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(54) **Titre** : POLYMERES AYANT DES PROPRIETES BACTERIOPHOBES ET, FACULTATIVEMENT, D'INHIBITION DE LA PROLIFERATION CELLULAIRE

(54) **Title:** POLYMERS HAVING BACTERIOPHOBIC AND OPTIONALLY CELL PROLIFERATION-INHIBITING PROPERTIES

(57) **Abrégé/Abstract:**

Disclosed is a water-insoluble, bacteriophobic and optionally cell proliferation-inhibiting polymer obtainable by free-radical polymerization of (a) at least one monomer of the general formula $R\text{-}(A)_a$, in which R is an aliphatically unsaturated organic radical with the valence a, A is a carboxyl group -COOH, sulfuric acid group $-OSO_2OH$, sulfonic acid group $-SO_3H$, phosphoric acid group $-OPO(OH)_2$, phosphonic acid group $-PO(OH)_2$, phosphorous acid group $-OP(OH)_2$, a phenolic hydroxyl group or a salt of one of the groups, and a is 1, 2 or 3; with the proviso that, if the monomer of the formula I contains a carboxyl group -COOH or a carboxylate group, either this monomer contains at least one further different radical A, or at least one further monomer of the formula I is also used in which A is different; and (b) at least one other aliphatically unsaturated monomer. The polymer is useful for the production of a bacteriophobic and optionally cell proliferation-inhibiting article.

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# ABSTRACT

Disclosed is a water-insoluble, bacteriophobic and optionally cell proliferation-inhibiting polymer obtainable by free-radical polymerization of (a) at least one monomer of the general formula $R-(A)_a$, in which R is an aliphatically unsaturated organic radical with the valence a, A is a carboxyl group -COOH, sulfuric acid group $-OSO_2OH$, sulfonic acid group $-SO_3H$, phosphoric acid group $-OPO(OH)_2$, phosphonic acid group $-PO(OH)_2$, phosphorous acid group $-OP(OH)_2$, a phenolic hydroxyl group or a salt of one of the groups, and a is 1, 2 or 3; with the proviso that, if the monomer of the formula I contains a carboxyl group -COOH or a carboxylate group, either this monomer contains at least one further different radical A, or at least one further monomer of the formula I is also used in which A is different; and (b) at least one other aliphatically unsaturated monomer. The polymer is useful for the production of a bacteriophobic and optionally cell proliferation-inhibiting article.

# POLYMERS HAVING BACTERIOPHOBIC AND OPTIONALLY CELL PROLIFERATION-INHIBITING PROPERTIES

## Field of Invention

The invention relates to a process for preparing bacteriophobic and optionally cell proliferation-inhibiting surfaces using certain water-insoluble polymers some of which are novel. The invention also relates to the novel polymers as such, which can be used as bacteriophobic and optionally at the same time cell proliferation-inhibiting materials, and to a process for their preparation. Finally, the invention relates to articles produced using the bacteriophobic and optionally cell proliferation-inhibiting, novel or known materials, and to the production processes.

## Prior Art

In medical examinations, treatments and interventions where articles, instruments or accessories come into direct contact with living tissue and/or body fluids, bacterial contamination may cause considerable difficulties which may even threaten the patient. This applies to short term contact just as much to medium- or long-term applications of implants, catheters, prostheses and other medicotechnical uses. For instance, it is known from P.A. Goldmann, G.B. Pier, Clin. Microbiol. Rev. 6 (1993), 176 ff. that infections in the course of operative interventions may give rise to considerable and costly complications. For the same reasons, catheters need changing after application periods of 2 to 6 days.

In the field of the food and drink industry, as well, colonization and propagation of bacteria on surfaces of pipelines, containers or packaging are extremely undesirable. In many cases coats of slime are formed which allow extreme rises in micropopulations, which have a persistent adverse effect on the quality of water, drinks and foods and may even lead to the decay of the product and to damage to the health of the consumers.

Bacteria must be kept away from all fields of life in which hygiene is important. This affects textiles for direct body contact, especially for the genital area and for the care of the elderly and sick. Bacteria must also be kept away from surfaces of furniture and instruments in wards, especially in the area of intensive care and neonatal care, in hospitals, especially in areas for medical interventions, and in isolation wards for critical cases of infection, and also in toilets.

At present, instruments and also surfaces of furniture and textiles are treated against bacteria as required or otherwise preventatively using chemicals or solutions thereof and using mixtures which, as disinfectants, have a more or less broad and heavy antimicrobial action. Such chemical compositions are nonspecific in their action, are frequently themselves toxic or irritant, or break down to form products which are objectionable from a health standpoint. In many cases there are also instances of incompatibility with individuals who are sensitized correspondingly.

A further measure taken against surface bacteria propagation is the incorporation of antimicrobial substances into surface layers, for example the incorporation of silver salts in accordance with WO 92/18098. The incorporation of quaternary ammonium salts into paintlike coatings, moreover, is known from WO 94/13748.

Composites of this kind, however, prove to have little resistance to aqueous solutions or body fluids. Leaching occurs, thereby reducing the concentration of the antimicrobial active substances with the period of application and lowering the action. Furthermore, when such formulations are used medically, active substance components pass into the physiological circulation, which is extremely undesirable because of toxicological anxieties and potential side-effects.

In a different technical field, U.S. Patent No. 5,278,200 discloses polymers which have a carboxylate group and a sulfonate group in a proportion which is comparable with that of natural heparin. These polymers have anticoagulant properties in relation to thrombocytes in the blood.

Furthermore, diverse attempts have been made to immobilize antimicrobial substances on polymeric and/or functionalized surfaces, preferably by means of covalent bonds (T. Ouchi, Y. Ohya, Prog. Polym. Sci., 20 (1995), 211 ff.). In this case, chemical bonding to a substrate leads to a reduction in the bactericidal action in comparison with the free active substances. In the case of medical applications, surfaces of this kind often display instances of incompatibility with the physiological system.

In addition, the bacteria which have been killed remain on antimicrobial surfaces and build up organic layers which, ultimately, completely mask the bactericidal actions. The covering of the surface with dead bacteria constitutes a particularly advantageous nutrient base for further microbial infestation (A. Kanazawa, T. Ikeda, T. Endo, J. Polym. Sci. A. Polym. Chem., 31 (1993), 1467 ff.).

In the case of certain medical uses, it is not only the bacteriophobic properties of the plastics used that are important but also cell proliferation-inhibiting properties. For example, cell colonization in the case of catheters applied intracorporally in the medium term (indwelling catheters) is just as harmful as in the case of cardiac valves or stents which are implanted for a long period. WO 94/16648 describes a process in which cell sorption and cell propagation on eye implant lenses, which cause clouding of the lens, are prevented by subsequent chemical modification of the surface of the implant. In accordance with EP 0 431 213, polymers are imparted with cell-repelling properties by rendering the surfaces of the polymers hydrophilic using strong mineral acids. This leads to a reduction in cell adhesion.

The subsequent chemical modification of surfaces of polymeric materials is in most cases irregular and/or nonuniform. Untreated areas remain in many cases, and may form starting points for cell colonization of the surface.

A major object of the present invention is to provide a process by which surfaces of polymers can be kept substantially free from bacteria and, optionally at the same time, from cell colonization in a physiologically compatible manner and without killed bacteria remaining on the surface. A further object is to provide novel, bacteriophobic and optionally at the same time cell proliferation-inhibiting polymers. Another object of the invention is to provide articles which consist of or comprise certain bacteriophobic and optionally at the same time cell proliferation-inhibiting materials.

## Bacteriophobic and Optionally Cell Proliferation-Inhibiting Polymer Surfaces

A first aspect of the present invention provides a process for preparing bacteriophobic and optionally cell proliferation-inhibiting polymer surfaces, which comprises using water-insoluble polymers A which are obtainable by free-radical polymerization of

(a) at least one monomer of the general formula:

$$R\text{-}(A)_a \qquad (I)$$

in which R is an aliphatically unsaturated organic radical with the valence a,

A is a carboxyl group -COOH, a sulfuric acid group $-OSO_2OH$, a sulfonic acid group $-SO_3H$, a phosphoric acid group $-OPO(OH)_2$, a phosphonic acid group $-PO(OH)_2$, a phosphorous acid group $-OP(OH)_2$, a phenolic hydroxyl group or a salt of one of the groups, and

<u>a</u> is 1, 2 or 3;

with the proviso that, when the monomer of the formula (I) contains a carboxyl group -COOH or a carboxylate group, either this monomer contains at least one further radical A having a different one of the definitions specified for A, or at least one further monomer of the formula (I) is also used in which A has a different one of the definitions specified for A; and

(b) at least one other aliphatically unsaturated monomer.

The invention is based on the observation that the polymers A are highly suitable for use as bacteriophobic and optionally cell proliferation-inhibiting materials, in bulk or for coating.

The term aliphatically unsaturated radical R as used here and below is intended to denote an organic radical comprising C-C double and/or triple bonds, preferably one or two olefinic double bonds. The organic radical R may have a hydrocarbon structure or may contain further atoms in addition to carbon and hydrogen, for example oxygen, nitrogen and/or silicon atoms. Preferably, R is a hydrocarbon radical having 2 to 10 carbon atoms which may be substituted by an alcoholic hydroxyl group. The hydrocarbon radical may contain a benzene ring.

The above restrictive proviso condition excludes the less effective copolymers which contain only one carboxyl or carboxylate group.

The salts of the acidic groups specified for A may be preferably physiologically acceptable such as alkali metal salts (in particular sodium salts) and ammonium and quarternary ammonium salts.

The common feature of the monomers of the formula (I) is that they have at least one aliphatically unsaturated bond, preferably 1 or 2 olefinic double bonds and also at least one acidic group or a salt of an acidic group, provided that the carboxyl and the carboxylate group alone is excluded.

The polymers A which are used in accordance with the first aspect of the invention are barely infested by bacteria. Consequently, the adhesion of bacteria on the surface is outstandingly suppressed. In addition to this bacteriophobic action, the polymers used in accordance with the invention are also bacteriostatic. In other words, the cell division of the few bacteria which have adhered to the surface of the polymers is greatly reduced. This means that the bacteriophobic action of the polymers according to the invention cannot be masked by the growth of bacteria which have already adhered. The reduction in the adsorption and multiplication of bacteria relates, for example, to the following types of Gram-positive and Gram-negative strains: Staphylococcus epidermidis, Streptococcus pyogenes, Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli and Enterobacter faecium.

The particular conditions in which a polymer A is bacteriophobic and at the same time inhibits cell proliferation will be explained later.

The surfaces of the polymers A are not only bacteriophobic and optionally cell proliferation-inhibiting but in addition are outstandingly compatible with tissue, blood or other body fluids, since antimicrobial active substances are not employed and thus are also unable to enter the body.

## New Bacteriophobic and Optionally Cell Proliferation-Inhibiting Polymers

A second aspect of the invention provides novel water-insoluble, bacteriophobic and optionally cell proliferation inhibiting polymers B, obtainable by free-radical copolymerization of:

(c) one or more aliphatically unsaturated monomers which contain a carboxyl group and/or a carboxylate group, or corresponding functionalized derivatives of these monomers, as component I,

(d) one or more aliphatically unsaturated monomers containing a sulfonic acid group and/or a sulfonate group, or corresponding functionalized derivatives of these monomers, as component II, and

(b) one or more further aliphatically unsaturated monomers, as component III,

the corresponding functionalized derivatives being converted if desired, after copolymerization and at least on the surface, into carboxyl or carboxylate groups or sulfonic acid or sulfonate groups, respectively.

A third aspect of the present invention provides a process for preparing the above-described water-insoluble, bacteriophobic polymers B, which comprises subjecting, to free radical copolymerization:

(c) one or more aliphatically unsaturated monomers which contain a carboxyl group and/or a carboxylate group, or corresponding functionalized derivatives of these monomers, as component I,

(d) one or more aliphatically unsaturated monomers containing a sulfonic acid group and/or a sulfonate group, or corresponding functionalized derivatives of these monomers, as component II, and

(b) one or more further aliphatically unsaturated monomers, as component III, and

where required, converting the correspondingly functionalized derivatives after copolymerization and at least on the surface, into a carboxyl or carboxylate group or a sulfonic acid or sulfonate group, respectively.

The novel copolymers B are a subgroup of the above-described polymers A which are used in accordance with the first aspect to prepare bacteriophobic surfaces. The statements regarding the properties for polymers A therefore also apply to the polymers B.

Functionalized derivatives of the carboxyl (or carboxylate) and sulfonic acid (or sulfonate) groups are, in particular, ester, amide and nitrile groups. They are optionally converted subsequently, at least on the surface (and it is only the surface which is important for the bacteriophobic and bacteriostatic and also the cell proliferation-inhibiting actions) into a carboxyl or carboxylate group or a sulfonic acid or sulfonate group, respectively, for example by means of acidic or basic hydrolysis.

Preferred polymers B contain carboxylate and sulfonate groups. In so far as these groups are not introduced by the choice of appropriate monomers, they can be generated subsequently, at least on the surface, by neutralizing carboxyl groups or sulfonic acid groups with a base, such as sodium hydroxide solution, or by basic hydrolysis of ester groups.

For the polymers B according to the invention it is also possible to employ an aliphatically unsaturated monomer which contains both a carboxyl (or carboxylate) group and a sulfonic acid (sulfonate) group. Bifunctional monomers of this kind function simultaneously as components I and II.

Aliphatically unsaturated monomers each containing two or more carboxyl and/or carboxylate groups or sulfonic acid and/or sulfonate groups, or correspondingly functionalized derivatives of these monomers, may also be used.

For the polymers B according to the invention a total content, of component I and of component II is preferably from 0.5 to 30 mol % of the polymer.

The molar ratio of the carboxyl and/or carboxylate groups present in the polymer B according to the invention to sulfonic acid and/or sulfonate groups is preferably from 0.4 to 10, preferably from 0.5 to 5. When the ratio is from 0.4 to less than 3, preferably from 0.4 to 2, the polymers B also exhibit pronounced cell proliferation-inhibiting properties.

Monomers of the Polymers A and B

Examples of components I and II for the preparation of the polymers B according to the invention include monomers of the general formulae II and III:

$(C_nH_{2n-q-x})(COOR^1)_x$ (for component I) Formula II

$(C_nH_{2n-q-x})(SO_3R^1)_x$ (for component II) Formula III

which come under the formula I and are preferred monomers for the preparation of polymers B. In the formulae II and III;

n independently at each occurrence is an integer from 2 up to and including 6;

q independently at each occurrence is 0 or 2;

x independently at each occurrence is 1 or 2; and the radical $R^1$, independently at each occurrence, is -H, an equivalent of a metal ion, especially an alkali metal ion, or a radical of an aliphatic, cycloaliphatic or araliphatic alcohol, preferably an alkanol having 1 to 6, especially 1 to 4 carbon atoms, a cycloalkanol having 5 to 12 carbon atoms, an arylalkanol having 7 to 10 carbon atoms, or an alkanol having oxygen and/or nitrogen atoms in the chain and up to 12 carbon atoms.

Where the groups $(COOR^1)_x$ and $(SO_3R^1)_x$ are ester groups, they are converted after polymerization, by hydrolysis, into carboxyl or carboxylate groups or sulfonic acid or sulfonate groups, respectively.

In accordance with the definitions given, the radical $(C_nH_{2n-q-x})$- independently at each occurrence is a straight-chain or branched monovalent alkenyl radical (q=0, x=1) or alkadienyl radical (q=2, x=1) or a straight-chain or branched divalent alkenylene radical (q=0, x=2) or alkadienylene radical (q=2, x=2).

Instead of two monomers of the formulae II and III it is also possible in turn to employ only one bifunctional monomer (II + III), which has both the $COOR^1$ and $SO_3R^1$ groups in the same molecule.

As a special case of monomers suitable as component I, mention may be made of the following monomers of the formula IV which come under the formula II:

$$(C_nH_{2n-q-x})(COOR^2)_x, \qquad \text{Formula IV}$$

where

$R^2$ is $-(CH_2-CH_2-O)_d-H$, $-(CH_2-CH(CH_3)-O)_d-H$, $-(CH_2-(CH_2-CH_2-O)_d-H$ or $-(CH_2)_d-NH_{2-e}(R^3)_e$, where $R_3$ is $-CH_3$ or $-C_2H_5$,

d is 0, 1, 2, 3 or 4 and

e is 0, 1 or 2,

<u>n</u> is 2, 3, 4, 5 or 6,

<u>q</u> is 0 or 2, and

<u>x</u> is 1 or 2.

Following polymerization, the carboxylic ester groups are hydrolysed and are then in the form of carboxyl or carboxylate groups. The aliphatically unsaturated monomers may be either straight-chain or branched.

As a special case of monomers which are suitable as component II, mention may be made of the following monomers of the general formula V, which fall under the formula III:

$$(C_nH_{2n-q-x})(SO_3R^2)_x \qquad \text{Formula V}$$

in which $R^2$, n, q and x are as defined above.

The sulfonic ester groups are hydrolysed after polymerization and are then in the form of sulfonic acid groups or sulfonate groups. The aliphatically unsaturated monomers may be either straight-chain or branched.

In addition, benzene-derived monomer components of the general formula VI:

$$(C_6H_{6-a-b-c})A_aB_b(OH)_c \qquad \text{Formula VI}$$

are also suitable as components I and II for the polymer B, where

A independently at each occurrence is a mono- or divalent straight-chain or branched radical of the formula $-(C_nH_{2n-1-q-x})(COOR^1)_x$ or $(C_nH_{2n-1-q-x})(SO_3R^1)_x$ in which $R^1$, n, q, x and y are as defined above;

B independently at each occurrence is $C_{1-4}$-alkyl, $-NH_2$, $-COOH$, $-SO_3H$, $-OSO_3H$, $-OPO(OH)_2$, $-PO(OH)_2$, $-OP(OH)_2$, $-PO(O^-)OCH_2CH_2N^+(CH_3)_3$, $-OP(O^-)-OCH_2CH_2N^+(CH_3)_3$ or is optionally a salt, especially an alkali metal salt, or an ester of these groups;

a is 1, 2, or 3;

b is 0, 1, 2 or 3; and

c is 0, 1, 2, or 3;

with the proviso that the total of a + b + c is not more than 6, preferably not more than 4.

Depending on the definition of A, the monomers of the formula VI are suitable as component I or as component II.

As a special case of monomers which fall under the general formula VI and which are suitable as component I, mention may be made of the following monomers of the general formula VII:

$(C_6H_{6-a-b-c})C_2D_b(OH)_c$ Formula VII

in which C is $(C_nH_{2n-q-x-1})(COOR^2)_x$, where

$R^2 =$ $-(CH_2-CH_2-O)_d-H$, $-(CH_2-CH(CH_3)-O)_d-H$, $-(CH_2-CH_2-CH_2-CH_2-O)_d-H$ or $-(CH_2)_d-NH_{2-e}(R^3)_e$, where $R^3$ is $-CH_3$ or $-C_2H_5$,

$n$ is 2, 3, 4, 5 or 6,

$q$ is 0 or 2,

$x$ is 1 or 2,

$d$ is 0, 1, 2, 3 or 4 and

$e$ is 0, 1 or 2;

D= $-COOH$, $-SO_3H$, $-NH_2$, $-N^+(CH_3)_3$, $-O-PO_3H-$, $-OSO_3H$, or $-O-PO_2-CH_2-CH_2-N^+(CH_3)_3$,

$a$ is 1, 2 or 3,

$b$ is 0, 1, 2 or 3, and

$c$ is 0, 1, 2 or 3;

with the proviso that $a + b + c \leq 6$, advantageously $\leq 4$.

As a special case of monomers which fall under the general formula VI and which are suitable as component II, mention may be made of the following monomers of the general formula VIII:

$(C_6H_{6-a-b-c})E_aD_b(OH)_c$ Formula VIII

in which E is $(C_nH_{2n-q-x-1})(SO_3R^2)_y$, where

$R^2$ is $-(CH_2-CH_2-O)_d-H$, $-(CH_2-CH(CH_3)-O)_d-H$,

$-(CH_2-CH_2-CH_2-O)_d-H$ or $-(CH_2)_d-NH_{2-e}(R^3)_e$,

where $R^3$ is $-CH_3$ or $-C_2H_5$,

n is 2, 3, 4, 5 or 6,

q is 0 or 2,

x is 1 or 2,

d is 0, 1, 2, 3 or 4 and

e is 0, 1 or 2;

D is $-COOH$, $-SO_3H$, $-NH_2$, $-N^+(CH_3)_3$, $-O-PO_3H$,

$-OSO_3H$, or $-O-PO_2-CH_2-CH_2-N^+(CH_3)_3$,

a is 1, 2 or 3,

b is 0, 1, 2 or 3; and

c is 0, 1, 2 or 3;

with the proviso that the total of a + b + c is not more than 6, preferably not more than 4.

In the two latter special cases as well, ester groups are hydrolysed after polymerization and are then in the form of the corresponding acidic or ionic neutralized groups.

Of the monomers of the general formulae I to VIII which are suitable for preparing the coating polymers and which contain one or more identical or different actual or potential (i.e. actual after-hydrolysis) radicals A in the molecule, mention may be made by way of example of:

acrylic acid, sodium acrylate, isobutyl acrylate, 2-ethylhexyl acrylate, 2-hydroxyethyl acrylate, 2-(2'-hydroxyethoxy)ethyl acrylate, 2-hydroxy-1-methylethyl acrylate, 2-N,N-dimethylaminoethyl acrylate, methacrylic acid, vinylacetic acid, sodium methacrylate, n-propyl methacrylate, 2-hydroxyethyl methacrylate, 2-(2′-hydroxyethoxy)ethyl methacrylate, 2-hydroxy-1-methylethyl methacrylate, 2-N,N-dimethylaminoethyl methacrylate, maleic acid, fumaric acid, diethylene glycol methacrylate, triethylene glycol diacrylate, allylsulfonic acid, methallylsulfonic acid, sodium allyl sulfate, sodium methallyl sulfate, 2-hydroxyethyl allyl sulfate, vinylsulfonic acid, sodium vinylsulfonate, 2-hydroxyethyl vinylsulfonate, styrenesulfonic acid (namely, vinylbenzene-sulfonic acid), vinyltoluenesulfonic acid, sodium vinyltoluene sulfonate, vinylxylenesulfonic acid, vinylsalicylic acid, 1,3-butadiene-1,4-diol diphosphate, sorbic acid, caffeic acid, 4- and 2-vinylphenol, 2-allylhydroquinone, 4-vinylresorcinol and carboxylstyrenesulfonic acid.

Further Monomers

Further aliphatically unsaturated monomers (b), in connection with the polymer B also referred to as component III, which are suitable for the polymers B and for the abovementioned polymers A are, preferably, nonionic monomers which carry no ionic groups. The aliphatically unsaturated monomers (b) make a predominant contribution to the insolubility of the polymers A and B in water. By means of guideline experiments, it is easy to determine which monomers in what amount should be employed as monomers (b) in order that the polymers A and B are insoluble in water. The polymers are regarded as being insoluble in water when they undergo no visible change even after a period of months in contact with aqueous media in the course of the use as intended of the articles produced from them or of the articles coated with them. Examples of the monomers which are suitable in principle as aliphatically unsaturated monomers (b) include vinyl compounds, for example vinylalkyl (e.g. of 1-8 C) ketones, such as vinyl ethyl ketone and vinyl n-butyl ketone; vinyl esters, such as vinyl acetate and vinyl propionate; allyl compounds; (meth)acrylic compounds, such as alkyl (e.g. 1-10C) (meth)acrylic esters, for example methyl acrylate, methyl methacrylate, n-butyl acrylate and 2-ethylhexyl acrylate; and also (meth)acrylonitrile and (meth)acrylamide; olefins and dienes, such as 1-butene, 1-hexene, 1,3-butadiene, isoprene and chloroprene; unsaturated halogenated hydrocarbons, such as vinyl chloride and vinylidene chloride; styrene and methyl- or halogeno-styrene; vinylsiloxanes, such as tris(trimethylsiloxy)methacryloyloxypropylsilane and tris(trimethylsiloxy)acryloyloxypropylsilane; and the correspondingly functionalized derivatives thereof. If, and in so far as, carboxylic ester groups, nitrile groups and carboxamide groups are not subsequently hydrolysed, the corresponding monomers are also valid as aliphatically unsaturated monomers (b). The content of the further monomers is often at least about 40 mol% and up to about mol%, preferably from about 60 to 85 mol%.

### Preparation of the Bacteriophobic and Optionally Cell Proliferation Inhibiting Polymers A and B

The polymers A and B according to the invention or to be used in accordance with the invention can be prepared, for example, by means of emulsion polymerization in accordance with the prior art (Hans-Georg Elias, Makromoleküle, Hüthig & Wepf Verlag, Heidelberg, 1981, p. 603 ff.).

Furthermore, to prepare the polymers B according to the invention, the components I, II and III can also be copolymerized in solution or in bulk by known methods (Hans-Georg Elias, Makromoleküle, Hüthig & Wepf Verlag, Heidelberg, 1981, p. 602 ff.).

For copolymerizing the components I, II and III in solution, it is possible to employ, for example, the following solvents (depending on the monomers employed): water, ketones, such as acetone, methyl ethyl ketone, butanone and cyclohexanone; ethers, such as diethyl ether, tetrahydrofuran dioxane; alcohols, such as methanol, ethanol, n- and isopropanol, n- and isobutanol and cyclohexanol; strongly polar solvents, such as dimethylacetamide, dimethyl sulfoxide and dimethylformamide; hydrocarbons, such as heptane, cyclohexane, benzene and toluene; halogenated hydrocarbons, such as dichloromethane and trichloromethane; esters, such as ethyl acetate, propyl acetate and amyl acetate; and also nitriles, such as acetonitrile.

Polymerization initiators which can be used include azo nitriles, alkyl peroxides, acyl peroxides, hydroperoxides, peroxoketones, peresters and peroxocarbonates, peroxodisulfate, persulfate and all customary photoinitiators. Polymerization can be initiated thermally or by means of electromagnetic radiation, such as UV light or gamma radiation.

If the monomers employed to prepare the

bacteriophobic and optionally cell proliferation-inhibiting polymers comprising monomers of the formulae II to VIII are not monomers which contain carboxyl and/or carboxylate groups or sulfonic acid and/or sulfonate groups, but the functionalized derivatives thereof, for example a carboxylic ester instead of a carboxylic acid, then following polymerization the functionalized derivatives must be converted into carboxyl or carboxylate groups and/or sulfonic acid or sulfonate groups, respectively. In the case of the esters this can be done by means of acid- or base-catalyzed hydrolysis. Polymeric materials can be derivatized by generally known methods (Hans Beyer, Lehrbuch der organischen Chemie, S. Hirzel Verlag, Stuttgart, 1988, p. 260 ff.).

## Use of the Polymers

A fourth aspect of the present invention is the use of the water-soluble polymers A and B as claimed for producing articles having a bacteriophobic and optionally cell proliferation-inhibiting surface. These include articles made wholly or in part of these polymers and articles made from plastic, ceramic or metal which are coated with the polymers. Suitable coating techniques are well known in the art, such as dipping, spraying, brushing, knife coating and spin coating. Coating with the polymers according to the invention makes it possible to continue to use known and well-established materials and production methods. This is particularly advantageous when the mechanical properties of the materials are important or when high levels of capital investment were required for the existing production plants in accordance with the production methods to date.

It is also possible to fix the polymers by means of primer layers or intermediate layers comprising bifunctional compounds on standard polymers, which may have been activated. Examples of such standard polymers are PVC, polystyrene, polyurethanes, polyacrylates, polymethacrylates, polyesters, polyethers, polyether-block-amides, polyamides, polycarbonates, polyolefins, silicones and polytetrafluorethylene.

The articles produced in accordance with the invention with a bacteriophobic and optionally cell proliferation-inhibiting surface are intended preferably for use in the fields of food and tobacco technology, water engineering, biotechnology, preventive hygiene and, in particular, medical engineering. For example, the polymers described here can be used to produce articles such as textiles, furniture and instruments, tubes and hoses, flooring, wall and ceiling surfaces, storage containers, packaging, window frames, telephone receivers, toilet seats, door handles, grips and holding straps in public transport, and medical articles which consist of the polymers or have a coating of these polymers on plastics, ceramics or metal as the substrate. Examples of medical articles are implants or accessories, such as drainage tubes, leads, cannulas, intraocular lenses, contact lenses, stents, vascular prostheses, artificial limbs, bone substitute materials, artificial ligaments, dental prostheses for plastic surgery, blood bags, dialysis membranes, suture materials, dressings, nonwoven products and surgical instruments. A preferred use of the materials according to the invention is for producing catheters.

Articles According to the Invention

A final aspect of the present invention provides articles which have been prepared using the water-insoluble, bacteriophobic and optionally cell proliferation-inhibiting polymers as described above, especially the abovementioned medical articles, and preferably catheters.

The examples which follow are intended to illustrate the invention in more detail but without restricting its scope as defined in the patent claims.

Examples

Test methods for bacterial adhesion

Measuring bacterial adhesion by scintillation

The samples of the respective polymers according to the invention, obtained by copolymerization, are dissolved in an appropriate solvent. The solutions are poured into a Petri dish and the solvent is evaporated, and the resulting polymer films are immersed for a period of one hour in 1 ml of a solution consisting of phosphate-buffered saline (PBS), 0.4 g/l bovine serum albumin (BSA) and 20 μg/ml purified human fibronectin. The samples thus coated with fibronectin are then placed with vigorous stirring for 1 hour at 37°C into the corresponding bacterial suspension, which has been radiolabeled by the incorporation of 3H-thymidine. After the predetermined time has elapsed the excess bacteria are removed and the membranes are rinsed 3 times with in each case 3 ml of

PBS-BSA solution and are placed in a sample chamber with 20 ml of scintillation solution in order to determine the number of bacteria which have adhered. The percentage of adhered bacteria is determined from the ratio of the radioactivity originating from the sample to the amount of radioactivity originally introduced by the bacteria. The reference sample used is a film prepared in the same way which is obtained by polymerization of component III of the respective polymer according to the invention. The inhibition of bacterial adhesion is expressed as a percentage quotient of the bacterial adhesion of the reference film to that of the polymer according to the invention.

**Measuring the bacterial adhesion of coated standard films using ATP (static)**

Following the adsorption of microbe cells on films of the respective polymer according to the invention, the bacteria which have not adhered are rinsed off using sterile PBS buffer solution. The adenosine triphosphate (ATP), a substance present in bacteria, is extracted from the bacteria which have adhered to the film and is measured using a customary commercial test combination in a bioluminometric assay. The number of light pulses measured is proportional to the number of bacteria which are adhering. Since the ATP content of the different bacterial strains is different, a plurality of standard films are employed in each case. The reference sample used is a film prepared in the same way which is obtained by polymerizing component III of the respective polymer according to the invention. The inhibition of bacterial adhesion is expressed as a percentage quotient of the bacterial adhesion of the reference film to that of the polymer according to the invention.

**Measuring the bacterial adhesion of coated standard films using ATP (dynamic)**

The bacteria are placed, together with the film of the respective polymer according to the invention that is to be tested, in a yeast extract/peptone/glucose nutrient solution, and the mixture is shaken at 37°C for 24 hours. Subsequently, the section of plastic is rinsed with tap water, transferred to a fresh flask containing nutrient solution and shaken for a further 24 hours at 37°C. After that, the latter procedure is repeated once, and the section of film is rinsed with tap water and immersed in sterile PBS. The adenosine triphosphate (ATP), a substance present in cells, is extracted from the bacteria which have adhered to the film and is measured using a customary commercial test combination in a bioluminometric assay. This value is proportional to the bacteria which have adhered. The reference sample used is a film prepared in the same way which is obtained by polymerizing component III of the respective polymer according to the invention. The inhibition of bacterial adhesion is expressed as a percentage quotient of the bacterial adhesion of the reference film to that of the polymer according to the invention.

The results set out in the following examples show that the adhesion of bacteria to polymers according to the invention, irrespective of the strain of bacteria and the measurement method, is from 95 to 99%, i.e. virtually complete. This action is also not masked by dead microorganisms.

**Method of determining the cell proliferation**

**Preparing the cell suspension**

Human fibroblasts (McCoy's) from ATCC No. CRL 1696 (Rockville, Maryland, USA) are grown in DMEM (Dulbecco's Modified Eagles Medium) with the addition of antibiotics, L-glutamine and 10% by volume of fetal calf serum at 37°C under an atmosphere of 5% $CO_2$, and 95% air. After separating the cells from the nutrient medium, both the number of living cells and the overall number of cells are determined by MTT staining test (MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide).

**Measuring the cell inhibition**

Samples of polymers according to the invention are placed in wells of standard microtiter plates and are held there by means of PTFE inserts which are sterilized beforehand with ethanol. Samples, wells and PTFE inserts are additionally sterilized by irradiation with ultraviolet light for 15 minutes. The cell suspension of known concentration is then added to the polymer samples, and the treated samples are kept at 37°C in an atmosphere of 95% air and 5% $CO_2$. After eight days have gone by, the cells are washed with phosphate buffer solution, suspended in 0.05% by weight trypsin solution and 0.02% by weight EDTA solution at pH 7.4, and counted with the aid of a Coulter counter.

The reference sample used is a sample prepared in the same way which is obtained by polymerizing component III of the respective polymer according to the invention. The inhibition of cell proliferation is expressed as a percentage quotient of the number of cells on the reference samples to the number of cells on the polymers according to the invention.

**Preparing samples of the polymers according to the invention.**

**Example 1:**

Under a nitrogen atmosphere, 218.2 g of methyl methacrylate, 12.1 g of methacrylic acid and 14.8 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Methacrylate: | 14 mol-% |
| Sodium Styrenesulfonate: | 11 mol-% |
| Methyl methacrylate: | 75 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 1.27.

**Example 2:**

Under a nitrogen atmosphere, 216.3 g of methyl methacrylate, 13.8 g of acrylic acid and 9.9 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Acrylic acid: | 10 mol-% |
| Sodium styrenesulfonate: | 9 mol-% |
| Methyl methacrylate: | 81 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 1.11.

**Example 3:**

Under a nitrogen atmosphere, 235 g of styrene, 6.1 g of methacrylic acid and 14.8 g of sodium sytrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at

50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Methacrylic acid: | 15 mol-% |
| Sodium styrenesulfonate: | 7 mol-% |
| Sytrene: | 78 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 2.14.

**Example 4:**

Under a nitrogen atmosphere, 227.5 g of styrene, 8.1g of acrylic acid and 24.7 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 20 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Acrylic acid: | 11 mol-% |
| Sodium sytrenesulfonate: | 12 mol-% |
| Styrene: | 77 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 0.9.

**Example 5:**

Under a nitrogen atmosphere, 310.0 g of n-butyl methacrylate, 12.1 g of methacrylic acid and 14.8 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 20 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Methacrylic acid: | 14 mol-% |
| Sodium styrenesulfonate: | 9 mol-% |
| n-butyl methacrylate: | 77 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 1.6.

**Example 6:**

Under a nitrogen atmosphere, 306.7 g of n-butyl methacrylate, 13.8 g of acrylic acid and 9.9 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Acrylic acid: | 10 mol-% |
| Sodium styrenesulfonate: | 8 mol-% |
| n-butyl methacrylate: | 82 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 1.3.

**Example 7:**

Under a nitrogen atmosphere, 220 g of styrene, 15.6g of acrylic acid and 14.8 g of sodium styrenesulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Acrylic acid: | 19 mol-% |
| Sodium styrenesulfonate: | 5 mol-% |
| Styrene: | 76 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 3.8.

**Example 8:**

Under a nitrogen atmosphere, 310.6 g of n-butyl methacrylate, 10.4 g of acrylic acid and 14.8 g of sodium styrenefulfonate were dissolved in 500 ml of dimethyl sulfoxide. The solution was heated to 70°C with stirring. Then 2.3 g of azobisisobutyronitrile dissolved in 30 ml of dimethylsulfoxide were added dropwise over the course of 2 minutes. The polymerization was conducted at 70°C over a period of 16 hours. The resulting product was subsequently precipitated in a fourfold excess of ice-water, then subjected to extraction with water in a Soxhlet for 24 hours and dried in vacuo at 50°C.

Subsequent analysis of the composition by $^1$H-NMR showed:

| | |
|---|---|
| Acrylic acid: | 8 mol-% |
| Sodium styrenesulfonate: | 11 mol-% |
| n-butyl methacrylate: | 81 mol-% |

From these values it was found that the ratio of carboxylate groups to sulfonate groups is 0.7.

**Preparing membranes from the polymers according to the invention**

**Example 9:**

A 5% strength dimethyl sulfoxide solution of a polymer according to the invention was prepared. The solution was poured into a Petri dish and the solvent was removed from the sample under reduced pressure at 80°C. The membrane was then cut into sections each of 0.5 cm$^2$ (for the scintillation measurement) or of 2 cm$^2$ (for the ATP measurements) and subjected to extraction with water for 24 hours. Before the following biological investigations, the membrane sections were washed three times for three hours in each case in Michaelis buffer solution (pH = 7.33) and were stored at -4°C until further examination.

The adhesion of the bacterial strains Staphylococcus epidermidis, Streptococcus pyogenes and Staphylococcus aureus was investigated on polymer samples obtained in accordance with Examples 1 to 8. The measurement of the bacterial adhesion to these samples by the scintillation technique and the static determination of the ATP gave bacterial adhesion inhibitions of more than 95%; dynamic determination of the ATP gave bacterial adhesion inhibitions of more than 93%.

## Preparing polymer coatings by dipping

### Example 10:

A 5% strength methyl ethyl ketone solution of a polymer according to the invention was prepared. A 10 cm x 8 cm x 0.04 cm polyamide film was immersed in this solution for 10 seconds. The film was removed and dried under reduced pressure at 50°C for 10 hours. The coated film was then cut into sections each of 0.5 $cm^2$ (for the scintillation measurement) or of 2 $cm^2$ (for the ATP measurements) and was subjected to extraction with water for 24 hours. Before the following biological investigations, the membrane sections were washed three times for three hours in each case in a Michaelis buffer solution (pH = 7.33) and stored at -4°C until further investigation.

The adhesion of the bacterial strains Staphylococcus epidermidis, Streptococcus pyogenes and Staphylococcus aureus was investigated on polymer samples obtained in accordance with Examples 1 to 8. The measurement of the bacterial adhesion to these samples by the scintillation technique and the static determination of the ATP gave bacterial adhesion inhibitions of more than 99%; dynamic determination of the ATP gave bacterial adhesion inhibitions of more than 96%.

**Example 11:**

A 5% strength acetone solution of a polymer according to the invention was prepared. A 10 cm x 8 cm x 0.03 cm polyethylene film whose surface had been activated beforehand by treatment for 3 minutes with the 172 nm radiation from an excimer source, was immersed in this solution for 15 seconds. The film was removed and dried under reduced pressure at 50°C for 10 hours. The coated film was then cut into sections each of 0.5 cm$^2$ (for the scintillation measurement) or of 2 cm$^2$ (for the ATP measurements) and was subjected to extraction with water for 24 hours. Before the following biological investigations, the membrane sections were washed three times for three hours in each case in a Michaelis buffer solution (pH = 7.33) and stored at -4°C until further investigation.

The adhesion of the bacterial strains Staphylococcus epidermidis, Streptococcus pyogenes and Staphylococcus aureus was investigated on polymer samples obtained in accordance with Examples 1 to 8. The measurement of the bacterial adhesion to these samples by the scintillation technique and the static determination of the ATP gave bacterial adhesion inhibitions of more than 98%; dynamic determination of the ATP gave bacterial adhesion inhibitions of more than 96%.

**Example 12:**

A 5% strength acetone solution of a polymer according to the invention was prepared. A 10 cm x 8 cm x 0.04 cm polyether-block-amide film, was immersed in this solution for 10 seconds. The film was removed and dried under reduced pressure at 50°C for 10 hours. The coated film was then cut into sections each of 0.5 $cm^2$ (for the scintillation measurement) or of 2 $cm^2$ (for the ATP measurements) and was subjected to extraction with water for 24 hours. Before the following biological investigations, the membrane sections were washed three times for three hours in each case in a Michaelis buffer solution (pH = 7.33) and stored at -4°C until further investigation.

The adhesion of the bacterial strains Staphylococcus epidermidis, Streptococcus pyogenes and Staphylococcus aureus was investigated on polymer samples obtained in accordance with Examples 1 to 8. The measurement of the bacterial adhesion to these samples by the scintillation technique and the static determination of the ATP gave bacterial adhesion inhibitions of more than 98%; dynamic determination of the ATP gave bacterial adhesion inhibitions of more than 95%.

**Conditioning the samples of polymers according to the invention**

**Example 13:**

A membrane according to Example 9 and the films coated with the polymers according to the invention, according to Examples 10 to 12, were sterilized by irradiation with ultraviolet light for 15 minutes. The samples pretreated in this way were then held three times for three hours in each case in 0.15 molar sodium chloride solution, and then washed for three hours with distilled water. In the following purification step, they were placed three times for three hours in each case in a phosphate buffer solution having the following composition:

| | |
|---|---|
| $CaCl_2H_2O$ | 0.132 g/l |
| KCl | 0.2 g/l |
| $KH_2PO_4$ | 0.2 g/l |
| $MgCl_26H_2O$ | 0.1 g/l |
| NaCl | 8 g/l |
| $Na_2HPO_4$ | 1.15 g/l |

The samples were subsequently irradiated again with ultraviolet light for 15 minutes. These samples were stored for about 16 hours at 37°C in a DMEM (Dulbecco's Modified Eagles Medium) solution. Finally, the samples were kept at 37°C under an atmosphere of 5% $CO_2$ and 95% air in a DMEM solution to which antibiotics, L-glutamine and 10% by volume of fetal calf serum had been added.

The polymers according to the invention prepared according to Examples 1, 2 and 5 were either processed to give a membrane (Example 9) or applied to standard polymers (Examples 10 to 12). These samples were subsequently conditioned as in Example 13, and the cell proliferation was determined in accordance with the method described.

For all samples, the inhibition of cell proliferation exceeded 98%.

CLAIMS:

1. A process for preparing a bacteriophobic and optionally cell proliferation-inhibiting polymer surface, which comprises using for this purpose a water-insoluble polymer A which is obtained by free-radical polymerization of:

(a) at least one monomer of the general formula:

$$R-(A)_a \qquad I$$

in which R is an aliphatically unsaturated organic radical having the valence a,

A is a carboxyl group -COOH, a sulfuric acid group $-OSO_2OH$, a sulfonic acid group $-SO_3H$, a phosphoric acid group $-OPO(OH)_2$, a phosphonic acid group $-PO(OH)_2$, a phophorous acid group $-OP(OH)_2$, a phenolic hydroxyl group or a salt of one of these groups, and

a is 1, 2 or 3;

with the proviso that, when the monomer of the formula I contains a carboxyl group -COOH or a carboxylate group, either this monomer contains at least one further radical A having a different one of the definitions specified for A, or at least one further monomer of the formula I is also used in which A has a different one of the definitions specified for A; and

(b) at least one other aliphatically unsaturated monomer.

2. A water-insoluble, bacteriophobic and optionally cell proliferation-inhibiting polymer obtained by free-radical copolymerization of:

(c) at least one aliphatically unsaturated monomer which contains a carboxyl or carboxylate group or a corresponding functionalized derivative thereof, as component I,

(d) at least one aliphatically unsaturated monomer containing a sulfonic acid or sulphonate group or a corresponding functionalized derivative thereof, as component II, and

(b) at least one further aliphatically unsaturated monomer, as component III;

the corresponding functionalized derivative being converted when required, after copolymerization and at least on a surface, into a carboxyl or carboxylate group or a sulfonic acid or sulfonate group, respectively; with the proviso that a molar ratio of the carboxyl or carboxylate group present in the polymer to the sulfonic acid or sulfonate group is from 0.4 to less than 3.

3. A polymer as claimed in claim 2, wherein a bifunctional, aliphatic unsaturated monomer containing a carboxyl or carboxylate group and a sulfonic acid or sulfonate group is used as the components I and II.

4. A polymer as claimed in claim 2 or 3, wherein a total content of the component I and the component II is from 0.5 to 30 mol% of the polymer.

5. A polymer as claimed in any one of claims 2 to 4, wherein a molar ratio of the carboxyl or carboxylate group present in the polymer to the sulfonic acid or sulfonate group is from 0.5 to 2.14.

6. A polymer as claimed in claim 5, wherein the molar ratio is from 0.7 to 2.14.

7. A polymer as claimed in any one of claims 2 to 4, wherein the polymer has a surface which is bacteriophobic and inhibits cell proliferation.

8. A polymer as claimed in claim 7, wherein the molar ratio is from 0.4 to 2.

9. A process for preparing a water-insoluble, bacteriophobic and optionally cell proliferation-inhibiting polymer B which comprises subjecting to free radical copolymerization:

(c) at least one aliphatically unsaturated monomer which contains a carboxyl or carboxylate group, or a corresponding functionalized derivative thereof, as component I,

(d) at least one aliphatically unsaturated monomer containing a sulfonic acid or sulphonate group, or a corresponding functionalized derivative thereof as component II, and

(b) at least one further aliphatically unsaturated monomer as component III;

the correspondingly functionalized derivative being converted where required, after copolymerization and at least on a surface, into a carboxyl or carboxylate group or a sulfonic acid or sulfonate group, respectively,

with the proviso that a molar ratio of the carboxyl or carboxylate group present in the polymer to the sulfonic acid or sulfonate group is from 0.4 to less than 3.

10. The process as claimed in claim 9, wherein a bifunctional, aliphatic unsaturated monomer containing a

carboxyl or carboxylate group and a sulfonic acid or sulfonate group is used as the components I and II.

11. The process as claimed in claim 9 or 10, wherein a total content of the component I and the component II is from 0.5 to 30 mol% of the polymer.

12. The process as claimed in any one of claims 9 to 11, wherein a molar ratio of the carboxyl or carboxylate group present in the polymer to the sulfonic acid or sulfonate group is from 0.5 to 2.14.

13. The process as claimed in claim 12, wherein the molar ratio is from 0.7 to 2.14.

14. The process as claimed in any one of claims 9 to 11, wherein the polymer has a surface which is bacteriophobic and inhibits cell proliferation.

15. The process as claimed in claim 14, wherein the molar ratio is from 0.4 to 2.

16. A process for producing an article having a bacteriophobic and optionally cell proliferation-inhibiting surface, which comprises making the article wholly or in part by the polymer as claimed in any one of claims 1 to 8 or coating a surface of an article made of a plastic, ceramic or metal material with the polymer as claimed in any one of claims 1 to 8.

17. The process as claimed in claim 16, wherein the article is selected from the group consisting of textiles, furniture, instruments, flooring, wall or ceiling surfaces, tubes, hoses, packaging, window frames and medical articles.

18. A process for producing an article having a bacteriophobic and optionally cell proliferation-inhibiting

coating, which comprises coating a surface of an article made of a plastic, ceramic or metal material with the polymer as claimed in any one of claims 2 to 8.

19. The process as claimed in claim 18, wherein the article is selected from the group consisting of textiles, furniture, instruments, flooring, wall or ceiling surfaces, tubes, hoses, storage containers, packaging, window frames and medical articles.

20. The process as claimed in claim 19, wherein the article is a medical article selected from the group consisting of catheters, drainage tubes and intraocular lenses.

21. An article having a bacteriophobic and optionally cell proliferation-inhibiting surface, the article being made of the water-insoluble bacteriophobic polymer as claimed in any one of claims 2 to 8.

22. An article as claimed in claim 21, wherein the article is selected from the group consisting of textiles, furniture, instruments, flooring, wall or ceiling surfaces, tubes, storage containers, packaging, window frames and medical articles.

23. An article comprising a substrate made of a plastic, ceramic or metal material and a bacteriophobic coating on a surface of the substrate, the coating comprising a water-insoluble, bacteriophobic polymer as claimed in any one of claims 2 to 8.

24. An article as claimed in claim 23, wherein the article is selected from the group consisting of textiles, furniture, instruments, flooring, wall or ceiling surfaces,

tubes, storage containers, packaging, window frames and medical articles.

25. An article as claimed in claim 24, which is a medical article selected from the group consisting of catheters, drainage tubes and intraocular lenses.

26. A polymer as claimed in claim 2, wherein:

the component I is a carboxylic acid selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, maleic acid, sorbic acid, caffeic acid and fumaric acid and is present in the polymer in a free carboxyl group or physiologically acceptable salt form;

the component II is a sulfonic acid selected from the group consisting of vinylsulfonic acid, allylsulfonic acid, methallylsulfonic acid, vinylbenzenesulfonic acid, vinyltoluenesulfonic acid and vinylxylenesulfonic acid or a physiologically acceptable salt thereof and is present in the polymer in the physiologically acceptable salt form;

the component III is a nonionic monomer contained in a sufficient content to make the polymer insoluble in water and is selected from the group consisting of vinyl alkyl ketones, vinyl esters, alkyl (meth)acrylates, (meth)acrylonitrile, (meth)acrylamide, 1-butene, 1-hexene, 1,3-butadiene, isoprene, chloroprene, vinyl chloride, vinylidene chloride, styrene, methylstyrene, halogenostyrene, tris(trimethylsiloxy)-methacryloyloxypropylsilane and tris(trimethylsiloxy)-acryloxypropylsilane; and

the components I and II are contained at a I/II molar ratio of from 0.4 to less than 3 and of a total content of 0.5 to 30 mol% based on the polymer.

27. A polymer as claimed in claim 26, wherein the I/II molar ratio is from 0.7 to 2.14.

28. A polymer as claimed in claim 26 or 27, wherein the component I is acrylic acid or methacrylic acid and is present in the free carboxyl group or salt form in the polymer; the component II is a physiologically acceptable salt of vinylsulfonic acid, allylsulfonic acid or vinylbenzenesulfonic acid and is present in the physiologically acceptable salt form in the polymer.

29. A polymer as claimed in claim 28, wherein the component II is an alkali metal salt of vinylbenzensulfonic acid and is present in the alkali metal salt form in the polymer.

30. A polymer as claimed in any one of claims 26 to 29, wherein the component III is a $C_1$-$C_{10}$ alkyl (meth)acrylate or styrene or both.

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