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Schwarcz

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[54] **METHOD FOR MAINTAINING THE NORMAL INTEGRITY OF BLOOD**

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[63] Continuation-in-part of Ser. No. 246,327, April 21, 1972, abandoned.

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[56] **References Cited**

UNITED STATES PATENTS

3,633,578	1/1972	Roth	3/1 X
3,663,288	5/1972	Miller	117/138.8 A X
3,722,599	3/1973	Robertson	128/334 R

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[57] **ABSTRACT**

Thromboresistant biomedical articles are provided which are useful in the fields of subdermal surgical implants, laboratory apparatus and blood containers. These articles have at least a thin surface coating of an organic polymeric material having fluoroalkyl side chains and simple anionic side groups.

19 Claims, No Drawings

METHOD FOR MAINTAINING THE NORMAL INTEGRITY OF BLOOD

This is a continuation-in-part of application Ser. No. 246,327, filed Apr. 21, 1972 and now abandoned.

BACKGROUND OF THE INVENTION

1. Field of the invention

This invention relates to biomedical articles that resist the clotting of human blood and generally that of warm blooded animals. It describes the structure of these articles and the various modes of their manufacture. One of such articles is a subdermal implant. Examples are subdermal prosthesis such as artificial blood vessels to correct atherosclerotic shrunken passageways or to eliminate aneurisms in cardiac assist devices and in artifical hearts and heart valves to replace or augment the function of the natural heart. Other subdermal prosthetic devices of this invention include reinforced and non reinforced sheetings, rubbers to reconstruct fractures, coronary arteries, denture soft liners, denture base materials, sponge subdermal implant materials, mammary prosthesis, testicular prosthesis, atoplasty prosthesis, rhinoplasty implants, scleral buckler designed for use with Everett technique, rubbers used to remedy defects following facial trauma and coiled capillary tubing membrane oxygenators for complete cardio-pulmonary bypass; also suction drainage of orthopedic wounds, arterial venous shunts, abdominal drains, catheters for intravenous administration of fluids for withdrawal of serial blood samples, for percutaneous flow-guided cardia catheterization, continuous monitoring of blood glucose, intestinal decompression tubes, various catheters and thoriac drains. Other implanted articles of this invention include circulatory assist devices, tubes for blood transfusion, the implants of electrical devices and mechanical devices such as prosthetic valves and sutures. Other biomedical articles of this invention include thromboresistant surgical instruments, laboratory apparatus used for blood handling and blood handling and blood containers for storage.

2. Description of the Prior Art

One of the most striking property of blood is its tendency to undergo clotting, or thrombosis. This has been the major problem encountered in the use of subdermal prosthesis.

The detailed mechanisme of thrombosis is still not established. Its normal course involves a series of complex reactions that, once initiated result in the formation of thrombosis. Two processes may occur:

1. The absorption of proteins leading to coagulation;

2. The adhesion of platelets at first to the solid, foreign surface, and then to each other. The growing mass of platelets forms a thrombosis which adheres to the solid surface.

Those surfaces that do not cause or significantly prolong the time of thrombosis are commonly called nonthrombogenic or thromboresistant surfaces. A major need exists for a great variety of thromboresistant articles. Various attempts have been made to find a suitable material which exhibits nonthrombogenic properties or a method of treating known materials to render them thromboresistant. Organic polymers are generally thrombogenic and therefore require the use by the patient of anticoagulant drugs such as heparin and coumarin derivatives.

Various organic polymers have been coated recently with heparin. Although this material displays some degree of thromboresistance, the coating eventually washes away with the flow of blood and it is difficult to fabricate.

There have been attempts to obtain thromboresistant biomedical articles from fluorinated polymers and sulfonated polymers. However, none of them are performing in a satisfactory manner. This is due, in the opinion of the author of the present invention, to the disposition, the length and the relative lengths of the various groups in the polymer.

SUMMARY OF THE INVENTION

My invention provides thromboresistant biomedical articles useful in the fields of subdermal implants, surgical instruments, laboratory apparatus and blood containers. These articles are composed, at least on their surface, of an organic polymeric material having side chains of the formula $C_nF_{2n+1}C_mH_{2m}$—, wherein n and m are integers, n ranging from 1 to 28 and the sum of n and m from 1 to 28, and an anionic group.

DESCRIPTION OF THE PREFERRED EMBODIMENT

The biomedical articles of this invention are characterized by their thromboresistant surface. The surface of the said articles are characterized by an organic polymeric material having fluoroalkyl side chains of the formula $C_nF_{2n+1}C_mH_{2m}$—, wherein n and m are integers, the range of n extending from 1 to 28 and the sum of n and m from 2 to 28. The number of fluoroalkyl side chains relative to the number of main-chain-atoms in one recurring unit ranges from 1:2 to 1:10, preferably from 1:2 to 1:5. The atoms that are in the main or linear direction of the polymer such as the carbon atoms in polyethylene and poly(vinyl alcohol), are the only ones considered main-chain-atoms. Linear fluoroalkyl side chains with values of the integer n ranging from 8 to 28 are particularly effective ones to give the articles of this invention a high degree of thromboresistance.

The presence of another, generally shorter side chain, which is an anion or one comprising an anion, generally enhances the thromboresistivity of the polymer. However, its presence is required only in the cases wherein the said fluoroalkyl side chain is branched (non linear) and in cases wherein the value of the integer n ranges from 1 to 7.

A feature of the said organic polymeric materials of this invention is that their thromboresistant character is provided by the side chains, the main chain having an essentially supportive role. This might be due to the fact that the fluoroalkyl side chained polymers of this invention have simultaneously low surface tension and negative zeta potential, properties thought necessary for thromboresistance according to certain theories.

The invention is described hereinafter in greater detail by reference to the examples which show preferred embodiments of the invention. It should be understood however that the examples hereinafter given are for the purposes of illustration only and that the invention in its broader aspects is not limited thereto.

Examples of the said fluorinated side chains are $CF_3(CF_2)_7$—, $CF_3(CF_2)_{11}(CH_2)_{16}$—, $CF_3(CF_2)_{22}CH_2$—, i-$C_4F_9(CH_2)_{10}$—, $CF_3(CH_2)_2$, C_3F_7—.

The anionic groups can be either in their acidic form, their salt or their partially neutralized form. Example of

simple anionic groups are carboxylate, sulfonate, sulfate, phosphate and phosphites. Examples of the salt forming positive ions are sodium, potassium, lithium, ammonium, magnesium, tertiary amines such as N-methylmorpholine.

The ratio of the number of the said fluoroalkyl groups to the number of said anionic groups ranges from 0.5:1 to 50:1, preferably from 1:1 to 20:1. In general, this ratio decreases as the ionic strength decreases. The number, strength and degree of neutralization of said anionic groups should be limited in order to avoid solvation or excessive swelling of the fluorinated polymer by the blood.

The said fluoroalkyl side chain may be directly attached to the main chain of the organic polymer. It can also be attached by an intermediate divalent radical, such as —O—, —CO—, —SO—, —SO_2—, —SO_2NH—, —CH_2O, —COO—, —NHCO—, —NHCOO—, —NHCONH—, —$POCH_3$—, —POC_2H_5, —, —SO_2NCH_3—, —$SO_2NC_2H_5$—.

Similarly, the anionic group may be directly attached to the main chain of the organic polymer or through an intermediate divalent radical. Such radicals are exemplified by —CH_2—, —C_2H_4—, —OC_2H_4—, —$(CH_2)_8$—, —$SO_2NHC_2H_4$—,—$(CF_2)_{15}$—.

Biomedical articles of this invention may be entirely composed of the said organic polymeric materials with the fluoroalkyl side chains. However, the particular mechanical and electrical properties required of the various biomedical articles, or the higher cost involved may require them to comprise a surface portion and a substrate portion. The surface portion is composed of the said thromboresistant organic polymer. The substrate portion may be any solid material that satisfies the properties required of the biomedical article. Thus, substrate materials comprise plastics, rubbers, metals, glass, ceramics. The use of a coating technic is particularly advantageous for making surgical instruments, laboratory apparatus, blood containers and heart valves.

Examples of plastic substrates are isotactic polyolefins, such as polypropylene, polystyrene, polyethylene, poly(4-methylpentane); polyesters such as poly(1,4-cyclohexylene terephthalate), poly(ethylene terephthalate); polyacrylates such as polymethylmethacrylate, polyco (ethylacrylate-acrylic acid); polyurethanes such as the ones prepared from a hydroxy terminated polyether or polyester and methylenebis (phenylisocyanate); polycarbonates such as poly(2,2-propanebis(4-phenyl carbonate); fluorinated polyolefins such as poly(tetrafluoroethylene); chlorinated polyolefins such as polyvinylchloride; proteins such as wool, casein; cellulose, cellulose derivatives such as cellulose acetate, cellulose acetate butyrate and other polysaccharides. Examples of rubber substrates are silicone rubbers such as poly(dimethylsiloxane poly(methylphenyl siloxane); hydrocarbon rubbers such as butyl rubber, ethylene-propylene rubber; nitrile rubbers such as polyco(butadieneacrylonitrile); fluorinated rubbers such as fluorinated ethylene-propylene rubber, fluorinated polyurethanes; urethane rubbers such as the ones prepared from hydroxy terminated polyethers or polyesters and methylenebis(-phenylisocyanate); polyether rubbers such as poly (propylene oxide) and chlorosulfonated rubbers such as chlorosulfonated ethylene-propylene rubber.

Metallic substrates include stainless steel, aluminum, alloys of chromium, nickel, cobalt and magnesium.

Examples of the said organic polymeric materials having linear fluoroalkyl side chains wherein the said integer *n* ranges between 8 and 28, the sum of *n* and *m* between 8 and 28 and the said polymer has no anionic groups attached to the main chain are:

poly(1,1,2,2- tetrahydropentadecafluorononyl acrylate)
poly(1,1-dihydropentacosafluorotridecyl acrylate)
poly(1,1-dihydropentatetracontafluorotricosyl methacrylate)
poly(1,1,2,2-tetrahydrononacosafluorohexadecyl vinyl ehter)
poly (vinylperfluorooctadecane)
poly (perfluoro-1-octadecene)
poly(vinyl perfluorostearate)
poly(N-1,1-dihydropentatriacontafluorooctadecyl hexamethylene urea)
poly(methyl-1,1,2,2-tetrahydrotritriacontafluorooctadecyl siloxane)
poly [di(1,1,2,2-tetrahydrotricosafluorotridecyl) siloxane]
poly(N-1,1-dihydropentatriacontafluorooctadecyl hexamethylene adipamide).

Examples of said organic polymeric materials having linear or branched fluoroalkyl side chains wherein the said integer *n* ranges between 1 and 28, the sum of *n* and *m* between 2 and 28 and the said anionic group is bonded to the main chain of the polymer, are (the propertion of monomers in the copolymers are expressed in mole %):

polyco(1,1-dihydropentadecafluorooctyl methacrylate — 10% sodium acrylate)
polyco (1,1,2,2,-tetrahydrotrifluoropropyl acrylate — 5% maleic acid)
polyco(1,1,2,2-tetrahydropentadecafluorononyl acrylate — 30% methacrylic acid — 15% sodium methacrylate)
poly(carboxyethyl-1,1,2,2-tetrahydrotrifluoropropyl siloxane)
polyco(methyl-3,3,3-trifluoropropyl siloxane — 20% carboxyethyl-methyl siloxane)
polymers of fluoroalkyl esters, amides and imides of maleic and fumaric acids
The copolymers with ethylene, styrene, methylvinyl ether and vinyl acetate of fluoroalkyl esters, amides and imides of maleic and fumaric acids
The copolymers with maleic, fumaric and acrylic acids and their anhydrides of fluoroalkyl esters, amides and imides of maleic and fumaric acids
the 1,1-dihydronanafluoropentyl monoester of polyco (50% ethylene — 23% maleic acid — 23% potassium maleate)
the 1,1-dihydropentadecafluorooctyl monoamide of polyco (80% methylvinyl ether — 10% fumaric acid — 10% sodium fumarate)
polyco(vinyl 1,1-dihydropentatriacontafluorooctadecyl carbamate — 15% vinyl disodium phosphite)
polyco (vinyl perfluoropropianate — 10% acrylic acid)

These compounds are all linear organic polymers having intrinsic viscosity values higher than 0.04, preferably higher than 0.07. They can be prepared by conventional polymerization techniques such as the free radical and ionic addition polymerization techniques or

condensation polymerization techniques of the monomers. Another method consists of introducing an anionic group to the polymer by carboxylation, sulfonation, phosphorilation, etc, and further reacting with a fatty fluorinated compound containing a functional group. Such compounds are, for example, perfluorooctadecanoyl chloride and 1,1-dihydrotricosafluorododecyl alcohol. These techniques are well documented in the art of polymer synthesis.

After preparation, the polymer is then shaped into the desired biomedical articles, e.g. heart valves, blood vessel, tubings etc. The shaping can be done by any conventional means, uch as extruding, molding, casting. After proper sterilization, the biomedical article is ready for use.

An effective way to prepare a thromboresistant biomedical article of this invention is to react the polymeric material of this invention containing the said anionic group with a stochiometrically defective amount of a cationic type polymer, such as poly-2-vinylpyridine, poly(vinylbenzyldimethylamine), polyco(styrene-4-vinylpyrridine).

Another way to prepare a thromboresistant biomedical article of this invention is to coat the potentially blood contacting surfaces of the shaped article made of a plastic, a rubber, a metal or glass with the said organic polymeric material having the fluoroalkyl side chains exemplified above. Any of the conventional coating procedures can be used, such as coating from a solution, emulsion, suspension followed by solvent evaporation, or a hot melt coating technique. The bond between he substrate and the coating can be improved, if necessary, by conventional surface treatment techniques, such as corona discharge, flame treatment, irradiation, or priming with a polar polymeric substance. These coating and priming procedures are well documented in the art of coating technology.

A biomedical article of this invention can be prepared by the use of still another technique. This technique consists of coating the shaped article, made of a plastic, a rubber, a metal or glass, with the monomers from which the said organic polymeric materials, having the fluoroalkyl side chains, and examplified above, are prepared, and let the polymerization proceed on the surface. Similar coating and priming procedures can be used as the ones described above. The polymerization on the surface of the article can be carried out by conventional techniques used in the art of polymer synthesis and coatings, such as the use of catalysts, heat, oxygen, moisture, radiation, peroxides etc.

Still another way to achieving the objectives of this invention is to graft an anionic group and the said perfluoroalkyl group $C_nF_{2n+1}C_mH_{2m}$—, onto the surface of a shaped biomedical article made of a plastic or a rubber. Examples of such surface grafting reactions are as follows:

the grafting of perfluorooctadecanoyl chloride onto a shaped biomedical article made of poly(tetramethylene urea), poly(tetramethylene hexamethylene dicarbamate), cellulose fibers, wool, silk, nylon;

the grafting of sulfuric acid and perfluorohexadecanoic acid onto the shaped article made of poly(vinylalcohol), cellulose, casein;

the grafting of 1,1,2,2-tetrahydroheptafluoropentanol, onto a preshaped article made of polyco(acrylic acid — 10% sodium acrylate);

the grafting of 1,1-dihydropentacosafluorotridecyl iodide onto a shaped article made of polyco(ethylene-monosodium maleate), and onto sodium cellulose sulfate;

the radiation grafting of 1,1,2,2-tetrahydrotritriacontafluorooctadecyl vinylether to a shaped article made of poly(ethylene terephtalate);

the grafting of 1,1-dihydrohencosafluoroundecyl amine onto a shaped biomedical article made of polyethylene which has been previously sulfonated with concentrated sulfuric acid and the sulfonate groups partially neutralized with a buffer solution having a pH of 7.5.

There are still other means to prepare the polymers of this invention. For example polymers having unbranched higher alkyl side chains can be fluorinated with fluorine gas. Examples of such polymers are polyvinylstearate, polyco(vinylacetate-docosylmaleate sodium salt).

EXAMPLE 1

Ninety (90) grams (0.1 moles) of 1,1-dihydrotritriacontafluoroheptadecyl acrylate and 1.14 grams (0.01 moles) of 1-hexenoic acid are copolymerized by using 0.5% azobisisobutyronitrile as the initiator and toluene as the solvent medium. The reaction is carried out in crew cup vials at 75–80°C. for 16 hours. The copolymer is then purified by adding methanol to the solution, filtered, redissolved in 1,2,2-trichlorotrifluoroethane, and this procedure is repeated three times. The solid polymer is then dried in a vacuum oven at 60°C. for 64 hours. The intrinsic viscosity measured in hexafluorodimethyl benzene is 0.2.

A glass tube is then treated with a 5% trichlorotrifluoroethylene solution of the copolymer by filling the tube, inverting it and allowing the excess liquid to drain out. Following evaporation of the solvent, the coated test tube is sterilized.

Five (5) ml of freshly drawn whole blood from the lower vena cava of a rabbit as added and the test tube is periodically tipped to observe clot formation. No evidence of clot formation is observed for several hours. A control test tube, not coated with a layer of the copolymer, is tested in an identical manner, and clotting occurs within 7 minutes.

EXAMPLE 2

A 1:1 molar mixture of potassium acrylate and 1,1-dihydroheptatriacontafluorononadecyl acrylate is grafted onto a bidirectionally oriented poly(ethylene terephtalate) film previously subjected to 2 MeV radiation at −80°C. A blood bag is formed from the surface-grafted film and sterilized. Plasma from the blood of a human donor is stored in the said bag for an extended period at 5°C. The plasma shows no signs of thrombus formation and it is physiologically acceptable for human use.

EXAMPLE 3

A copolymer of octadecyl vinyl ether with 1-dodecenoic acid sodium salt is used to coat, from a 5% toluene solution, a commercially available fluoropolymer heart valve previously submitted to electron radiation to obtain better adhesion. It is then fluorinated in the dark by exposure to 5% fluorine diluted with 95% nitrogen at room temperature for 2 weeks. The coated heart valve is then sterilized and when implanted in an

animal, such as a dog, the implant, in accordance with this invention, will be found to sustain the life of the animal.

EXAMPLE 4

A silicone rubber having a fluoroalkyl side chain is prepared by the following customary procedure. Methyl trichlorosilane is reacted with 1,1,2,2,3,3,4,4-octahydropentadecafluorohexadecyl magnesium chloride, the dichloro product separated from the reactive mixture by vacuum distillation and followed by polymerization with the addition of water. It is then mixed with 2% dimethyltindilaurate catalyst, molded into a tube of 0.05 inch inside diameter and cured at 150°C. for 48 hours under nitrogen.

The tubing is tested in vivo using a jugular vein of a dog. The vein is exposed and severed in a standard surgical manner. The tube, after sterilization, is formed into a loop and to each end of the vein is attached one end of the tubing. Circulation through the vein is resumed and blood now is passing through the tubing.

The implanted artifical vein, in accordance with this invention, will not be found to be harmful to the life of the animal.

EXAMPLE 5

1-perfluorooctadecene, 88.1 g (0.1 mol), is copolymerized with maleic anhydride, 9.6 g(0.1 mole), using a technique similar to that described in Example 1. The copolymer is then boiled in an aqueous sodium hydroxide solution containing a small amount of a fluorinated anionic surfactant. This reaction yields the sodium salt of the maleic acid portion of the polymer. The polymer is then purified by a repeated solutionpreceipitation technique.

A cannula made of polypropylene is surface oxidized in a circulating air oven at 110° C. to obtain better adhesion. It is then coated with a 5% trichlorotrifluoroethylene solution of the polymer prepared in this example and the solvent evaporated in an air iven at 60°C. After sterilization, the cannula is used as conduit replacement in a heart-lung machine. After several months of use no evidence of thrombus formation on the cannula will be reported.

EXAMPLE 6

Poly(vinyl alcohol) of 120,000 molecular weight, 45 g(1 mole), is sulfated with sulfur trioxide dissolved in sulfuric acid to yield the sulfate ester. As deduced by titration with sodium hydroxide one out of every 10 hydroxyl groups is sulfated. The polymer is further reacted with perfluorohexadecanoyl chloride in N-methyl morpholine to yield polyco(vinyl perfluorohexadecanoate-vinyl sulfate N-methylmorpholine salt), which then is purified by successive crystallizations. The copolymer is then coated on a Nylon cannula and sterilized, all in the similar way as described in Example 5. The coated cannula is used as conduit tubing in a blood machine. Equivalent results to those described in Example 5 are obtained.

EXAMPLE 7

A 1:1 copolymer of methylvinylether maleic anhydride, 15.6 g (0.1 mole) having an intrinsic viscosity of 2.5 in methylethyl ketone, is reacted in 500 ml of methylethyl ketone at the boil with 1,1,2,2-tetrahydrohencosafluorododecyl amine, 66.3 g (0.1 mole). The fluorinated acid-amid is then precipitated in methanol, filtered, washed, and reacted with sodium hydroxide dissolved in alcohol. The polymer thus obtained is polyco[methylvinyl ether-sodium salt of maleic acid mono(1,1,2,2-tetrahydrohencosafluorododecyl)amide], which is then purified by repeated solvation-precipitation.

The fluorinated copolymer is then molded in a hot press into a 0.05 in. inside diameter catheter having a wall thickness of 0.005 in. and sterilized. When surgically implanted in the jugular vein of a dog, similar results to those obtained in Example 4 will be reported.

EXAMPLE 8

Vinyl perfluorodocosyl ether, 11.8 g (0.1 mole) is polymerized and purified using a technique similar to that described in Example 1. The intrinsic viscosity measured in trichlorotrifluoroethane is 0.2. A stainless steel tubing is coated with a 5% trichlorotrifluoroethylene solution of this polymer, and the solvent evaporated at 60°C. in a vacuum oven. After sterilization the tubing is used as an arterialvenous bypass in a hemidialysis machine. No thrombus formation will be evident after usage of the machine for several months.

EXAMPLE 9

A cannula made of polyethylene is phosphorilated on the surface with phosphorous trichloride at 60°C. in the presence of oxygen, and then boiled in aqueous sodium hydroxide. This procedure provides sodium phosphate groups at the surface. A subsequent grafting of perfluorotetradecene using an electron radiation techniques yields the desired surface, which is then cleaned with bis(trifluoromethyl) benzene and ethanol. After through sterilization, the cannula, when tested in a heart-lung machine, will yield comparable result to those obtained in Example 5.

EXAMPLE 10

101.6 grams (0.1 mole) of perfluorooctadecyl-perfluorovinyl ether and 16 grams (0.02 moles) of perfluoro-1-hexadecenoic acid are dissolved in bis(trifluoro)benzene and coated on a commercially available silicone rubber heart valve previously primed to obtain better adhesion. After solvent evaporation, the coated heart valve is then irradiated with an electron beam of 5 MeV under argon to polymerize the coating. Following extraction of the residual monomers and sterilization, the heart valve, when evaluated as in Example 3, yields similar results.

It will be apparent that many widely different embodiments of this invention may be made without departing from the spirit and scope thereof. Therefore, the invention is not intended to be limited except as indicated in the appended claims.

EXAMPLE 11

Polyco(methacrylic acid-3,3,3,3',3',3'-hexafluoroisobutyl methacrylate) is prepared in emulsion at 65°C for 6 hours with the following recipe, added in the order shown:

	Parts
Water	30.0
Trimethyloctodecylammonium bromide	1.0
Methacrylic acid	2.0

-Continued

3,3,3,3',3',3' - hexafluoroisobutyl methacrylate	10.0
Acetone	5.0
Azodiisobutyramidine dihydrochloride	0.2

A cannula made out of chlorosulfonated ethylene-propylene rubber is coated with a thin layer of polyco(-styrene-2-vinylpyrridine) of 0.9 intrinsic viscosity. It is subsequently coated with a latex prepared in this example to leave at the surface a thin film of the fluorinated polymer chemically bonded to the underlaying polymeric substance and said fluorinated polymer having free, unreacted carboxyl groups. The coated cannula is used as a conduit in a blood machine. Equivalent results to those described in Example 5 are obtained.

EXAMPLE 12

A thromboresistant artificial heart is molded from poly(methyl-3,3,3-trifluoropropyl siloxane) wherein about one fifth of the methyl groups is replaced with carboxyethyl groups. This copolymer is prepared as follows: Methyldichlorosilane is reacted with acrylonitrile under reflux conditions (60–115°C) for about ten hours by using catalytic amounts of the following materials: cuprous chloride, tetramethylethylene diamine and triethylamine. The reaction product, which is cyanoethyl-methyldichlorosilane, is hydrolyzed in the presence of a 10% HCl solution under reflux conditions until complete diappearance of the nitrile group. After separation from the aqueous layer, the organic layer consists of poly(carboxyethylmethylsiloxane). This is equilibrated at 60–100°C, for 4–6 hours, with 20% by weight of 3,3,3-trifluoropropyl-methylsiloxane fluid commercially available from Dow Corning Co., Inc until constant viscosity is reached. The product is then washed with aqueous sodium carbonate, water, separate from the aqueous layer, and stripped off from the low boilers by distillation. It is then blended with 100 phr finely divided silica and 1 phr dicumyl peroxide, molded into a human heart and cured at 125°C for 5 hours.

EXAMPLE 13

Acrylic acid, 20 mole % is copolymerized with 80 mole % of bis [2-(N-ethyl perfluorohexylsulfonamido) ethyl] itaconate, as in Example 1. After purification and coating on a test tube, the polymer passes the same test as the one described in Example 1.

Having thus described my invention and in what manner it may be manufactured and used, what I claim and desire to protect by Letters Patent is:

1. A method or maintaining the normal integrity of blood which comprises placing it in contact with a physiologically acceptable article at least the surface of which consists of an organic polymeric material having fluoroalkyl side chains of the formula $C_nF_{2n+1}C_mH_{2m}$—, wherein *n* and *m* are integers, *n* ranging 1 to 28, and the sum of *n* and *m* from 2 to 28, the number of said fluoroalkyl side chains relative to the number of main chain atoms in one recurring unit ranges from 1:2 to 1:10; and said polymeric material having another side group chemically bonded to the main chain, said side group being selected from the group consisting of Hydrogen, hologen, aryl, lower alkyl and anionic groups.

2. The method defined in claim **1** wherein the said fluoroalkyl side chains are linear, the said integers *n* and *m* range from 8 to 28 and the sum of *n* and *m* from 8 to 28.

3. The method defined in claim **1** wherein the said integer *n* ranges from 1 to 7, the sum of *n* and *m* from 2 to 28 and the said side group is an anionic group.

4. The method defined in claim **1** wherein said physiological acceptable article comprises a substrate portion and a surface coating portion, said surface coating portion at least being of said polymeric material defined in claim **1**.

5. The method defined in claim **1** wherein the said anionic group is a member selected from the group consisting of the acid form of a carboxylate, sulfonate, sulfate, phosphate, phosphite and the salt forms of these groups.

6. The method defined in claim **1** wherein the ratio of the number of said fluoroalkyl side chains to the number of said anions is in the range of 1:1 to 20:1.

7. The method defined in laim **1** wherein the said fluoroalkyl side chain is bonded to the main chain of the said organic polymeric material by an intermediate divalent radical.

8. The method defined in claim **1** wherein the said anionic group is bonded to the said organic polymeric material by an intermediate divalent radical.

9. The method defined in claim **7** wherein the said intermediate divalent radical is a member selected from the group consisting of —O—, —CO—, —SO—, $—SO_2—$, $—SO_2NH—$, $—CH_2O—$, —COO—, —NHCO—, —NHCONH—, $—POCH_3—$, $—POC_2H_5—$, $—SO_2NCH_3—$, $—SO_2NC_2H_5—$.

10. The method defined in claim **8** wherein the said intermediate divalent radical is a member selected from the group consisting of $—CH_2—$, $—C_2H_4—$, $—OC_2H_4—$, $—(CH_2)_8—$, $—(CF_2)_{15}—$, $—SO_2NHC_2H_4—$.

11. The method defined in claim **1** wherein said physiologically acceptable article is a subdermal surgical implant.

12. The method defined in claim **1** wherein said physiologically acceptable article is a surgical instrument.

13. The method defined in claim **1** wherein said physiologically acceptable article is a laboratory apparatus used for handling blood.

14. The method defined in claim **1** wherein said physiologically acceptable article is a blood container.

15. The method defined in claim **4** wherein the said substrate portion is selected from the group consisting of plastics, rubbers, metals, glass and ceramics.

16. The method defined in claim **1** wherein said organic polymeric material is selected from the group consisting of copolymers prepared from a fluoroalkyl acrylate and acrylic acid, a fluoroalkyl methacrylate and methacrylic acid and the mixtures of these monomers.

17. The method defined in claim **16** wherein said polymeric acrylates are selected from the group consisting of:

poly(1,1- dihydropentacosafluorotridecyl acrylate)

poly(1,1-dihydropentatetracontafluorotricosyl methacrylate)

polyco(1,1-dihydropentadecafluorooctyl methacrylate — 10% sodium acrylate)

polyco(1,1,2,2-tetrahydrotrifluoropropyl acrylate — 5% maleic acid)

polyco(1,1,2,2-tetrahydropentadecafluorononyl acrylate — 30% methacrylic acid — 15% sodium methacrylate)

18. The method defined in claim 1 wherein said organic polymeric material is selected from the group consisting of:

poly(methyl-1,1,2,2-tetrahydrotriacontafluorooctadecyl siloxane)

poly[di(1,1,2,2-tetrahydrotricosafluorotridecyl) siloxane].

poly(carboxyethyl-1,1,2,2-tetrahydrotrifluoropropyl siloxane) and

poly(methyl-3,3,3- trifluoropropyl siloxane) wherein a minor part of the methyl groups is replaced with carboxyethyl groups.

19. The method defined in claim 1 wherein said organic polymeric material is selected from the group consisting of:

polymers of fluoroalkyl esters, amides and imides of maleic and fumaric acids,

the copolymers with ethylene, styrene, methylvinyl ether and vinyl acetate of fluoroalkyl esters, amides and imides of maleic and fumaric acids,

the copolymers with maleic, fumaric and acrylic acids and their anhydrides of fluoroalkyl esters, amides and imides of maleic and fumaric acids.

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