholok, vinilpirrolidonok, akrilamidok, metakrilátok, akrilsavak és ezek keverékei csoportjából van kiválasztva.

11. Az 1. igénypont szerinti eljárás, ahol az oldat tartalmaz továbbá egy térhálósító szert.

12. Az 1. igénypont szerinti eljárás, ahol a hidrofil bevonat a felszínhez a hidrofil bevonat és a felszín között kovalens kölcsönhatások nélkül van rögzítve.

13. A 11. igénypont szerinti eljárás, ahol a térhálósítószer UV fénnyel aktiválható térhálósítószerek, karbodiimidek, aziridinek, melamin-formaldehidek és több funkciós csoportot tartalmazó karbonsav típusú térhálósítószerek csoportjából van kiválasztva.

14. Az 1. igénypont szerinti eljárás, amely tartalmazza továbbá az orvosi eszköznek egy térhálósítószert tartalmazó oldattal történő érintkeztetését.

15. Orvosi eszköz, amely egy, az 1. igénypont szerinti eljárás szerint kialakított hidrofil bevonattal van ellátva, amely tartalmaz

egy orvosi eszközt, amely legalább részben duzzadt és nem duzzadt állapotú, vízben duzzasztható anyagot tartalmazó felszíne van; és

egy a felszínen elhelyezett behatoló polimerhálózatot, a behatoló polimerhálózat az orvosi eszköz felszíne és egy oldat érintkeztetésével van kialakítva, amely oldat duzzasztja a vízben duzzasztható anyagot, az említett oldat tartalmazza a következők legalább egyikét: (i) egy vízoldható polimer, amely térhálósodásra képes térhálósított síkos hidrofil bevonatot képezve, és (ii) egy vízoldható monomer, amely polimerizálni képes térhálósított síkos hidrofil bevonatot képezve, a vízben duzzasztható anyag duzzadt állapotának jelenlétében, ezáltal a hidrofil bevonatot a felszínhez rögzíti.

16. A 15. igénypont szerinti orvosi eszköz, amely orvosi eszköz tartalmaz egy első réteget és egy második réteget, amely első réteg tartalmazza a vízben duzzasztható anyagot.

17. A 16. igénypont szerinti orvosi eszköz, ahol a második réteg tartalmaz egy vízben nem duzzasztható anyagot.

18. A 15. igénypont szerinti orvosi eszköz, amely orvosi eszköz orvosi implantámok, intravaszkuláris implantátumok, katéterek és kontaktlencsék csoportjából van kiválasztva.

19. A 15. igénypont szerinti orvosi eszköz, ahol a vízben duzzasztható anyag tartalmaz egy blokk kopolimert, amely vízben duzzasztható poliamid-alapú kopolimerek, vízben duzzasztható poliészter alapú kopolimerek, vízben duzzasztható uretán alapú kopolimerek és ezek keverékei csoportjából van kiválasztva.

20. A 15. igénypont szerinti orvosi eszköz, ahol a vízoldható polimer poliakrilsavak, akrilsav-kopolimerek, poli-N-vinil-laktámok, polivinilalkoholok, polivinilalkohol-kopolimerek és ezek keverékei csoportjából van kiválasztva.