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(54) **Title:** HYDROPHILIC COATING

(57) **Abstract:** The invention relates to a coating formulation for preparing a hydrophilic coating, wherein the hydrophilic coating formulation comprises a supporting monomer and/or polymer comprising at least 2 reactive moieties capable of undergoing polymerization reactions, a polyelectrolyte, a Norrish Type I photoinitiator, and a Norrish Type II photoinitiator.

HYDROPHILIC COATING

This invention relates to a hydrophilic coating formulation for preparing a hydrophilic coating. The invention further relates to a coating system, a hydrophilic coating, a lubricious coating, use of a Norrish Type I and a Norrish Type II photoinitiator in a lubricious coating, an article, a medical device or component and a method of forming a hydrophilic coating on a substrate.

Many medical devices, such as guide wires, urinary and cardiovascular catheters, syringes, and membranes need to have a lubricant applied to the outer and/or inner surface to facilitate insertion into and removal from the body and/or to facilitate drainage of fluids from the body. Lubricious properties are also required so as to minimize soft tissue damage upon insertion or removal. Especially, for lubrication purposes, such medical devices may have a hydrophilic surface coating or layer which becomes lubricious and attains low-friction properties upon wetting, i.e. applying a wetting fluid for a certain time period prior to insertion of the device into the body of a patient. A coating or layer which becomes lubricious after wetting is hereinafter referred to as a hydrophilic coating. A coating obtained after wetting is hereinafter referred to as a lubricious coating.

It has now been observed that such lubricious coatings are often prone to wear and as such may lose coating material in the tortuous path (e.g. in a blood vessel). Moreover, they may lose their lubricious properties upon use.

Therefore it is an object of the present invention to provide a lubricious coating that exhibits an improved wear resistance in addition to a high lubricity.

Surprisingly it has now been found that a lubricious coating with an improved wear resistance can be obtained by using a coating formulation for preparing a hydrophilic coating, wherein the hydrophilic coating formulation comprises

(a) a supporting polymer comprising a backbone and at least 2 reactive moieties capable of undergoing polymerization reactions,
(b) a polyelectrolyte;
(c) a Norrish Type I photoinitiator; and
(d) a Norrish Type II photoinitiator.

It has been found that the hydrophilic coatings obtainable by curing the hydrophilic coating formulation according to the invention are extremely wear resistant in tortuous tests compared to similar coatings known in the art. For example,

subjecting the coatings according to the invention to a particulates release test, as described in the examples, results in a surprisingly low number of particles released from the coating. This is particularly advantageous for cardiovascular applications such as guide wires and catheters, in which the hydrophilic coating experiences serious torture and no particle release is tolerated.

Within the context of the invention “lubricious” is defined as having a slippery surface. A coating on the outer or inner surface of a medical device, such as a catheter, is considered lubricious if (when wetted) it can be inserted into the intended body part without leading to injuries and/or causing unacceptable levels of discomfort to the subject. In particular, a coating is considered lubricious if it has a friction as measured on a Harland FTS5000 Friction Tester (HFT) of 20 g or less, preferably of 15 g or less, at a clamp-force of 300 g, a pull speed of 1 cm/s, and a temperature of 22°C. The term “wetted” is generally known in the art and – in a broad sense – means “containing water”. In particular the term is used herein to describe a coating that contains sufficient water to be lubricious. In terms of the water concentration, usually a wetted coating contains at least 10 wt% of water, based on the dry weight of the coating, preferably at least 50 wt%, based on the dry weight of the coating, more preferably at least 100 wt% based on the dry weight of the coating. For instance, in a particular embodiment of the invention a water uptake of about 300-500 wt% water is feasible. Examples of wetting fluids are treated or untreated water, water-containing mixtures with for example organic solvents or aqueous solutions comprising for example salts, proteins or polysaccharides. In particular a wetting fluid can be a body fluid.

The Norrish Type I and Norrish Type II photoinitiators are used to cure the hydrophilic coating formulation according to the invention, for example using visible light or UV, electro-beam, or gamma radiation to form the hydrophilic coating. Herein both Norrish Type I and Norrish Type II photoinitiators are free-radical photoinitiators, but are distinguished by the process by which the initiating radicals are formed. Compounds that undergo unimolecular bond cleavage of the chromophore upon irradiation to generate radicals that initiate polymerization are termed Norrish Type I or homolytic photoinitiators. A Norrish Type II photoinitiator generates radicals indirectly by hydrogen abstraction from a suitable synergist, which may be a low molecular weight compound or a polymer.

Compounds that undergo unimolecular bond cleavage upon irradiation are termed Norrish Type I or homolytic photoinitiators, as shown by formula

(1):

		hν		
PI		→ PI*	→	$R^{1\bullet} + {}^{\bullet}R^{2}$ (1)
photoinitiator		excited PI		free radicals

Depending on the nature of the functional group and its location in the molecule relative to the carbonyl group, the fragmentation can take place at a bond adjacent to the carbonyl group (α-cleavage), at a bond in the β-position (β-cleavage) or, in the case of particularly weak bonds (like C-S bonds or O-O bonds), elsewhere at a remote position. The most important fragmentation in photoinitiator molecules is the α-cleavage of the carbon-carbon bond between the carbonyl group and the alkyl residue in alkyl aryl ketones, which is known as the Norrish Type I reaction.

If the photoinitiator, while being in the excited state, interacts with a second molecule (a coinitiator COI) to generate radicals in a bimolecular reaction as shown by formula (2), the photoinitiator is termed a NorrishType II photoinitiator. In general, the two main reaction pathways for Norrish Type II photoinitiators are hydrogen abstraction by the excited initiator or photoinduced electron transfer, followed by fragmentation. Bimolecular hydrogen abstraction is a typical reaction of excited diaryl ketones. Photoinduced electron transfer is a more general process, which is not limited to a certain class of compounds.

		hν		
PI		→ PI* + COI	→	$R^{1\bullet} + {}^{\bullet}R^{2}$ (2)
photoinitiator		exited PI		free radicals

Examples of suitable Norrish Type I or free-radical photoinitiators are benzoin derivatives, methylolbenzoin and 4-benzoyl-1,3-dioxolane derivatives, benzilketals, α,α-dialkoxyacetophenones, α-hydroxy alkylphenones, α-aminoalkylphenones, acylphosphine oxides, bisacylphosphine oxides, acylphosphine sulphides, halogenated acetophenone derivatives, and the like. Commercial examples of suitable Type I photoinitiators are Irgacure 2959 (2-hydroxy-4'-(2-hydroxyethoxy)-2-methyl propiophenone), Irgacure 651 (benzildimethyl ketal or 2,2-dimethoxy-1,2-diphenylethanone, Ciba-Geigy), Irgacure 184 (1-hydroxy-cyclohexyl-phenyl ketone as

the active component, Ciba-Geigy), Darocur 1173 (2-hydroxy-2-methyl-1-phenylpropan-1-one as the active component, Ciba-Geigy), Irgacure 907 (2-methyl-1-[4-(methylthio)phenyl]-2-morpholino propan-1-one, Ciba-Geigy), Irgacure 369 (2-benzyl-2-dimethylamino-1-(4-morpholinophenyl)-butan-1-one as the active component, Ciba-Geigy), Esacure KIP 150 (poly {2-hydroxy-2-methyl-1-[4-(1-methylvinyl)phenyl]propan-1-one}, Fratelli Lamberti), Esacure KIP 100 F (blend of poly {2-hydroxy-2-methyl-1-[4-(1-methylvinyl)phenyl]propan-1-one} and 2-hydroxy-2-methyl-1-phenyl-propan-1-one, Fratelli Lamberti), Esacure KTO 46 (blend of poly {2-hydroxy-2-methyl-1-[4-(1-methylvinyl)phenyl]propan-1-one}, 2,4,6-trimethylbenzoyldiphenyl-phosphine oxide and methylbenzophenone derivatives, Fratelli Lamberti), acylphosphine oxides such as Lucirin TPO (2,4,6-trimethylbenzoyl diphenyl phosphine oxide, BASF), Irgacure 819 (bis (2,4,6-trimethylbenzoyl)-phenyl-phosphine-oxide, Ciba-Geigy), Irgacure 1700 (25:75% blend of bis (2,6-dimethoxybenzoyl)2,4,4-trimethyl-pentyl phosphine oxide and 2-hydroxy-2-methyl-1-phenyl-propan-1-one, Ciba-Geigy), and the like. Also mixtures of type I photoinitiators can be used.

Examples of Norrish Type II photoinitiators that can be used in the hydrophilic coating formulation according to the invention include aromatic ketones such as benzophenone, xanthone, derivatives of benzophenone (e.g. chlorobenzophenone), blends of benzophenone and benzophenone derivatives (e.g. Photocure 81, a 50/50 blend of 4-methyl-benzophenone and benzophenone), Michler's Ketone, Ethyl Michler's Ketone, thioxanthone and other xanthone derivatives like Quantacure ITX (isopropyl thioxanthone), benzil, anthraquinones (e.g. 2-ethyl anthraquinone), coumarin, or chemical derivatives or combinations of these photoinitiators.

Preferred are Norrish Type I and Norrish Type II photoinitiators which are water-soluble or can be adjusted to become water-soluble, also preferred photoinitiators are polymeric or polymerisable photoinitiators.

Generally the total amount of photoinitiator in the hydrophilic coating formulation is between 0.2 and 10 wt%, preferably between 0.8 and 8 wt%, based on the total weight of dry the coating.

Hereinafter all percentages of components given in the application are based on the total weight of the dry coating. i.e. the hydrophilic coating formed upon curing the hydrophilic coating formulation.

Typically the weight ratio Norrish Type I photoinitiator: Norrish Type II photoiniatiator is between 10:1 and 1:10, preferably between 5:1 and 1:5.

The hydrophilic coating formulation also comprises a supporting polymer comprising a backbone and at least 2 reactive moieties capable of undergoing polymerization reactions. Herein the supporting polymer may also contain hydrophilic functional groups.

Within the context of the invention the term polymer is used for a molecule comprising two or more repeating units. In particular it may be composed of two or more monomers which may be the same or different. As used herein, the term includes oligomers and prepolymers. Usually polymers have a number average weight (M_n) of about 500 g/mol or more, in particular of about 1000 g/mol or more, although the M_n may be lower in case the polymer is composed of relatively small monomeric units. Herein and hereinafter the M_n is defined as the M_n as determined by light scattering, optionally in combination with Size Exclusion Chromatography (SEC).

A supporting network can be formed upon curing said supporting polymer. The reactive moiety of the supporting polymer may be selected from the group consisting of radically reactive groups, such as alkenes, amino, amido, sulfhydryl (SH), unsaturated esters, such as acrylate and methacrylate, unsaturated ethers, unsaturated amides, and alkyd/dry resins. The supporting polymer has a backbone and at least one of the above-mentioned reactive moieties. The backbone of the supporting polymer may be selected from the group consisting of polyethers, polyurethanes, polyethylenes, polypropylenes, polyvinyl chlorides, polyepoxides, polyamides, polyacrylamides, poly(meth)acrylics, polyoxazolidones, polyvinyl alcohols, polyethylene imines, polyesters like polyorthoesters and alkyd copolymers, polypeptides, or polysaccharides such as cellulose and starch or any combination of the above. In particular, polymers with unsaturated esters, amides or ethers, thiol or mercaptan groups may suitably be used in the invention.

Preferably the supporting polymer has a number average molecular weight in the range of about 750 to 20,000 g/mol, more preferably in the range of about 1,000 to about 15,000 g/mol, most preferably in the range of about 1,100 to about 10,000 g/mol, in particular in the range of about 1,200 to about 7,000 g/mol, more in particular in the range of about 1,400 to about 5,000 g/mol. The advantage of using a relatively high molecular weight supporting polymer, i.e. having molecular weight of more than about 750 g/mol, preferably more than about 1,000 g/mol, is that a relatively open supporting network will be formed. Such a relatively open supporting network will swell more easily and therewith provide the coating with a higher lubricity and/or an improved dry-out time.

The average number of reactive groups per molecule of the supporting polymer is preferably in the range of about 1.2 to about 64, more preferably in the range of about 1.2 to about 16, most preferably in the range of about 1.2 to about 8. This means that apart from supporting polymer molecules comprising at least 2 reactive moieties also supporting polymer molecules comprising 1 reactive moiety, i.e. monofunctional polymers, may be present. The monofunctional supporting polymers may also be part of the formed supporting network.

The supporting polymer may be used in more than 1 wt%, for example more than 10 %, more than 20 wt%, more than 30 wt% or more than 40 wt%, based on the total weight of the dry coating. The supporting polymer can be present in the hydrophilic coating formulation up to 90 wt%, however, more often the supporting polymer will be used up to 50 or 60 wt%, based on the total weight of the dry coating.

The hydrophilic coating formulation according to the invention also comprises a polylectrolyte. Herein a polyelectrolyte is understood to be a high molecular weight linear, branched or crosslinked polymer composed of macromolecules comprising constitutional units, in which between 5 and 100 % of the constitutional units contain ionized groups when the polyelectrolyte is in the lubricious coating. Herein a constitutional unit is understood to be for example a repeating unit, for example a monomer. A polyelectrolyte herein may refer to one type of polyelectrolyte composed of one type of macromolecules, but it may also refer to two or more different types of polyelectrolytes composed of different types of macromolecules.

The presence of a polyelectrolyte is particularly advantageous to improve the dry-out time of the hydrophilic coating. Herein dry-out time is defined as the duration of the hydrophilic coating remaining lubricious in the open air after the device comprising the hydrophilic coating has been taken out of the wetting fluid wherein it has been stored and/or wetted. Hydrophilic coatings with an improved dry-out time, i.e. wherein the duration of the hydrophilic coating remaining lubricious is longer, will have a lower tendency of losing water and drying out prior to insertion into the body, or in the body when it comes in contact with e.g. a mucous membrane or vein. This may result in complications when the device comprising the lubricious coating is inserted into the body or removed from the body. The dry-out time can be determined by measuring the friction in gram as a function of time the catheter had been exposed to air on the HFT.

Considerations when selecting a suitable polyelectrolyte are its solubility and viscosity in aqueous media, its molecular weight, its charge density, its

affinity with the supporting network of the coating and its biocompatibility. Herein biocompatibility means biological compatibility by not producing a toxic, injurous or immunological response in living mammalian tissue.

For a decreased migrateability, the polyelectrolyte is preferably a polymer having a weight average molecular weight of at least about 1000 g/mol, as determinable by light scattering, optionally in combination with size exclusion chromatography. A relatively high molecular weight polyelectrolyte is preferred for increasing the dry-out time and/or reduced migration out of the coating. The weight average molecular weight of the polyelectrolyte is preferably at least 20,000 g/mol, more preferably at least 100,000 g/mol, even more preferably at least about 150,000 g/mol, in particular about 200,000 g/mol or more. For ease of applying the coating it is preferred that the average weight is 1000,000 g/mol or less, in particular 500,000 g/mol or less, more in particular 300,000 g/mol or less.

Examples of ionized groups that may be present in the polyelectrolyte are ammonium groups, phosphonium groups, sulfonium groups, carboxylate groups, sulfate groups, sulfinic groups, sulfonic groups, phosphate groups, and phosphonic groups. Such groups are very effective in binding water. In one embodiment of the invention the polyelectrolyte also comprises metal ions. Metal ions, when dissolved in water, are complexed with water molecules to form aqua ions $[M(H_2O)_x]^{n+}$, wherein x is the coordination number and n the charge of the metal ion, and are therefore particularly effective in binding water. Metal ions that may be present in the polyelectrolyte are for example alkali metal ions, such as Na^+, Li^+, or K^+, or alkaline earth metal ions, such as Ca^{2+} and Mg^{2+}. In particular when the polyelectrolyte comprises quaternary amine salts, for example quaternary ammonium groups, anions may be present. Such anions can for example be halogenides, such as Cl^-, Br^-, I^- and F^-, and also sulphates, nitrates, carbonates and phosphates.

Suitable polyelectrolytes are for example salts of homo- and co-polymers of acrylic acid, salts of homo- and co-polymers of methacrylic acid, salts of homo- and co-polymers of maleic acid, salts of homo- and co-polymers of fumaric acid, salts of homo- and co-polymers of monomers comprising sulfonic acid groups, homo- and co-polymers of monomers comprising quarternary ammonium salts and mixtures and/or derivatives thereof. Examples of suitable polyelectrolytes are poly(acrylamide-co-acrylic acid) salts, for example poly(acrylamide-co-acrylic acid) sodium salt, poly(acrylamide-co-methacrylic acid) salts, for example poly(acrylamide-co-methacrylic acid) sodium salt, poly(methacrylamide-co-acrylic acid) salts, for example

poly(methacrylamide-co-acrylic acid) sodium salt, poly(methacrylamide-co-methacrylic acid) salts, for example poly(methacrylamide-co-methacrylic acid) sodium salt poly(acrylic acid) salts, for example poly(acrylic acid) sodium salt, poly(methacrylic acid) salts, for example poly(methacrylic acid) sodium salt, poly(acrylic acid-co-maleic acid) salts, for example poly(acrylic acid-co-maleic acid) sodium salt, poly(methacrylic acid-co-maleic acid) salts, for example poly(methacrylic acid-co-maleic acid) sodium salt, poly(acrylamide-co-maleic acid) salts, for example poly(acrylamide-co-maleic acid) sodium salt, poly(methacrylamide-co-maleic acid) salts, for example poly(methacrylamide-co-maleic acid) sodium salt, poly(acrylamido-2-methyl-1-propanesulfonic acid) salts, poly(4-styrene sulfonic acid) salts, poly(acrylamide-co-dialkyl ammonium chloride), quaternized poly[bis-(2-chloroethyl)ether-alt-1,3-bis[3-(dimethylamino)propyl]urea], polyallylammonium phosphate, poly(diallyldimethylammonium chloride), poly(sodium trimethyleneoxyethylene sulfonate), poly(dimethyldodecyl(2-acrylamidoethyl) ammonium bromide), poly(2-N methylpyridiniumethylene iodine), polyvinylsulfonic acids, and salts of poly(vinyl)pyridines, polyethyleneimines, and polylysines.

Particularly suitable polyelectrolytes for use in the current invention are copolymeric polyelectrolytes, which may be random or block copolymers, wherein said copolymeric polyelectrolyte is a copolymer comprising at least two different types of constitutional units, wherein at least one type of constitutional units comprises ionizable or ionized groups and at least one type of constitutional units is absent of ionizable or ionized groups. Herein “ionizable” is understood to be ionizable in neutral aqueous solutions, i.e. solutions having a pH between 6 and 8. An example of such a copolymeric polyelectrolyte is a poly(acrylamide-co-acrylic acid) salt.

The hydrophilic coating composition according to the invention typically comprises 1-90 wt%, 3-50 wt%, 5-30 wt%, or 10-20 wt% of polyelectrolyte based on the total weight of the dry coating.

In one embodiment of the invention the hydrophilic coating formulation may further comprise a non-ionic hydrophilic polymer. Herein a non-ionic hydrophilic polymer is understood to be a high molecular weight linear, branched or cross-linked polymer composed of macromolecules comprising constitutional units, in which less than 5 % of the constitutional units contain ionized groups when the hydrophilic polymer is in the lubricious coating.

The hydrophilic polymer is capable of providing hydrophilicity to a coating and may be synthetic or bio-derived and can be blends or copolymers of both.

The hydrophilic polymers include but are not limited to poly(lactams), for example polyvinylpyrollidone (PVP), polyurethanes, homo- and copolymers of acrylic and methacrylic acid, polyvinyl alcohol, polyvinylethers, maleic anhydride based copolymers, polyesters, vinylamines, polyethyleneimines, polyethyleneoxides, poly(carboxylic acids), polyamides, polyanhydrides, polyphosphazenes, cellulosics, for example methyl cellulose, carboxymethyl cellulose, hydroxymethyl cellulose, and hydroxypropylcellulose, heparin, dextran, polypeptides, for example collagens, fibrins, and elastin, polysacharrides, for example chitosan, hyaluronic acid, alginates, gelatin, and chitin, polyesters, for example polylactides, polyglycolides, and polycaprolactones, polypeptides, for example collagen, albumin, oligo peptides, polypeptides, short chain peptides, proteins, and oligonucleotides.

Generally the hydrophilic polymer has a molecular weight in the range of about 8,000 to about 5,000,000 g/mol, preferably in the range of about 20,000 to about 3,000,000 g/mol and more preferably in the range of about 200,000 to about 2,000,000 g/mol.

In one embodiment of the invention the hydrophilic polymer may be used in more than 1 wt%, for example more than 10 wt%, more than 20 wt%, or more than 30 weight %, based on the total weight of the dry coating. The hydrophilic polymer can be present up to 95 wt%, however, more often the hydrophilic polymer will be used up to 50, 60, 70 or 80 wt%, based on the total weight of the dry coating.

In the hydrophilic coating formulation the weight ratio of the total weight of polyelectrolyte and hydrophilic polymer to supporting polymer may for example vary between 10 : 90 and 90 : 10, such as between 25 : 75 and 75: 25 or such as between 60 : 40 and 40 : 60.

The invention relates to a hydrophilic coating formulation which when applied to a substrate and cured results in a hydrophilic coating. Herein a hydrophilic coating formulation refers to a liquid hydrophilic coating formulation, e.g. a solution or a dispersion comprising a liquid medium. Herein any liquid medium that allows application of the hydrophilic coating formulation on a surface would suffice. Examples of liquid media are alcohols, like methanol, ethanol, propanol, butanol or respective isomers and aqueous mixtures thereof, acetone, methylethyl ketone, tetrahydrofuran, dichloromethane, toluene, and aqueous mixtures or emulsions thereof or water. The hydrophilic coating formulation further comprises components which when cured are converted into the hydrophilic coating, and thus remain in the hydrophilic coating after curing. Herein curing is understood to refer to physical or chemical hardening or

solidifying by any method, for example heating, cooling, drying, crystallization or curing as a result of a chemical reaction, such as radiation-curing or heat-curing. In the cured state all or part of the components in the hydrophilic coating formulation may be cross-linked forming covalent linkages between all or part of the components, for example by using UV or electron beam radiation. However, in the cured state all or part of the components may also be ionically bonded, bonded by dipole-dipole type interactions, or bonded via Van der Waals forces or hydrogen bonds.

The term "to cure" includes any way of treating the formulation such that it forms a firm or solid coating. In particular, the term includes a treatment whereby the hydrophilic polymer further polymerizes, is provided with grafts such that it forms a graft polymer and/or is cross-linked, such that it forms a cross-linked polymer.

The invention also relates to a hydrophilic coating obtainable by applying the hydrophilic coating formulation according to the invention to a substrate and curing it. The invention further relates to a lubricious coating obtainable by applying a wetting fluid to said hydrophilic coating, and to the use of a Norrish Type I and a Norrish Type II photo-initiator in a lubricious coating in order to improve its wear resistance. Further the invention relates to an article, in particular a medical device or a medical device component comprising at least one hydrophilic coating according to the invention and to a method of forming on a substrate the hydrophilic coating according to the invention.

The hydrophilic coating comprises a polyelectrolyte, optionally a hydrophilic polymer, and a supporting network, which may be a hydrophilic supporting network, and which is formed from the supporting polymer. Said hydrophilic coating is formed by curing a hydrophilic coating formulation comprising the polyelectrolyte, optionally the hydrophilic polymer, the supporting polymer, the Norrish Type I photoinitiator and the Norrish Type II photoinitiator. Preferably the polyelectrolyte and/or the supporting network are covalently linked and/or physically bound to each other and/or entrapped to form a polymer network after curing. If a hydrophilic polymer is present this may also be covalently linked and/or physically bound to one or more of the other components and/or entrapped to form a polymer network after curing.

The fact that polyelectrolyte, optionally the hydrophilic polymer and/or the supporting polymer are covalently and/or physically bound in the hydrophilic coating as part of a polymer network has the advantage that the polyelectrolyte and the hydrophilic polymer (if present) will not leak out into the environment of the hydrophilic coating, for example when it is coated on a medical device. This is particularly useful

when the medical device is inside the human or animal body.

In one embodiment of the invention a polyelectrolyte is present in a wetting fluid and introduced into the hydrophilic coating when wetting the hydrophilic coating according to the invention. This is particularly useful for medical devices with a hydrophilic coating which are packed in a fluid, or wherein the hydrophilic coating is wetted in a separate wetting fluid that contains the polyelectrolyte. The invention therefore also relates to coating system for preparing a lubricious coating, said coating system comprising the coating formulation according to the invention and a wetting fluid comprising a polyelectrolyte.

In one embodiment of the invention the hydrophilic coating formulation according to the invention further comprises at least one surfactant, which can improve the surface properties of the coating. Surfactants constitute the most important group of detergent components. Generally, these are water-soluble surface-active agents comprised of a hydrophobic portion, usually a long alkyl chain, attached to hydrophilic or water solubility enhancing functional groups. Surfactants can be categorized according to the charge present in the hydrophilic portion of the molecule (after dissociation in aqueous solution): ionic surfactants, for example anionic or cationic surfactants, and non-ionic surfactants. Examples of ionic surfactants include Sodium dodecylsulfate (SDS), Sodium cholate, Bis(2-ethylhexyl)sulfosuccinate Sodium salt, Cetyltrimethylammoniumbromide (CTAB), Lauryldimethylamine-oxide (LDAO), N-Lauroylsarcosine Sodium salt and Sodium deoxycholate (DOC). Examples of non-ionic surfactants include Alkyl Polyglucosides such as TRITON™ BG-10 Surfactant and TRITON CG-110 Surfactant, Branched Secondary Alcohol Ethoxylates such as TERGITOL™ TMN Series, Ethylene Oxide / Propylene Oxide Copolymers, such as TERGITOL L Series, and TERGITOL XD, XH, and XJ Surfactants, Nonylphenol Ethoxylates such as TERGITOL NP Series, Octylphenol Ethoxylates, such as TRITON X Series, Secondary Alcohol Ethoxylates, such as TERGITOL 15-S Series and Specialty Alkoxylates, such as TRITON CA Surfactant, TRITON N-57 Surfactant, TRITON X-207 Surfactant, Tween 80 and Tween 20.

In the above embodiment typically 0.001 to 1 wt% of surfactant can be applied, preferably 0.05-0.5 wt%, based on the total weight of the dry coating.

In one embodiment of the invention the hydrophilic coating formulation according to the invention further comprises at least one plasticizing agent, which can enhance the flexibility of the coating, which may be preferable when the object to be coated is likely to bend during use. Said plasticizing agent may be included

in the hydrophilic coating formulation in a concentration of from about 0.01 wt% to about 15 wt% based on the total weight of the dry coating, preferably from about 1 wt% to about 5.0 wt%. Suitable plasticizers are high boiling compounds, preferably with a boiling point at atmospheric pressure of >200 °C, and with a tendency to remain homogeneously dissolved and/or dispersed in the coating after cure. Examples of suitable plasticizers are mono- and polyalcohols and polyethers, such as decanol, glycerol, ethylene glycol, diethylene glycol, polyethylene glycol and/or copolymers with propylene glycol and/or fatty acids.

The hydrophilic coating according to the invention can be coated on an article. The hydrophilic coating can be coated on a substrate which may be selected from a range of geometries and materials. The substrate may have a texture, such as porous, non-porous, smooth, rough, even or uneven. The substrate supports the hydrophilic coating on its surface. The hydrophilic coating can be on all areas of the substrate or on selected areas. The hydrophilic coating can be applied to a variety of physical forms, including films, sheets, rods, tubes, molded parts (regular or irregular shape), fibers, fabrics, and particulates. Suitable surfaces for use in the invention are surfaces that provide the desired properties such as porosity, hydrophobicity, hydrophilicity, colorisability, strength, flexibility, permeability, elongation abrasion resistance and tear resistance. Examples of suitable surfaces are for instance surfaces that consist of or comprise metals, plastics, ceramics, glass and/or composites. The hydrophilic coating may be applied directly to the said surfaces or may be applied to a pretreated or coated surface where the pretreatment or coating is designed to aid adhesion of the hydrophilic coating to the substrate.

In one embodiment of the invention the hydrophilic coating according to the invention is coated on a biomedical substrate. A biomedical substrate refers, in part, to the fields of medicine, and the study of living cells and systems. These fields include diagnostic, therapeutic, and experimental human medicine, veterinary medicine, and agriculture. Examples of medical fields include ophthalmology, orthopedics, and prosthetics, immunology, dermatology, pharmacology, and surgery; nonlimiting examples of research fields include cell biology, microbiology, and chemistry. The term “biomedical” also relates to chemicals and compositions of chemicals, regardless of their source, that (i) mediate a biological response in vivo, (ii) are active in an in vitro assay or other model, e.g., an immunological or pharmacological assay, or (iii) can be found within a cell or organism. The term “biomedical” also refers to the separation sciences, such as those involving processes

of chromatography, osmosis, reverse osmosis, and filtration. Examples of biomedical articles include research tools, industrial, and consumer applications. Biomedical articles include separation articles, implantable articles, and ophthalmic articles. Ophthalmic articles include soft and hard contact lenses, intraocular lenses, and forceps, retractors, or other surgical tools that contact the eye or surrounding tissue. A preferred biomedical article is a soft contact lens made of a silicon-containing hydrogel polymer that is highly permeable to oxygen. Separation articles include filters, osmosis and reverse osmosis membranes, and dialysis membranes, as well as bio-surfaces such as artificial skins or other membranes. Implantable articles include catheters, and segments of artificial bone, joints, or cartilage. An article may be in more than one category, for example, an artificial skin is a porous, biomedical article. Examples of cell culture articles are glass beakers, plastic petri dishes, and other implements used in tissue cell culture or cell culture processes. A preferred example of a cell culture article is a bioreactor micro-carrier, a silicone polymer matrix used in immobilized cell bioreactors, where the geometry, porosity, and density of the particulate micro-carrier may be controlled to optimize performance. Ideally, the micro-carrier is resistant to chemical or biological degradation, to high impact stress, to mechanical stress (stirring), and to repeated steam or chemical sterilization. In addition to silicone polymers, other materials may also be suitable. This invention may also be applied in the food industry, the paper printing industry, hospital supplies, diapers and other liners, and other areas where hydrophilic, wettable, or wicking articles are desired.

The medical device can be an implantable device or an extracorporeal device. The devices can be of short-term temporary use or of long-term permanent implantation. In certain embodiments, suitable devices are those that are typically used to provide for medical therapy and/or diagnostics in heart rhythm disorders, heart failure, valve disease, vascular disease, diabetes, neurological diseases and disorders, orthopedics, neurosurgery, oncology, ophthalmology, and ENT surgery.

Suitable examples of medical devices include, but are not limited to, a stent, stent graft, anastomotic connector, synthetic patch, lead, electrode, needle, guide wire, catheter, sensor, surgical instrument, angioplasty balloon, wound drain, shunt, tubing, infusion sleeve, urethral insert, pellet, implant, blood oxygenator, pump, vascular graft, vascular access port, heart valve, annuloplasty ring, suture, surgical clip, surgical staple, pacemaker, implantable defibrillator, neurostimulator, orthopedic device, cerebrospinal fluid shunt, implantable drug pump, spinal cage, artificial disc,

replacement device for nucleus pulposus, ear tube, intraocular lens and any tubing used in minimally invasive surgery.

Articles that are particularly suited to be used in the present invention include medical devices or components such as catheters, for example intermittent catheters, balloon catheters, PTCP catheters, stent delivery catheters, guide wires, stents, syringes, metal and plastic implants, contact lenses and medical tubing.

The hydrophilic coating formulation can be applied to the substrate by for example dip-coating. Other methods of application include spray, wash, vapor deposition, brush, roller and other methods known in the art.

The concentration of ionic or ionizable groups in the hydrophilic coating and the thickness of the hydrophilic coating according to the invention may be controlled by altering the type of polyelectrolyte, polyelectrolyte concentration in the hydrophilic coating formulation, soaking time, drawing speed, viscosity of the hydrophilic coating formulation and the number of coating steps. Typically the thickness of a hydrophilic coating on a substrate ranges from 0.1-300 μm, preferably 0.5-100 μm, more preferably 1-30 μm.

The invention further relates to a method of forming on a substrate a hydrophilic coating which has a low coefficient of friction when wetted with a water-based liquid, wherein said hydrophilic coating comprises an polyelectrolyte.

To apply the hydrophilic coating on the substrate, a primer coating may be used in order to provide a binding between the hydrophilic coating and the substrate. The primer coating is often referred to as the primary coating, base coat or tie coat. Said primer coating is a coating that facilitates adhesion of the hydrophilic coating to a given substrate, as is described in for example WO02/10059. The binding between the primer coating and the hydrophilic coating may occur due to covalent or ionic links, hydrogen bonding, physisorption or polymer entanglements. These primer coatings may be solvent based, water based (latexes or emulsions) or solvent free and may comprise linear, branched and/or cross-linked components. Typical primer coatings that could be used comprise for example polyether sulfones, polyurethanes, polyesters, including polyacrylates, as described in for example US6,287,285, polyamides, polyethers, polyolefins and copolymers of the mentioned polymers.

In particular, the primer coating comprises a supporting polymer network, the supporting network optionally comprising a functional hydrophilic polymer entangled in the supporting polymer network as described in WO2006/056482 A1. The

information with respect to the formulation of the primer coating is herewith incorporated by reference.

A primer coating as described above is in particular useful for improving adherence of a coating comprising a hydrophilic polymer such as a polylactam, in particular PVP and/or another of the above identified hydrophilic polymers, in particular on polyvinylchloride (PVC), silicone, polyamide, polyester, polyolefin, such as polyethylene, polypropylene and ethylene-propylene rubber (e.g. EPDM), or a surface having about the same or a lower hydrophilicity.

In general there is no restriction as to the thickness of the primer coating, but typically the thickness is less than 5 µm, less than 2 µm or less than 1 µm.

In an embodiment, the surface of the article is subjected to oxidative, photo-oxidative and/or polarizing surface treatment, for example plasma and/or corona treatment in order to improve the adherence of the coating which is to be provided. Suitable conditions are known in the art.

Application of the formulation of the invention may be done in any manner. Curing conditions can be determined, based on known curing conditions for the photo-initiator and polymer or routinely be determined.

In general, curing may be carried out at any suitable temperature depending on the substrate, as long as the mechanical properties or another property of the article are not adversely affected to an unacceptable extent.

Intensity and wavelength of the electromagnetic radiation can routinely be chosen based on the photoinitiator of choice. In particular, a suitable wavelength in the UV, visible or IR part of the spectrum may be used.

The invention will be further illustrated by the following examples.

Examples

A primer coating formulation was prepared as indicated below.

Primer coating formulation (Examples 1 and 2 and Comparative Experiments A and B

PTGL1000(T-H)$_2$ *	:	5.00 % (w/w)
Irgacure 2959 (Aldrich)	:	0.20 % (w/w)
Ethanol (Merck, 96 % extra pure PH EUR, BP)	:	94.8 % (w/w)

* Synthesized as described below

The above mentioned components were added to a brown colored glass flask and mixed overnight (~16 hours) at room temperature. The next morning the primer formulation was a homogeneous liquid with a viscosity of 7 mPa.s. Herein the viscosity was measured on a Brookfield CAP1000, v.1.2 in combination with cone nr. 1 at 25 ºC.

The above primer coating formulation was applied to Pebax ® 7233 catheter tubing (shafts) with an outer diameter of 0.034" (0.86mm) using a Harland 175-24 PCX coater. The application parameters were used as listed in Table 1.

Table 1. Application conditions of the primer coating formulation

	Primer coating formulation
Solids primer [w/w %]	5
Viscosity [mPa.s]	7
Draw speed primer [cm/s]	1.0
Cure time primer [s]	15

Synthesis of PTGL1000(T-H)$_2$

In a dry inert atmosphere toluene diisocyanate (TDI or T, Aldrich, 95% purity, 87.1 g, 0.5 mol), Irganox 1035 (Ciba Specialty Chemicals, 0.58 g, 1 wt% relative to hydroxy ethyl acrylate (HEA or H)) and tin(II) 2-ethyl hexanoate (Sigma, 95% purity, 0.2 g, 0.5 mol) were placed in a 1 liter flask and stirred for 30 minutes. The reaction mixture was cooled to 0 °C using an ice bath. HEA (Aldrich, 96 % purity, 58.1 g, 0.5 mol) was added dropwise in 30 min, after which the ice bath was removed and the mixture was allowed to warm up to room temperature. After 3 h the reaction was complete. Poly(2-methyl-1,4-butanediol)-alt-poly(tetramethyleneglycol) (PTGL1000, Hodogaya, M_n = 1000 g/mol, 250 g, 0.25 mol) was added dropwise in 30 min. Subsequently the reaction mixture was heated to 60 °C and stirred for 18 h, upon which the reaction was complete as indicated by GPC (showing complete consumption of HEA), IR (displayed no NCO related bands) and NCO titration (NCO content below 0.02 wt%).

Example 1

A hydrophilic coating formulation (1) was prepared comprising both a Norrish Type I (Irgacure 2959) and a Norrish Type II (benzophenone) photoinitiator.

PEG4000DA *	2.00 wt%
Polyvinylpyrollidone (PVP, 1.3M, Aldrich)	1.33 wt%
Poly(acrylamide-co-acrylic acid) partial sodium salt (14.5 wt% of Na^+), 20 wt% acrylamide, M~200,000 (PAcA) (Aldrich)	0.67 wt%
Benzophenone (Aldrich)	0.08 wt%
Irgacure 2959	0.04 wt%
Tween 80 (surfactant, Merck)	0.04 wt%
Water	47.92 wt%
MeOH (Merck pa)	47.92 wt%

* Synthesized as described below

Comparative Experiment A

For comparison hydrophilic coating formulation A was prepared without Norrish Type II photoinitiator.

PEG4000DA *	2.00 w%
PVP	1.33 w%
PAcA	0.67 w%
Benzophenone	-
Irgacure 2959	0.04 w%
Tween 80	0.04 w%
Water	47.96 w%
MeOH	47.96 w%

* Synthesized as described below

The above mentioned components of Example 1 and Comparative Experiment A were added to brown colored glass flasks and mixed overnight (~16 hours) at room temperature. The next morning the hydrophilic coating formulations were homogeneous liquids with a viscosity as indicated in Table 2. Herein the viscosity was measured on a Brookfield CAP1000, v.1.2 in combination with cone nr. 1 at 25 °C.

Synthesis of PEG4000DA

150 g (75 mmol OH) of polyethyleneglycol (PEG4000, Biochemika Ultra from Fluka, OH value 28.02 mg KOH/g, 499.5 mew/kg, M_n = 4004 g/mol) was dissolved in 350 ml of dry toluene at 45 °C under nitrogen atmosphere. 0.2 g (0.15 wt%) of Irganox 1035 was added as a radical stabilizer. The resulting solution was distilled azeotropically overnight (50 °C, 70 mbar) leading the condensed toluene over 4Å mol sieves. For each batch of PEG the OH value was accurately determined by OH titration, which was performed according to the method described in the 4th edition of the European Pharmacopoeia, paragraph 2.5.3, Hydroxyl Value, page 105. This made it possible to calculate the amount of acryloyl chloride to be added and to determine the degree of acrylate esterification during the reaction. 9.1 g (90 mmol) of triethylamine was added to the reaction mixture, followed by a dropwise addition of 8.15 g (90 mmol) of acryloyl chloride dissolved in 50 ml of toluene in 1 h. Triethylamine and acryloyl chloride were colorless liquids. The reaction mixture was stirred for 2 to 4 h at 45 °C under nitrogen atmosphere. During the reaction the temperature was kept at 45 °C to prevent crystallization of PEG. To determine the conversion a sample was withdrawn from the reaction mixture, dried and dissolved in deuterated chloroform. Trifluoro acetic anhydride (TFAA) was added and a ^{1}H-NMR spectrum was recorded. TFAA reacts with any remaining hydroxyl groups to form a trifluoro acetic ester, which can be easily detected using ^{1}H-NMR spectroscopy (the triplet signal of the methylene protons in the α-position of the trifluoro acetic acid group (g, 4.45 ppm) can be clearly distinguished from the signal of the methylene groups in the α-position of the acrylate ester (d, 4.3 ppm)). At a degree of acrylate esterification lower than 98 % an additional 10 mmol of acryloyl chloride and triethylamine were added to the reaction mixture allowing it to react for 1 h. At a degree of acrylate esterification higher than 98 % the warm solution was filtered to remove triethylamine hydrochloride salts. Approximately 300 ml of toluene was removed under vacuum (50 °C, 20 mbar). The remaining solution was kept at 45 °C in a heated dropping funnel and added dropwise to 1 liter of diethyl ether (cooled in an ice bath). The ether suspension was cooled for 1 h before PEG4000DA was obtained by filtration. The product was dried overnight at room temperature under reduced air atmosphere (300 mbar). Yield: 80-90 % as white crystals.

The hydrophilic coating formulations of Example 1 and Comparative Experiment A were applied on the Pebax® 7233 shafts with primer coating using a Harland 175-24 PCX coater. The relevant application conditions used are represented in Table 2.

Table 2: Application conditions for hydrophilic coating formulations of Example 1 and Comparative Experiment A

	1	A
Solids topcoat [w/w %]	4	4
Viscosity [mPa.s]	23	24
Draw speed topcoat [cm/s]	1.0	1.0
Cure time topcoat [s]	360	360

The coated length of the Pebax catheter shafts was 27 cm for the primer coating and the hydrophilic coating.

On average the UV light intensity in the PCX coater is 60 mW/cm^2 between 250-400nm, measured with a Harland UVR335 (IL1400) light meter in combination with detector SED005#989 and filter WBS320#27794. The primer coating was exposed 15 seconds, while the topcoat was exposed 360 seconds to the UV light. This correspondings with a UV-dose of respectively 0.9 J/cm^2 and 21.6 J/cm^2. During the application the temperature was 21 °C and 50% RH. For applied coating parameters see Table 3.

Table 3. Applied process parameters in PCX coater

Harland Coating parameters selection table			
Dipping Cycle	Primer	Hydrophilic coating	Units
Move device carrier to position	134.5	134.5	Cm
speed	6.5	6.5	cm/sec
acceleration time	0.1	0.1	Sec
Operator Prompt	"Remove dip cover"		
Operator Prompt	"Switch funnels"		
Move device carrier down	24.5	24.5	Cm
speed	4	4	cm/sec
acceleration time	0.1	0.1	cm/sec/sec
Operator Prompt	Check alignment of the devices above the funnels		
Move device carrier down	27	27	Cm
speed	2	2	0cm/sec
acceleration time	0.1	0.1	Sec
Time Pause	10	10	Sec
Move device carrier up	30	30	
speed	1.0	1.0	cm/sec
acceleration time	0.1	0.1	Sec
Move device carrier to position	170	170	Cm
Speed	6.5	6.5	cm/sec
acceleration time	0.1	0.1	Sec
Operator Prompt	"Close doors"		
Cure Cycle			
Rotator On	4	4	Rpm
UV lights Full Power	E - G and L - N		
Time pause	15	360	Sec
Close Shutter			
UV lights Standby Power	E - G and L - N		
Rotator Off			

The coated catheter shafts were tested in a particulate release test as described below.

Sample preparation for particulates release test

10 g of Congo-red was weighed and dissolved in 1 L of milli-Q purified water in a measuring flask. The resulting 1 wt% Congo-red solution was used to dye the hydrophilic coatings on the coated Pebax™ catheter shafts. The coated catheter shafts were impregnated in this solution for 30 minutes. The coated catheter shafts were air dried for 15 minutes. Wetting again in purified water was performed to remove the excess of Congo-red. Now the coated catheter shafts were air dried again to an extend that they showed no stickiness (approximately 1 hour). The congo-red coloured coated catheter shafts were exposed to the wear test described below.

Particulates release wear test

The particulates release wear test was conducted on a Zwick 1474 ZmartPro tensile tester with 10N KAP-Z loadcell (hereinafter referred to as "Zwick tensile tester", see Figure 1). The following materials and set-up were used:

- 950 mm of 0.022" (0.56 mm) Nitinol SE metal guide wire (diameter 0.0022", New England Precision Grinding) as reinforcing core wire inside each coated catheter shaft.
- 625 mm top-part of Medtronic Pro-Flo 6F pigtail 2.00 mm, 110 cm, cardio-vascular angiographic catheter (hereinafter referred to as "Pro-Flo guiding catheter" or, in Figure 1, "Pro-Flo guiding catheter") as outer counter surface for the wear test. The connector on the proximal end was used to connect a syringe.
- 60 ml of Milli-Q water
- Mould to support the outer catheter in the Zwick 1474 ZmartPro tensile tester. The mould has a 180 ºC curvature of ∅40mm
- 150 mm of coated catheter shaft (in Figure 1: "colored CV catheter shaft") as described above.

The coated catheter shaft was glued onto the Nitinol guide wire using Loctite, to prevent sliding of the coated catheter shaft during testing, 200 mm from the end of the Nitinol guide wire (from the load cell). This ensured that the coated catheter shaft was placed just before entering the ∅ 40 mm curvature when inserting into the

test set-up (see Figure 1). The coated catheter shaft was placed in milli-Q water for 30 seconds to ensure proper wetting of the hydrophilic coating. During wetting of the sample for 30 seconds, the Congo-red indicator partly dissolved in the water. The Nitinol guide wire and the glued coated catheter shaft were inserted into the straightened and pre-wetted Pro-Flo guiding catheter, at the catheter entrance part. The Pro-Flo guiding catheter and the inserted coated catheter shaft were placed in the polymer supporting mould, with the specific 180 ° curvature of 40 mm, and extra milli-Q water was carefully flushed into the Pro-Flo guiding catheter to ensure complete wetting of the inner space.

The polymer mould and Pro-Flo guiding catheter comprising the inserted coated catheter shaft were placed into the Zwick tensile tester and attached to the load cell by a clamp, which was placed 350 mm above the top of the mould. The end part of the catheter shaft was now inside the Pro-Flo guiding catheter just before entering the curvature where friction (and wear) mainly takes place.

Using the Zwick tensile tester, the coated catheter shaft was inserted over a length of 100 mm and withdrawn over the same length with a speed of 200 mm/min. One insertion and withdrawal is defined as 1 cycle. Each sample was conducted to the test during 5 cycles.

Particulates collection

After the particulates release wear test as described above, one side of the Pro-Flo guiding catheter was released from the mould and placed above a jar collecting the milli-Q water out of the Pro-Flo guiding catheter. A syringe, containing 10 ml of milli-Q water was attached to the catheter entrance part of the Pro-Flo guiding catheter, flushing the Pro-Flo guiding catheter. The Nitinol guide wire and attached coated catheter shaft were removed and flushed with 10ml of milli-Q water. The Pro-Flo guiding catheter was flushed with 4x 10ml of milli-Q water. The 60 ml of collected milli-Q water was subjected to particulates measurements (see below), while the Pro-Flo guiding catheter was dried for further visual check of contamination with coloured particles. No particles were found.

A 0.45-micron filter Millipore type HAWP was used to filtrate the collected milli-Q water solution. With this filter also particles smaller than 10 micron are collected, while such small particles do not need to be included in the counting according to the USP28 standard. However, the image analysis as described below could clearly distinguish between sizes bigger and smaller than 10 micron. A Millipore

glass Büchner funnel system was used for this procedure.

The filter was wetted with pure water first to make sure the filter did not colour red too much. A slightly pink colour could not be prevented. This background colour was corrected with the white and colour balance. This correction did not affect the final result.

Imaging

Microscopy images were recorded using a LEICA MA FLIII equipped with a CC-12 Soft Imaging System. The filter was illuminated in 180 ° backscattering mode with a LEICA CLS 150X with light guides fixed to the microscope. The upper switch was set on value 4 and the lower was set at position 6. A 10x ocular was used and the zoom factor was 5. The white balance was auto set using white paper. The illumination time per photo capture was set at 3.900 ms. The filter was partially imaged with 9 photos in total representing an area of 2.71 x 2.12 mm equals 5.7 mm^2 each. A piece of paper with a grid of 9 sections was placed under the filter enabling to record images out of every section. The total filter surface is 1020 mm^2. The correction factor for the total filter is 1020/(9 x 5.75) = 20.

Image analysis

The image analysis comprised the following steps:

- Background subtraction
- Object analysis
- Data visualization

Due to a varying background due to variation in Congo-red dye absorption by the filter, a background correction had to be Performed.

Opening the image in Bersoft imaging software "Image Measurement Professional 4.02" and taking a pixel slice through the center revealed the background curvature. The following procedure was used: a vertical and a horizontal slice were taken through the approximate center of the image. The pixel values were exported to Excel, wherein a fit was made of both slices.

The quadratic curves were then used in a Mathematica Workbook to subtract the background (see code below).

Mathematica code used for the background subtraction.

```
fMain=Import["D:\\image.jpg"];
```

```
fTotal=fMain; {n1,n2,n3}=Dimensions[fMain[[1,1]]];
nx=n1; ny=n2;
(*-- Fit of Red background--*)
tabelRed=Table[fMain[[1,1,x,y,1]],{x,nx},{y,ny}];
(*---Generate table t.b.v. "Fit". *)
tabelFit=Flatten[Table[{x,y,tabelRed[[x,y]]},{x,nx},{y,ny}],1];
(*---Fit, calculate parameters. *)
opl=Fit[tabelFit,{1,x,x^2,y,y^2},{x,y}];
r0=opl[[1]]; {r1,r2,r3,r4}=Table[opl[[i,1]],{i,2,5}];
Print["pLijst=",{r0,r1,r2,r3,r4}];
tabelRed=.
tabelFit=.

fTotal[[1,1]]=Table[{Abs[(fMain[[1,1,i,j,3]]-(r0+r1*i+r2*i^2+r3*j+r4*j^2)-10)*2-40],0,0},
                    {i,n1},{j,n2}];
Export["D:\\BackgroundRSubtracted.jpg",fTotal,"JPEG"];
fTotal=.
fMain=.
opl=.
```

All RGB colours were combined to one value and put in RGB Red. The resulting picture was saved as a JPG file. The image was then opened in Bersoft imaging software to detect all objects which had a RGB Red pixel value above 24. The level was chosen such that it is just above the remaining overall background value.

After analysing all objects, the data was exported to Excel wherein the visualization is done. The result of all nine images was put together and corrected for the fraction of the total filter surface.

Interpretation

Particles were analysed on the filter. Particles which were smaller than 10 micron in all directions were ignored according to the USP28. Particles which were larger than 10 micron in at least one direction were counted and related to the USP28 standard. Particle surfaces were converted to particle volumes, assuming that the particles were rigid spheres. It was taken into account that the catheter has a coating thickness of 2 micron.

Criteria:

Particles > 10 micron (particle volume between 500 μm^3 and 8000 μm^3): less than 3000 per release test (= per filter).

Particles > 25 micron (particle volume > 8000 μm^3): less than 300 per release test (= per filter).

Particulate release wear test results of Example 1 and Comparative Example A

The hydrophilic coatings 1 and A on the catheter shafts were both subjected to the particulates release wear test as described above. The particulates release of these two coatings is represented in Table 4.

Table 4: Particulates count related to the USP criteria

Sample	> 10 micron	> 25 micron	Passed
Example 1	80	20	Yes
Comparative example A	6340	1260	No

A significant reduction in particulates release was obtained due to the addition of a Norrish Type II photoinitiator (benzophenone).

CLAIMS

1. Coating formulation for preparing a hydrophilic coating, wherein the hydrophilic coating formulation comprises
   (a) a supporting monomer and/or polymer comprising at least 2 reactive moieties capable of undergoing polymerization reactions; wherein the supporting polymer has a number average molecular weight in the range 750-20,000 g/mol, preferably 1,000-15,000 g/mol, more preferably 1,100-10,000, in particular 1,200-7,000, more in particular 1,400-5,000 g/mol;
   (b) a polyelectrolyte;
   (c) a Norrish Type I photoinitiator; and
   (d) a Norrish Type II photoinitiator

2. Coating formulation according to claim 1, wherein the Norrish Type I photoinitiator is chosen from the group consisting of benzoin derivatives, methylolbenzoin and 4-benzoyl-1,3-dioxolane derivatives, benzilketals, α,α-dialkoxyacetophenones, α-hydroxy alkylphenones, α-aminoalkylphenones, acylphosphine oxides, bisacylphosphine oxides, acylphosphine sulphides, and halogenated acetophenone derivatives.

3. Coating formulation according to claim 1 or claim 2, wherein the Norrish Type II photoinitiator is chosen from the group consisting of aromatic ketones such as benzophenone, xanthone, derivatives of benzophenone (e.g. chlorobenzophenone), blends of benzophenone and benzophenone derivatives (e.g. Photocure 81, a 50/50 blend of 4-methyl-benzophenone and benzophenone), Michler's Ketone, Ethyl Michler's Ketone, thioxanthone and other xanthone derivatives like Quantacure ITX (isopropyl thioxanthone), benzil, anthraquinones (e.g. 2-ethyl anthraquinone), coumarin, or chemical derivatives or combinations of these photoinitiators.

4. Coating formulation according to any one of claims 1-3, wherein the supporting polymer comprises a backbone selected from the group consisting of polyethers, polythioethers, polyurethanes, polyethylenes, polypropylenes, polyvinyl chlorides, polyepoxides, polyamides, polyacrylamides, poly(meth)acrylics, polyoxazolidones, polyvinyl alcohols, polyethylene imines, polyesters like polyorthoesters and alkyd copolymers, polypeptides, and

polysaccharides such as cellulose and starch or any combination of the above and at least 2 reactive moieties selected form the group consisting of radically reactive groups, such as alkenes, amino, amido, sulfhydryl (SH), unsaturated esters such as acrylate and methacrylate, unsaturated ethers, unsaturated amides, and alkyd/dry resins.

5. Coating formulation according to any one of claims 1-4, wherein the polyelectrolyte is chosen from the group consisting of salts of homo- and co-polymers of acrylic acid, salts of homo- and co-polymers of methacrylic acid, salts of homo- and co-polymers of maleic acid, salts of homo- and co-polymers of fumaric acid, salts of homo- and co-polymers of sulfonic acid, quarternary ammonium salts and mixtures and/or derivatives thereof.

6. Coating formulation according to claim 5, wherein the polyelectrolyte is a poly(acrylamide-co-acrylic acid) salt.

7. Coating formulation according to any one of claims 1-6, further comprising a hydrophilic polymer selected from the group consisting of poly(lactams), for example polyvinylpyrollidone (PVP), polyurethanes, homo- and copolymers of acrylic and methacrylic acid, polyvinyl alcohol, polyvinylethers, maleic anhydride based copolymers, polyesters, vinylamines, polyethyleneimines, polyethyleneoxides, poly(carboxylic acids), polyamides, polyanhydrides, polyphosphazenes, cellulosics, for example methyl cellulose, carboxymethyl cellulose, hydroxymethyl cellulose, and hydroxypropylcellulose, heparin, dextran, polypeptides, for example collagens, fibrins, and elastin, polysacharrides, for example chitosan, hyaluronic acid, alginates, gelatin, and chitin, polyesters, for example polylactides, polyglycolides, and polycaprolactones, polypeptides, for example collagen, albumin, oligo peptides, polypeptides, short chain peptides, proteins, and oligonucleotides.

8. Coating formulation according to any one of claims 1-7, the hydrophilic coating formulation further comprising at least one surfactant or levelling agent.

9. Coating formulation according to any one of claims 1-8, the hydrophilic coating formulation further comprising at least one plasticizer.

10. Hydrophilic coating obtainable by curing a hydrophilic coating formulation according to any one of claims 1-9.

11. Lubricious coating obtainable by applying a wetting fluid to a hydrophilic coating according to claim 10.

12. Lubricious coating having a wear resistance, as measured according to the

particulates release wear test, corresponding to less than 3000, preferably less than 2000, more preferably less than 1000, in particular less than 500 particles larger than 10 µm.

13. Coating system for preparing a lubricious coating, said coating system comprising a coating formulation according to any one of claims 1-9 and a wetting fluid comprising a polyelectrolyte.

14. Use of a Norrish Type I and a Norrish Type II photo-initiator in a lubricious coating wherein the wear resistance, as measured as measured according to the particulates release wear test, corresponding to less than 3000, preferably less than 2000, more preferably less than 1000, in particular less than 500 particles larger than 10 µm.

15. Article comprising at least one hydrophilic coating or lubricious coating according to any one of claims 10-12.

16. Article according to claim 15, wherein the article is a medical device or component.

17. Medical device or component according to claim 16 comprising a catheter, a medical tubing, a guide wire, a stent, or a membrane.

18. Method of forming on a substrate a hydrophilic coating, the method comprising

- applying a coating formulation according to any one of claims 1-9 to at least one surface of the article;
- and allowing the coating formulation to cure by exposing the formulation to electromagnetic radiation thereby activating the initiator.

FIGURE 1/1

Schematic setup of the particulates release wear test