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(71) Applicant *(for all designated States except US):* RIJKSUNIVERSITEIT GRONINGEN [NL/NL]; Broerstraat 5, NL-9712 CP Groningen (NL).

(72) Inventors; and

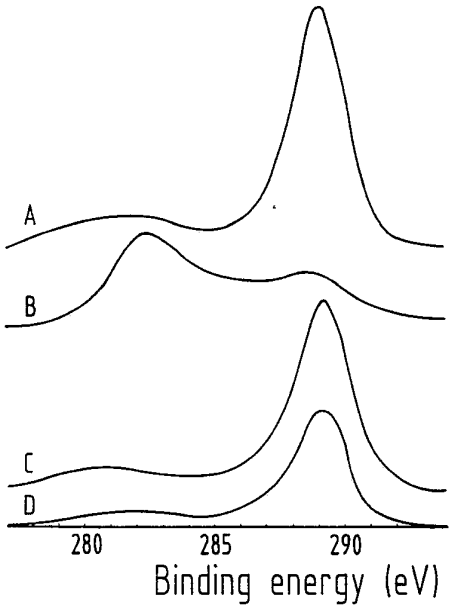
(75) Inventors/Applicants *(for US only) :* SCHAKENRAAD, Josephus, Maria [NL/NL]; Ruskenstukken 17, NL-9761 KL Eelde (NL). BUSSCHER, Hendrik, Jan [NL/NL]; G.N. Schutterlaan 4, NL-9797 PC Thesinge (NL).

(74) Agent: PRINS, Hendrik, Willem; Arnold & Siedsma, Sweelinckplein 1, NL-2517 GK The Hague (NL).

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(54) Title: METHOD FOR MODIFYING FLUORINE-CONTAINING PLASTIC, MODIFIED PLASTIC AND BIO-MATERIAL CONTAINING THIS PLASTIC



(57) Abstract

The invention relates to a method for modifying at least a part of the surface of a fluorine-containing plastic, which comprises making the surface hydrophobic by: i) ion-etching the plastic surface; and ii) subsequently cleaning the treated plastic surface, to a fluorine-containing plastic, whereof the surface is at least partially hydrophobe modified by ion-etching followed by a cleaning treatment, and to materials, such as bio-materials, in which the plastic is incorporated.

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METHOD FOR MODIFYING FLUORINE-CONTAINING PLASTIC, MODIFIED PLASTIC AND BIO-MATERIAL CONTAINING THIS PLASTIC

The present invention relates to the modifying of a fluorine-containing plastic, to the modified fluorine-containing plastic and to materials, particularly bio-materials, containing such a modified, fluorine-containing plastic, possibly as coating (plasmapolymers). The invention relates particularly to a method with which the surface of the fluorine-containing plastic can be made superhydrophobic, and according to a preferred embodiment the fluorine-containing plastic is modified such that a portion of the surface becomes superhydrophobic and another portion of the surface hydrophilic. In preference both types of surface are located on either side of a fluorine-containing plastic sheet.

Fluorine-containing plastics, such as polytetrafluoroethylene (PTFE) offer interesting technical applications because of the material properties such as a high thermal and chemical resistance and the hydrophobic nature of the surface. The materials seem very suitable as bio-material. PTFE is for example strong, flexible and bio-inert and can be made elastic and if necessary porous (e-PTFE). This hydrophobic material can be used as bio-material when a small adhesion to body tissues is required, for example at the lumen side of vascular prostheses, paradontological membranes and the visceral side of stomach wall patches. If a good interaction with body tissue is necessary, as for instance on the dermal side of stomach wall patches, the use of PTFE poses problems.

The invention has for its object to modify the surface of fluorine-containing plastics such that the applicability in industrial products and in bio-materials is thereby increased, particularly in that the hydrophobic character of the surface is greatly increased. This is achieved according to the invention with a method for modifying at least a part of the surface of a fluorine-containing plastic, which method comprises making the surface hydrophobic by:

i) ion-etching the plastic surface; and

ii) subsequently cleaning the treated plastic surface.

It has been found that due to the combined treatment consisting of ion-etching and glow discharging the hydrophobic character of the fluorine-containing plastic is greatly enlarged. If as a measure of the hydrophobic character the mean contact angle of water on the modified surface is used, the method according to the invention results in an increase of the average contact angle of 108° to more than 125°, preferably more than 130° and even to more than 140°. It is noted that ion-etching alone results in a smaller increase in the hydrophobic character (mean contact angle of water approximately 120°) and that glow discharging alone results in a lessening of the hydrophobic character (mean contact angle of water 100°).

Ion-etching is a per se conventional treatment technique well known to a person skilled in the art.

The cleaning treatment which must be performed on the plastic surface treated by ion-etching after the ion-etching has for its object to remove from the plastic surface substances or structures generated on the plastic surface by the ion-etching. This cleaning treatment can comprise a chemical, physical and/or physical-chemical treatment of the plastic surface treated by ion-etching such as a treatment with acid, base, salts, solvents and/or combinations thereof, assuming that the effect according to the present invention is thereby not adversely affected to any great extent. A cleaning treatment preferred at this moment comprises glow discharging, which is a per se conventional treatment technique.

Suitable for use as fluorine-containing plastic in the modification method according to the invention are those plastics whose mechanical properties are such that the ion-etching and the glow discharging treatment, while optionally the plastic is cooled, does not result in a serious deterioration in the physical and chemical properties of the plastic. In general can be used fluorine- and fluorochlorine-containing plastics such as the polymers polyfluoroethene-propylene (FEP), polytetrafluoroethylene (PTFE), polychlorotrifluoroethylene (PCTFE), polyvinyl fluoride (PVF), polyvinylidene fluoride (PVDF) and copolymers thereof with (C_2-C_6)

alkylene, fluorinated (C_2-C_6) alkylene such as hexafluoropropylene, fluorinated (C_1-C_6) alkylvinylether such as perfluoropropylvinylether. Preferred plastics are FEP and PTFE.

As a consequence of the modification method according to the invention the chemical composition of the hydrophobe modified surface layer is also altered. The hydrophobe modified surface has an oxygen-carbon concentration ratio (O/C) of generally 0.100-0.200, preferably 0.120-0.180 and a fluorine-carbon concentration ratio (F/C) of generally 1.00-2.000, preferably 1.400-1.800 (measured with XPS).

As a result of the pronounced hydrophobic character of the surface modified according to the invention, these modified plastics can be used on surfaces where adhesion of for instance cells, micro-organisms, proteins and other particles or organisms is undesired, such as in heat exchangers employed in the food industry, on ship shells and other surfaces coming into contact with water over long periods. As biomaterial the modified plastic according to the invention can be used in clinical and dental situations where the adhesion and/or spread of cells and/or micro-organisms is undesirable, such as on the inside of vascular prostheses, heart valves, the visceral side of reconstruction materials for the stomach wall and with vocal assist devices in the case of a tracheal-oesophageal shunt. In the case of these bio-materials it can be advantageous that there is also a surface present which lends itself to cell adhesion and cell spread (the outside of vascular prostheses and the dermal side of stomach wall reconstruction materials). According to the invention another portion of the surface of the fluorine-containing plastic is hydrophile modified in accordance with a specific embodiment by:

i) ion-etching the other portion of the plastic surface; and

ii) placing the surface in contact with water.

This hydrophile modified surface has a contact angle with water on the modified surface of $6^\circ \pm 5^\circ$.

Mentioned and other features of the modification method according to the invention and the fluorine-containing plastics modified according to the invention and their appli-

cations will be further elucidated hereinbelow with reference to a number of non-limitative examples.

Example 1

FEP-Teflon was obtained from Fluorplast B.V. (Raamsdonkveer, The Netherlands), cut into pieces of 1x2 cm and thoroughly cleaned with acetone and dried.

The samples were subjected to ion-etching making use of a so-called Ion Tech saddle field ion source (Teddington, England) at an argon pressure of $1x10^{-5}$ to $1x10^{-4}$ torr, while the ion energy was varied from 5-10 kV. Depending on the argon pressure the ion source flow varied between 8-10 mA. If a fixed sample holder was used the radiating time varied between 5 and 120 minutes, and preferably between 10 and 60 minutes. With the use of a rotating target holder the radiating time amounted to 1-10 hours, and preferably 2-7 hours, for example 5 hours.

After ion-etching the samples were treated with oxygen glow discharging in a PLASMOD (Tegal Corporation, Richmond, California), an inductively coupled instrument (13.56 MHz) with a cylindrical reaction chamber made of quartz (internal diameter 8 cm, length 15 cm). The glow discharging was performed under an oxygen pressure of 15 mbar and at a power of 50W. The glow discharging treatment lasted 0.5 to 10 minutes, and in general 1 to 5 minutes.

In the case of a number of samples, another portion of the surface was hydrophile modified by ion-etching of this portion of the surface followed by water contact. Making use for instance of a rotating target holder with an ion bundle treatment at 6mA, 6kV and an argon pressure of $4x10^{-4}$ torr for about 45 minutes. The samples were subsequently stored in water for 24 hours.

The contact angle of the various samples with a number of liquids, namely water, formamide, diiodomethane and α-bromonaphthalene, was measured using a SUPCON EC90 (accuracy 0.5°). The results are shown in table 1.

Using X-ray photoelectron spectroscopy (XPS) the surface concentration ratios for a number of elements were measured on the basis of the C_{1s}, O_{1s}, and F_{1s} peaks and the concentration ratios relative to carbon were calculated using

the Wagner sensitivity factors. The results are shown in table 2.

Using infrared spectroscopy it could be demonstrated that the chemical effects of the modification treatment according to the invention are limited to the outer surface of the plastic.

The stylus surface roughness R_A of the diverse samples was calculated from 4.8 mm tracings taken with a perthometer C5D equipped with a 5 μm stylus (opening angle 90°). Ten tracings were recorded and averaged for each sample. The results are shown in table 3.

Using a scanning electron microscope (SEM) micrographs were made at two magnifications after ion-etching and/or oxygen glow discharging.

In the figures:

Fig. 1A is untreated

Fig. 1B is 1 min. glow discharging (15 mbar oxygen pressure/ 50W)

Fig. 1C is 5 min. glow discharging (15 mbar oxygen pressure/ 50W)

Fig. 1D is 10 min. ion-etching (8 mA/6 kV/4x10^{-4} torr argon pressure)

Fig. 1E is 30 min. ion-etching (8 mA/6 kV/4x10^{-4} torr argon pressure)

Fig. 1F is 60 min. ion-etching (8 mA/6 kV/4x10^{-4} torr argon pressure)

Fig. 1G is ion-etching according to D followed by glow discharging according to C

Fig. 1H is ion-etching according to E followed by glow discharging according to C

Fig. 1I is ion-etching according to F followed by glow discharging according to C

(the bars show respectively 10 μm and 3 μm).

Fig. 2 shows XPS spectra of

A - untreated FEP-teflon

B - 45 min. ion-etching (8 mA/6 kV/4x10^{-4} torr argon pressure)

C - 5 min. glow discharging (15 mbar oxygen pressure/50W)

D - 10 min. ion-etching (8 mA/6 kV/4x10^{-4} torr argon pressure) followed by 5 min. glow discharging (15 mbar oxygen pressure/50W).

The figures 1A-C show that the glow discharging treatment as such does not affect the topography of the surface. It can be seen from figures 1D-F that a typical micro-surface roughness results after ion-etching formed by stalk-like projections with a diameter generally of 20-60 nm, for example approximately 40 nm, and a length generally of several hundred nanometers, which cover the whole surface homogeneously. Glow discharging of these surfaces results in a melting down of the upper portions of these projections, as can be seen in figures 1G-I.

In figure 2 spectrum B shows that ion-etching leads to the generation of substances and/or structures with an average binding energy of approximately 282-283 eV. These substances and/or structures are not generated during glow discharging (spectrum C) but are removed by the cleaning treatment, such as glow discharging (spectrum D).

Example 2

The effect of the hydrophobic modification according to the invention on the adhesion and spreading of cells was studied using human fibroblasts. For comparison the same tests were performed using conventional tissue culture polystyrene (TCPS), normal FEP (FEP) and hydrophile modified FEP.

Human skin fibroblasts were cultured in RPMI 1640 medium (Gibco) with 15% foetal calf serum (Gibco) and 100 μ/ml of penicillin/streptomycin (Gibco) at 37°C in air with 5% CO_2. Every other day the cells were sub-divided by trypsination (0.15 w/w % 1:250 trypsin) in calcium- and magnesium-free Hanks balance salt solution.

After trypsination 10^4 cells per cm^2 were set out on Greiner plates. The different substrata (n=6) were positioned on the bottom. After 120 minutes photos were taken of the cells and the number of adhered cells per cm^2 x 10^4 (cell density), the mean cell spreading area (MCSA) in μm^2 and the spreading area distribution (SEM) were determined per material by morphometric image analysis (Cambridge Instruments, Quantimet 520). The experiment was performed in triplicate. The results are shown in table 4.

Example 3

An elastic vascular prosthesis of e-PTFE (Gore-Tex from W.L.Gore & Associates Inc, Flagstaff, USA) with a length of 1 cm, an internal diameter of 1.55 mm and a pore size of 30 μm was cut open longitudinally, whereafter the luminal surface was hydrophobe modified according to the invention in the same manner as described in example 1. After the hydrophobic treatment according to the invention the vascular prosthesis was closed with a continuous stitch (Ethylon 9-0, BV-4 needle, Ethicon).

A rabbit (New Zealand White) was anaesthetized with Nembutal (0.5 ml/kg), after which the neck was shaved. Oxygen/nitrous oxide was then used as anaesthetic. Pain-killing was carried out using Temgesic, 0.1 ml.

The left-hand arteria carotis was exposed over a length of about 2 cm. After arranging two clamps, 1 cm of the arteria carotis was removed and replaced by the luminal vascular prosthesis hydrophobe modified according to the invention which was joined at both ends to the arteria carotis using eight stitches (Ethylon 9-0, BV-4 needle, Ethicon).

After the clamps were removed, it was checked and confirmed after 10 minutes and after two hours that blood could pass through the prosthesis. The wound was then closed and the rabbit returned to its hutch. Standard rabbit food and water were provided ad libitum.

One week later the prosthesis was once again exposed under the same standard anaesthetic as described above and it was determined that blood was still passing through the prosthesis. Before removing the prosthesis heparin was administered to the rabbit in order to avoid coagulation in the removed prosthesis.

Although no cleaning treatment other than glow discharging is described in the examples, it will be apparent that any cleaning treatment is suitable insofar as substances and/or structures are removed (spectrum B) with a binding energy of about 282-283 eV and the modified hydrophobe character of the plastic surface is substantially not adversely affected.

Table 1 Contact angle (°) after ion-etching (IE) and/or oxygen (15 mbar) glow discharge (Gld, 50W) for modified FEP-Teflon. ± indicates the standard deviation for three separately manufactured samples.

treatment duration	water	formamide	diiodo-methane	α-bromo naphthalene
untreated	109±2	90±4	77±3	73±1
Modified				
IE[a], 10 min	121±4	98±16	87±14	41±14
IE[a], 30 min	120±6	102±16	95±9	75±16
IE[a], 60 min	118±10	80±21	81±11	51±10
Modified				
Gld, 1 min	104±7	87±6	74±6	69±5
Gld, 3 min	99±6	77±9	73±5	71±3
Gld, 5 min	99±7	80±7	69±4	69±4
Hydrophobe modified according to the invention				
IE[a], 10 min + Gld, 5 min	131±7	110±7	96±10	85±13
IE[a], 30 min + Gld, 5 min	>140[c]	123±3	111±5	97±14
IE[b], 30 min + Gld, 5 min	>140[c]	122±7	110±10	107±10
Hydrophile modified				
IE, 45 min/ water contact	6	10	26	16

[a] IE; 8 mA, 6kV and 4×10^{-4} torr argon pressure
[b] IE; 10 mA, 10kV and 2×10^{-4} torr argon pressure
[c] drops did not remain on the surface, angles determined between 140 and 150° (possibly higher)

Table 2 Surface concentration ratios measured with XPS after ion-etching (IE) (8 mA, 6kV and $4x10^{-4}$ argon pressure) and/or oxygen glow discharging (15 mbar oxygen pressure at 50W for 5 minutes) of FEP-Teflon surfaces.

IE	Gld	O/C	F/C
no	no	0.018	1.931
10 min	no	0.208	0.629
45 min	no	0.142	1.059
60 min	no	0.097	0.670
no	yes	0.016	1.757
10 min	yes	0.133	1.511
30 min	yes	0.173	1.526
45 min	yes	0.169	1.745

Table 3 Stylus surface roughness R_A after ion-etching (8 mA, 6kV and $4x10^{-4}$ torr argon pressure) and/or after oxygen glow discharging (15 mbar oxygen pressure at 50W) of FEP-Teflon surfaces. ± indicates the standard deviation over ten tracings.

IE	Gld	R_A [μm]
no	no	0.44±0.22
10 min	no	0.54±0.07
60 min	no	0.74±0.07
no	5 min	0.48±0.09
45 min	10 min	0.49±0.04
45 min	30 min	0.35±0.02

Table 4 Spreading of human skin fibroblasts. A total of 400 cells were measured per material. The standard deviation of the standard error of the mean (SEM) of the mean cell spreading area MCSA is given in %.

Material	TCPS	FEP	FEP hydrophobe modified according to the invention	FEP hydrophile modified
Cell density	4.5	2.8	2.8	2.3
MCSA	270	209	158	257
SEM	6	6	14	9
Significance (a)	#	*	*#	#

(a): * indicates a significant difference relative to TCPS, $p<0.01$, student t-test;
# indicates a significant difference relative to FEP

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CLAIMS

1. Method for modifying at least a part of the surface of a fluorine-containing plastic, which comprises making the surface hydrophobic by:

i) ion-etching the plastic surface; and

ii) subsequently cleaning the treated plastic surface.

2. Method as claimed in claim 1, wherein the cleaning is performed by means of glow discharging.

3. Method as claimed in claim 1 or 2, wherein the fluorine-containing plastic is selected from the group comprising the polymers polyfluoroethenepropylene (FEP), polytetrafluoroethylene (PTFE), polychlorotrifluoroethylene (PCTFE), polyvinyl fluoride (PVF), polyvinylidene fluoride (PVDF) and copolymers thereof with (C_2-C_6) alkylene, fluorinated (C_2-C_6) alkylene, fluorinated (C_1-C_6) alkylvinylether.

4. Method as claimed in claim 3, wherein the fluorine-containing polymer is FEP or PTFE.

5. Method as claimed in claims 1-4, wherein the average contact angle of water on the hydrophobe modified surface amounts to more than 125°, preferably more than 130°, and more preferably more than 140°.

6. Method as claimed in claims 1-5, wherein the hydrophobe modified surface has;

- an oxygen-carbon concentration ratio (O/C) of 0.100-0.200; and
- a fluorine-carbon concentration ratio (F/C) of 1.000-2.000.

7. Method as claimed in claim 6, wherein

- the O/C ratio amounts to 0.120-0.180; and
- the F/C ratio amounts to 1.400-1.800.

8. Method as claimed in claims 1-7, wherein the hydrophobe modified surface is provided with stalk-like projections with a diameter in the range of 20-60 nm, the free ends whereof are melted down.

9. Method as claimed in claim 8, wherein the hydrophobe modified surface has a structure as according to figures 1G-1I.

10. Method as claimed in claims 1-9, wherein another portion of the surface of the fluorine-containing plastic is hydrophile modified by:

i) ion-etching the other portion of the plastic surface; and

ii) placing the surface in contact with water.

11. Method as claimed in claim 10, wherein the contact angle of water on the hydrophile modified surface amounts to $6^{\circ}\pm5^{\circ}$.

12. Fluorine-containing plastic, the surface of which is at least partially hydrophobe modified by ion-etching followed by a cleaning treatment.

13. Plastic as claimed in claim 12, wherein the cleaning treatment comprises glow discharging.

14. Plastic as claimed in claim 12 or 13, wherein the mean contact angle of water on the hydrophobe modified surface amounts to more than 125°.

15. Plastic as claimed in claims 12-14, wherein the mean contact angle of water on the hydrophobe modified surface amounts to more than 130°, and preferably more than 140°.

16. Plastic as claimed in claims 12-15, wherein the hydrophobe modified surface has;

- an oxygen-carbon concentration ratio (O/C) of 0.100-0.200; and
- a fluorine-carbon concentration ratio (F/C) of 1.000-2.000.

17. Plastic as claimed in claims 12-16, wherein

- the O/C ratio amounts to 0.120-0.180; and
- the F/C ratio amounts to 1.400-1.800.

18. Plastic as claimed in claims 12-17, wherein the hydrophobe modified surface is provided with stalk-like projections with a diameter in the range of 20-60 nm, the free ends whereof are melted down.

19. Plastic as claimed in claim 18, wherein the hydrophobe modified surface has a structure as according to figures 1G-1I.

20. Plastic as claimed in claims 12-19, wherein the fluorine-containing plastic is selected from the group comprising polymers of polyfluoroethenepropylene (FEP), polytetrafluoroethylene (PTFE), polychlorotrifluoroethylene

(PCTFE), polyvinyl fluoride (PVF), polyvinylidene fluoride (PVDF) and copolymers thereof with (C_2-C_6) alkylene, fluorinated (C_2-C_6) alkylene, fluorinated (C_1-C_6) alkylvinylether.

21. Plastic as claimed in claim 20, wherein the fluorine-containing polymer is FEP or PTFE.

22. Plastic as claimed in claims 12-21, whereof another portion of the surface is hydrophile modified.

23. Plastic as claimed in claim 22, wherein the surface is hydrophile modified by ion-etching followed by water contact.

24. Bio-material containing a fluorine-containing plastic with a modified surface as claimed in the claims 12-23 and/or obtained according to the method as claimed in the claims 1-11.

25. Vascular prosthesis comprising a luminal surface that is hydrophobe modified according to the method as claimed in any of the claims 1-11.

26. Material containing a fluorine-containing plastic with a modified surface as claimed in claims 12-23 and/or obtained according to the method as claimed in claims 1-11.

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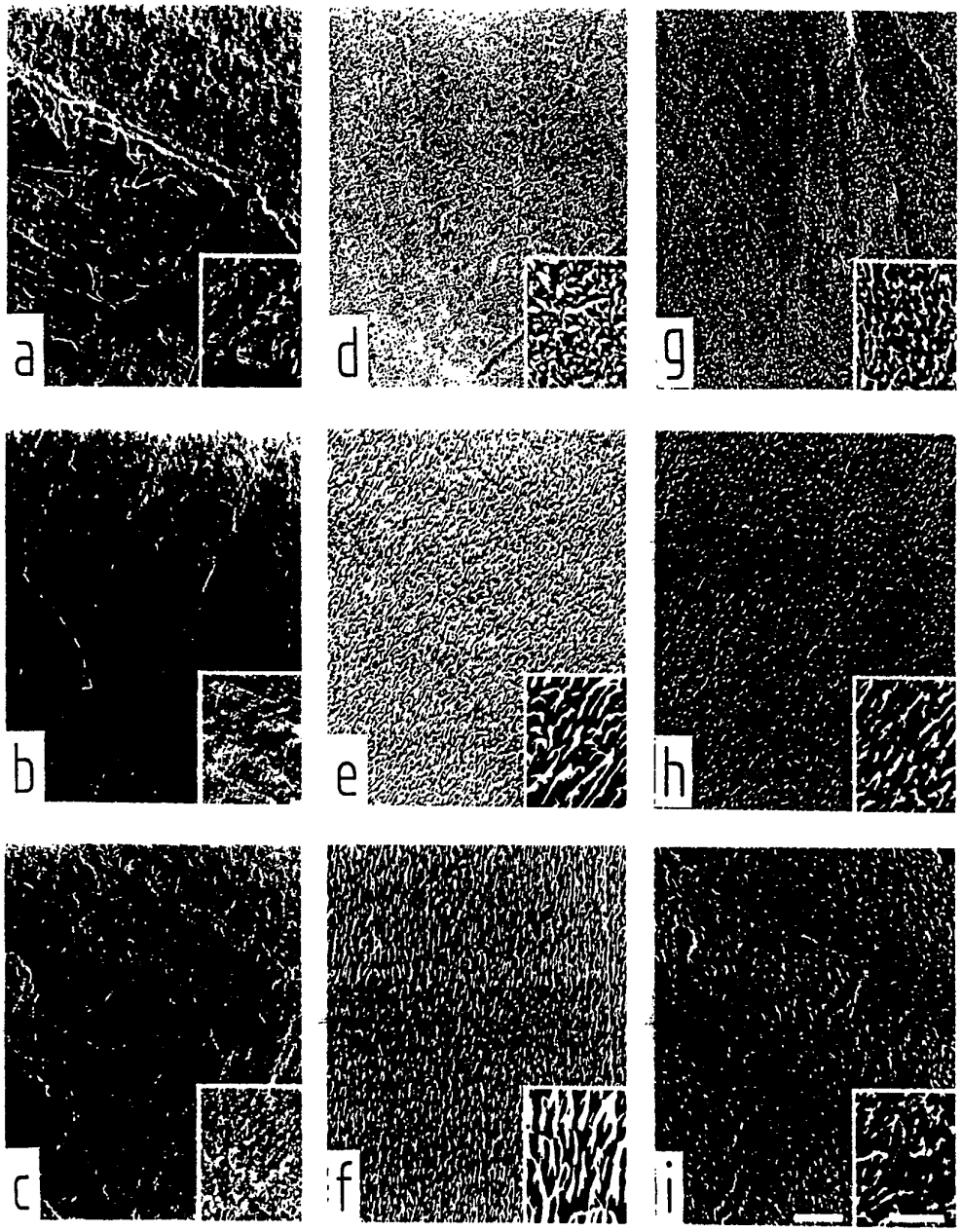


FIG. 1

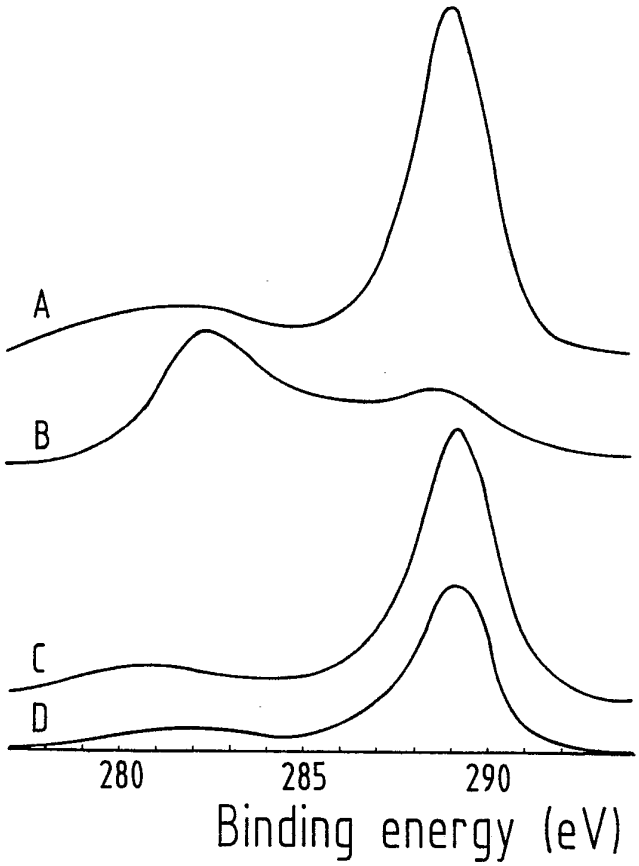


FIG. 2

INTERNATIONAL SEARCH REPORT

PCT/NL 92/00069

International Application No

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 B29C59/16; B29C59/10

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	B29C ; C08J

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category °	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
A	US,A,4 199 650 (MIRTICH ET AL.) 22 April 1980 see column 1, line 61 - line 68	1-26
A	DE,A,3 806 770 (AGION) 21 September 1989 see column 1, line 51 - column 2, line 25; figures 2,3	1-26
A	Polym. Mater. Sci. Eng., vol. 62, 1990 H.J.GRIESSER 'Long Term Behaviour of Contact Angles on Modified Fluorocarbon Surfaces' page 872 to 875 see figures	1-26
A	CHEMICAL ABSTRACTS, vol. 94, no. 18, 1980, Columbus, Ohio, US; abstract no. 145301Z, G. PICHA: 'Tissue Response to Peritoneal Implants' see abstract	1-26

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° Special categories of cited documents :[10]

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IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
08 JULY 1992	15. 07. 92
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Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
A	US,A,4 632 842 (KARWOSKI ET AL.) 30 December 1986 see column 2, line 52 - column 3, line 13	1-26
A	Adhäsion, vol. 23, no. 5, 1979, München J.Hansmann 'Corona-Oberflächenbehandlung' page 136 to 142 see figure 7	1-26

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. NL 9200069 SA 59183

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-4199650	22-04-80	None	
DE-A-3806770	21-09-89	None	
US-A-4632842	30-12-86	None	