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(54) Title: HYDROPHOBIC ACRYLIC INTRAOCULAR LENS MATERIALS

(57) Abstract: Disclosed are low-tack, hydrophobic, high refractive index, acrylic materials. These materials, especially useful as intraocular lens materials, contain one or more aryl acrylic hydrophobic monomers as principal device-forming monomers, a tack-reducing macromer additive and a glistening-reducing additive. In addition to their use as intraocular lens materials, the present materials are also suitable for use in other implantable ophthalmic devices.

HYDROPHOBIC ACRYLIC INTRAOCULAR LENS MATERIALS

Field of the Invention

This invention is directed to acrylic device materials. In particular, this invention relates to low-tack, high refractive index, glistening resistant, low surface scatter acrylic device materials particularly suited for use as intraocular lens ("IOL") materials, which can be injected trough small incisions of less than 2.5 mm.

Background of the Invention

With the recent advances in small-incision cataract surgery, increased emphasis has been placed on developing soft, foldable materials suitable for use in artificial lenses. In general, these materials fall into one of three categories: hydrogels, silicones, and acrylics.

In general, hydrogel materials have a relatively low refractive index, making them less desirable than other materials because of the thicker lens optic necessary to achieve a given refractive power. Silicone materials generally have a higher refractive index than hydrogels, but tend to unfold explosively after being placed in the eye in a folded position. Explosive unfolding can potentially damage the corneal endothelium and/or rupture the natural lens capsule. Acrylic materials are desirable because they typically have a higher refractive index than silicone materials and unfold more slowly or controllably than silicone materials.

U.S. Patent No. 5,290,892 discloses high refractive index, acrylic materials suitable for use as an IOL material. These acrylic materials contain, as principal components, two aryl acrylic monomers. They also contain a cross-linking component. The IOLs made of these acrylic materials can be rolled or folded for insertion through small incisions.

U.S. Patent No. 5,331,073 also discloses soft acrylic IOL materials. These materials contain as principal components, two acrylic monomers which are defined by the properties of their respective homopolymers. The first monomer is defined as one in which its homopolymer has a refractive index of at least about 1.50. The second monomer is defined as one in which its homopolymer has a glass transition temperature less than about 22 °C. These IOL materials also contain a cross-linking component. Additionally, these materials may optionally contain a fourth constituent, different from the first three constituents, which is derived from a hydrophilic monomer. These materials preferably have a total of less than about 15% by weight of a hydrophilic component.

U.S. Patent No. 5,693,095 discloses foldable ophthalmic lens materials comprising a total of at least 90% by weight of only two principal lens-forming monomers. One lens-forming monomer is an aryl acrylic hydrophobic monomer. The other lens-forming monomer is a hydrophilic monomer. The lens materials also comprise a cross-linking monomer and optionally comprise a UV absorber, polymerization initiators, reactive UV absorbers and reactive blue-light absorbers.

U.S. Patent No. 6,653,422 discloses foldable ophthalmic lens materials consisting essentially of a single device-forming monomer and at least one cross-linking monomer. The materials optionally contain a reactive UV absorber and optionally contain a reactive blue-light absorber. The single device-forming monomer is present in an amount of at least about 80% by weight. The device-forming monomer is an aryl acrylic hydrophobic monomer.

Some foldable acrylic materials are tacky. Foldable ophthalmic lenses made of tacky acrylic materials are difficult to manufacture and handle. Attempts have been made to reduce tackiness so that the lenses are easier to process or handle, easier to fold or deform, and have shorter unfolding times.

For example, U.S. Patent No. 6,713,583 discloses ophthalmic lenses made of a material that includes branched chain alkyl groups in an amount effective to reduce tackiness. U.S. Patent No. 4,834,750 discloses intraocular lenses made from materials that optionally include a fluoroacrylate component to reduce surface tackiness. U.S. Patent No. 5,331,073 discloses acrylic materials that optionally include a hydrophilic component that is present in an amount sufficient to reduce the materials' tackiness. U.S. Patent No. 5,603,774 discloses a plasma treatment process for reducing the tackiness of a soft acrylic article. U.S. Patent No. 7,585,900 discloses the use of a dimethylacryloxypropyl-terminated polydimethylsiloxane macromer as a tack-reducing additive for certain acrylic ophthalmic device materials, including IOL materials.

Summary of the Invention

Improved soft, foldable acrylic materials which are particularly suited for use as IOLs, but which are also useful as other implantable ophthalmic devices, such as keratoprostheses, corneal rings, corneal implants, and corneal inlays have now been discovered. These materials contain at least one principal lens-forming component, which is an aryl acrylic hydrophobic monomer, in an amount of 30 – 60 % by weight. The materials also contain 0.1 - 3 % by weight of a dimethacryloxypropyl-terminated polydimethylsiloxane macromer. Importantly, in order to reduce or eliminate haze and produce a clear, optically acceptable material, the copolymeric materials of the present invention contain 10 – 40 % of 2-ethylhexyl acrylate or n-octyl acrylate, and 3 – 25 % by weight of a hydrophilic additive to reduce glistenings. The material also comprises a cross-linking monomer, a UV-light absorbing compound, and optionally a blue-light absorbing compound. The resulting copolymeric device materials are hydrophobic, which as used herein means that they have an equilibrium water content at 35 °C of 4 % or less, preferably 3 % or less, and more preferably 2.5 % or less.

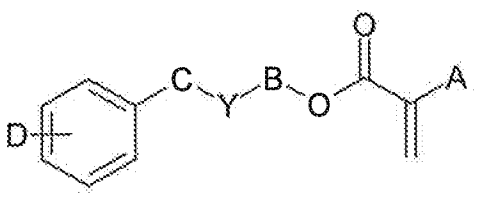
For IOLs, it is not enough that they have low tack as they need to be optically clear as well. The implantable ophthalmic device materials of the present invention are optically clear such that they are suitable for use as IOLs and they have low tack, low surface scatter, and good delivery properties. Among other factors, the present invention is based on the finding that a multi-component, copolymeric, high refractive index device material obtained by copolymerizing the ingredients mentioned above is soft, glistening-free, has low tack and low haze, has low surface light scatter, and is capable of going through small (2.5 mm or less) incisions with good unfolding properties.

Detailed Description of the Invention

Unless indicated otherwise, all component amounts are presented on a % (w/w) basis ("wt.%").

The ophthalmic device materials of the present invention comprise at least one principal device-forming monomer. For convenience, the device-forming monomer may be referred to as a lens-forming monomer, particularly with reference to an IOL. The materials of the present invention, however, are also suitable for use as other implantable ophthalmic devices such as such as keratoprostheses, corneal rings, corneal implants, and corneal inlays.

The aryl acrylic hydrophobic monomers suitable for use as principal lens-forming monomers in the materials of the present invention have the formula



(I)

wherein: A is H;

B is $(CH_2)_m$, $S(CH_2)_u$, $O(CH_2)_v$, or $[O(CH_2)_2]_n$;

u is 1 – 4;

v is 1 – 4;

C is $(CH_2)_w$;

m is 1 – 6;

n is 1 – 10;

Y is nothing, O, S, or NR, provided that if Y is O, S, or NR, then B is $(CH_2)_m$;

R is H, CH_3, C_nH_{2n+1} (n=1-10), iso-OC_3H_7, C_6H_5, or $CH_2C_6H_5$;

w is 0 – 6, provided that m + w ≤8; and

D is H, C_1 – C_4 alkyl, C_1 – C_4 alkoxy, C_6H_5, $CH_2C_6H_5$, Br, F, Cl, or I.

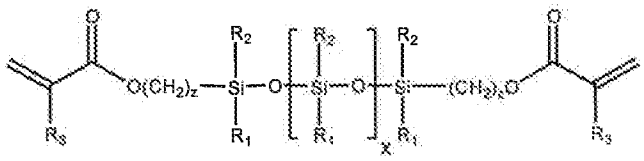
Preferred aryl acrylic hydrophobic monomers for use in the materials of the present invention are those wherein B is $(CH_2)_m$, m is 1 - 5, Y is nothing, O, or S, w is 0 – 1, and D is H. Most preferred are benzyl acrylate, 2-phenylethyl acrylate, 2-phenoxyethyl acrylate, 4-phenylbutyl acrylate, 5-phenylpentyl acrylate, 2-benzyloxyethyl acrylate, 3-benzyloxypropyl acrylate, 3-phenylpropyl acrylate, 3-phenoxypropyl acrylate, 2-(phenylthio)propyl acrylate, and 2-(phenylthio)ethyl acrylate. In one embodiment, the materials of the present invention comprise only one principal lens-forming monomer. In another embodiment, the materials of the present invention comprise two principal lens-forming monomers. Particularly preferred lens-forming monomers are 2-phenylethyl acrylate; 2-phenoxyethyl acrylate; benzyl acrylate; and 2-(phenylthio)ethyl acrylate.

Monomers of structure I can be made by known methods. For example, the conjugate alcohol of the desired monomer can be combined in a reaction vessel with methyl acrylate, tetrabutyl titanate (catalyst), and a polymerization inhibitor such as 4-benzyloxy phenol. The vessel can then be heated to facilitate the reaction and distill off the reaction by-products to drive

the reaction to completion. Alternative synthesis schemes involve adding acrylic acid to the conjugate alcohol and catalyzing with a carbodiimide or mixing the conjugate alcohol with acryloyl chloride and a HCl acceptor such as pyridine or triethylamine.

The materials of the present invention comprise 30 – 60 %, preferably 35 – 50 %, and more preferably 40 – 50% of the principal lens-forming monomer(s).

In addition to the principal lens-forming monomer, the materials of the present invention contain a macromer additive of formula (II) in an amount sufficient to reduce the material's tackiness. Generally, the amount of macromer additive in the materials of the present invention will range from 0.1 - 3.9 % (w/w), and preferably will range from 1 – 3 % (w/w), most preferably 1.5 – 2.5 % (w/w). The macromer is a dimethylacryloxypropyl-terminated polydimethylsiloxane macromer of the formula:



wherein

R_1 and R_2 are independently $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$, $-C_6H_5$, $-CH_2C_6H_5$, $-CH_2CH_2C_6H_5$, $-CH_2CH_2CH_2C_6H_5$, or $-CH_2CH_2CH_2CH_2C_6H_5$;

R_3 is H, CH_3, or CH_2CH_3;

z is 2-11; and

x indicates the number of repeating units and determines the molecular weight of the macromer.

Preferred macromers of formula (II) are those wherein

$R_1 = R_2 = CH_3$;

R_3 is H, CH_3, or CH_2CH_3; and

z = 3; and
x = 0 – 43.

More preferred macromers of formula (II) are those wherein R_1, R_2, R_3, and z are as defined above for the preferred macromers and x is 0 – 22. In one embodiment, x is 5 – 14 (generally corresponding to a macromer molecular weight (M_n) of 800 – 1400). In another embodiment, x is 2 – 5 (generally corresponding to a macromer molecular weight (M_n) of 550 – 700).

Dimethylacryloxypropyl-terminated polydimethylsiloxanes of formula (II) ("PDMS"), also known as methacryloxypropyl terminated polydimethyl siloxanes, can be made by known methods. Some PDMS compounds are commercially available from Gelest, Inc. in molecular weights (M_n) ranging from 800 - 1400 (mid-range M_n estimated as 1000). There are higher (M_n 4K - 6K, 5K - 20K, 20K - 30K) and lower (M_n 386, 550 - 700) molecular weight grades of dimethacryloxypropyl-terminated siloxane commercially available. The macromer additive selection is limited by solubility (in the remainder of the copolymer material formulation) and formulation clarity (the copolymer material should be clear). Generally, PDMS used in the present invention will have a molecular weight (M_n) of about 300 – about 3500 and preferably about 350 – about 2000. In one embodiment, an especially preferred PDMS has a M_n from about 800 – about 1400. In another embodiment, an especially preferred PDMS has a M_n from about 550 - about 700.

In order to make the macromer of formula II and other components compatible in the final composition, the materials of the present invention contain 10 – 40 %, preferably 15 – 35 %, and most preferably 17 – 32 % of 2-ethylhexyl acrylate or n-octyl acrylate. Preferably, the compositions of the present invention contain n-octyl acrylate.

In order to reduce glistening, the materials of the present invention also contain a hydrophilic monomer selected from the group consisting of: hydroxy(C_2 – C_4 alkyl)methacrylates, glycerol methacrylate, and *N*-vinyl

pyrrolidone (NVP). Hydroxy(C_2 – C_4 alkyl)methacrylates are preferred. The most preferred hydrophilic monomer is 2-hydroxyethyl methacrylate. The materials of the present invention contain a total amount of hydrophilic monomer of 5 – 30 %, preferably 10 – 25 %, and most preferably 15 – 25 %. In one embodiment the materials of the present invention contain at least one hydrophilic monomer selected from the list recited above and at least one hydrophilic monomer of a different type, such as poly(ethylene glycol) monomethyl ether macromer (Mn ~ 4100 Daltons) or the monomers and macromers described in U.S. Published Patent Application Nos. 20090088493, 20090088544, and 20090093604, respectively. Regardless of their identities, the total amount of hydrophilic monomers contained in the materials of the present invention should be limited such that the equilibrium water content (at 35°C) of the polymerized device material of the present invention is less than 4%.

The copolymer materials of the present invention are cross-linked. The copolymerizable cross-linking agent used in the copolymers of this invention may be any terminally ethylenically unsaturated compound having more than one unsaturated group. Suitable cross-linking agents include, for example low molecular weight cross-linking agents having a molecular weight from 100 – 500 Daltons and high molecular weight cross-linking agents having a molecular weight from 501 – 6,000 Daltons. Low molecular cross-linking agents will typically be present in a total amount from 0.5 – 3 %, whereas high molecular weight cross-linking agents will typically be present in a total amount from 2 – 10 %. In general, the total amount of cross-linking agent in the materials of the present invention will range from 0.5 – 10 %, and will preferably range from 1 – 3%. For purposes of determining the total amount of cross-linker in the present invention, the macromer of formula (II) is not considered to be part of the cross-linking component and is ignored. Suitable low molecular weight cross-linking agents include: ethylene glycol dimethacrylate; diethylene glycol dimethacrylate; allyl methacrylate; 1,3-propanediol dimethacrylate; 2,3-propanediol dimethacrylate; 1,6-hexanediol

dimethacrylate; 1,4-butanediol dimethacrylate; triethylene glycol dimethacrylate; and their corresponding acrylates. Preferred low molecular cross-linking monomers include 1,4-butanediol dimethacrylate and triethylene glycol dimethacrylate. Suitable high molecular weight cross-linking agents include poly(ethylene glycol) diacrylate (M_n = 700 Daltons) and poly(ethylene glycol) dimethacrylate (M_n = 2000 Daltons).

In a preferred embodiment, the materials of the present invention contain 0.5 - 2 % triethyleneglycol dimethacrylate (TEGDMA).

In addition to the aryl acrylic hydrophobic lens-forming monomer component, the macromer of formula (II), the hydrophilic additive to reduce glistenings, the 2-ethylhexyl arcrylate or n-octyl acrylate, and the cross-linking component, the lens materials of the present invention also contain reactive UV and/or blue-light absorbers.

Many reactive UV absorbers are known. Preferred reactive UV absorbers are 2-(2'-hydroxy-3'-methallyl-5'-methylphenyl)benzotriazole, commercially available as o-Methallyl Tinuvin P ("oMTP") from Polysciences, Inc., Warrington, Pennsylvania, and 3-(2*H*-benzo[*d*][1,2,3]triazol-2-yl)-4-hydroxyphenylethyl methacrylate ("Norbloc 7966"). UV absorbers are typically present in an amount from about 0.1 - 5 % (w/w). In one embodiment, the materials of the present invention contain 1.5 – 2.5%, preferably 1.5 - 2%, of a reactive UV absorber.

Many reactive blue-light absorbing compounds are known. Preferred reactive blue-light absorbing compounds are those described in U.S. Patent No. 5,470,932, U.S. Published Patent Application No. 20110003910, and in co-pending, commonly assigned U.S. Patent Application Serial No. 13/008,409. the entire contents of which are hereby incorporated by reference. A preferred blue-light absorbing dye is N-2-[3-(2'-methylphenylazo)-4-hydroxyphenyl]ethyl

methacrylamide. Blue-light absorbers are typically present in an amount from about 0.01 - 1 % (w/w), preferably 0.02 – 0.5 % (w/w).

The implantable ophthalmic device materials of the present invention are prepared by combining the ingredients described above and polymerizing the resulting mixture. Suitable polymerization initiators include thermal initiators and photoinitiators. Preferred thermal initiators include peroxy free-radical initiators, such as 2,2'-(diazene-1,2-diyl)bis(2,4-dimethylpentanenitrile; t-butyl (peroxy-2-ethyl)hexanoate; and di-(tert-butylcyclohexyl) peroxydicarbonate (commercially available as Perkadox® 16 from Akzo Chemicals Inc., Chicago, Illinois). A preferred photoinitiator is phenylphosphorylbis(mesitylmethanone), which is commercially available as Irgacure 819. Initiators are typically present in an amount of about 5% (w/w) or less, and preferably about 1 % or less. Customarily, the total amount of initiator is not included when determining the amounts of other ingredients in copolymeric compositions.

The identity and amount of the principal lens-forming monomer component described above and the identity and amount of any additional components are determined by the desired properties of the finished ophthalmic lens. Preferably, the ingredients and their proportion are selected so that the acrylic lens materials of the present invention possess the following properties, which make the materials of the present invention particularly suitable for use in IOLs which are to be inserted through incisions of 2.5 mm or less, and preferably 2.0 mm or less.

The lens material preferably has a refractive index in the dry state of at least about 1.50 as measured by an Abbe' refractometer at 589 nm (Na light source). For a given optic diameter, optics made from materials having a refractive index lower than 1.50 are necessarily thicker than optics of the same power which are made from materials having a higher refractive index. As such, IOL optics made from materials having a refractive index lower than about 1.50 generally require relatively larger incisions for IOL implantation.

The glass-transition temperature ("Tg") of the lens material, which affects the material's folding and unfolding characteristics, is preferably below about 25 °C, and more preferably below about 15 °C. Tg is measured by differential scanning calorimetry at 10 °C/min., and is determined as the half-height of the heat capacity increase.

The lens material will have an elongation (strain at break) of at least 100 %, preferably at least 125 %, and most preferably at least 150 %. This property indicates that the lens generally will not crack, tear or split when folded. Elongation of polymer samples is determined on dumbbell shaped tension test specimens with a 20 mm total length, length in the grip area of 11 mm, overall width of 2.49 mm, 0.833 mm width of the narrow section, a fillet radius of 8.83 mm, and a thickness of 0.9 mm. Testing is performed on samples at standard laboratory conditions of 23 ± 2°C and 50 ± 5 % relative humidity using a tensile tester. The grip distance is set at 11 mm and a crosshead speed is set at 500 mm/minute and the sample is pulled to failure. The strain at break is reported as a fraction of the displacement at failure to the original grip distance. Stress at break is calculated at the maximum load for the sample, typically the load when the sample breaks, assuming that the initial area remains constant. The Young's modulus is calculated from the instantaneous slope of the stress-strain curve in the linear elastic region. The 25% secant modulus is calculated as the slope of a straight line drawn on the stress-strain curve between 0% strain and 25% strain. The 100% secant modulus is calculated as the slope of a straight line drawn on the stress-strain curve between 0% strain and 100% strain.

IOLs constructed of the materials of the present invention can be of any design capable of being rolled or folded into a small cross section that can fit through a relatively smaller incision. For example, the IOLs can be of what is known as a one piece or multipiece design, and comprise optic and haptic components. The optic is that portion which serves as the lens. The haptics are attached to the optic and hold the optic in its proper place in the eye. The optic

and haptic(s) can be of the same or different material. A multipiece lens is so called because the optic and the haptic(s) are made separately and then the haptics are attached to the optic. In a single piece lens, the optic and the haptics are formed out of one piece of material. Depending on the material, the haptics are then cut, or lathed, out of the material to produce the IOL.

The invention will be further illustrated by the following examples, which are intended to be illustrative, but not limiting.

EXAMPLE 1

The formulations shown in Table 1 were prepared as follows. Single piece IOLs and test samples measuring 20 x 10 x 0.9 mm (length x width x thickness) were made via thermal or photo-curing. Thermally cured samples were cured using a 70 °C → 105 °C cure cycle. Samples were first ramp heated from ambient temperature to 70 °C over 15 minutes, soaked at 70 °C for 1 hour, ramp heated from 70 °C to 105 °C over 20 minutes, and then soaked at 110 °C for 2 hours. Photo-cured samples were cured by heating test samples in a nitrogen filled glove box for 10 minutes at 55 °C and then irradiating with a Philips TLK 40W/03 24-inch fluorescent lamp for 50 minutes. Cured samples were extracted in acetone for 15 hours at ambient temperature, air dried slowly at ambient temperature for 15 hours, and then vacuum dried at low pressure (0.1 mm Hg) for a minimum of 15 hours at 60 °C.

TABLE 1

Form	PEA	HEMA	HEA	EHA	n-OA	PDMS-1000-DMA	TEGDMA	DEGDA	BDDA	TEGDA	UV ABS-BB / wt %	INITIATOR / wt %
A	68.2	15	10	-	-	2.5	2.5	-	-	-	oMTP/1.8	PERK/1.0
B	61.75	18	-	18.2	-	-	1	-	-	0.75	WL-2/0.3	AIBN/1.0
C	45	20	-	-	29.7	2.0	-	-	-	1.5	oMTP/1.8	IRG819/0.2
D	45.2	20	-	-	30	2	-	1	-	-	oMTP/1.8	IRG819/0.2
E	44.2	21	-	-	30	2	-	-	1	-	oMTP/1.8	IRG819/0.2
F	45.2	20	-	-	29.5	2	-	-	-	1.5	oMTP/1.8 BB/0.04	IRG819/0.2
G	43.16	21	-	-	30	2	-	-	-	2	oMTP/1.8 BB/0.04	IRG819/0.2
H	45.16	20	-	-	29.5	2	-	-	-	1.5	oMTP/1.8 BB/0.04	IRG819/0.27
I	45.16	20	-	-	29.5	2	-	-	-	2	oMTP/1.8 BB/0.04	IRG819/0.27
J	46.16	20	-	-	30.5	-	-	-	-	1.5	oMTP/1.8 BB/0.04	IRG819/0.27

PEA= 2-phenylethyl acrylate

HEMA= 2-hydroxyethyl methacrylate

HEA= 2-hydroxyethyl acrylate

EHA= 2-ethylhexyl acrylate

n-OA= n-octyl acrylate

PDMS-1000-DMA= methacryloxypropyl terminated dimethylsiloxane. The PDMS-1000-DMA polymer has a molecular weight about 1,000 Daltons and viscosity ranges between 12 – 18 cst.

TEGDMA= triethylene glycol dimethacrylate

DEGDA= diethylene glycol diacrylate

BDDA: 1,4-butanediol diacrylate

TEGDA = triethylene glycol diacrylate

oMTP= o-methallyl Tinuvin P, 2-(*2H*-benzo[*d*][1,2,3]-triazol-2-yl)-4-methyl-6-(2-methylallyl)phenol

WL-2= 3-(5-fluoro-2H-benzo[d][1,2,3]triazol-2-yl)-2-hydroxy-5-methoxybenzyl methacrylate

BB= blue light attenuating chromophore (AL8739) = N-(4-hydroxy-3-(o-tolyldiazenyl)phenethyl)methacrylamide

PERK: Perkadox 16, bis(4-*tert*-butylcyclohexyl) peroxydicarbonate

AIBN: 2,2' azobisisobutyronitrile

Irgacure 819 = phenylphosphorylbis(mesitylmethanone)

EXAMPLE 2

Before and after acetone extraction weight measurements were carried out on the test samples to calculate weight percent extractables. Then, dried test samples were equilibrated in deionized water at 35 °C for a minimum of 24 hours. Weight percent extractables, equilibrium water content (EWC at 35°C), and refractive index (hydrated at 35°C) values were subsequently measured as shown in Table 2. Sample clarity was qualitatively assessed on dry and hydrated lenses using a Dolan-Jenner Fiber-Lite Fiber Optic Illuminator (model 190). Hydrated lenses were placed in the light path while rotating the samples in the x, y, and z directions to determine relative haze. As shown in Table 2, sample A that contained HEA was hazy, mostly because of the incompatibility between shorter chain length HEA and PDMS-1000-DMA. Good compatibility was achieved with EHA and n-OA resulted clear material. Glistening evaluation

was carried out on IOLs casted 21.0D lens molds. Samples were placed in BSS at 45 °C for 24 hours and then cooling to ambient temperature. Samples were inspected after 2 hours using an optical microscope under bright field (BF) and dark field (DF) settings using a magnification of 100X. No BF glistenings were observed under the conditions described. DF setting has more sensitive to pick up smaller glistenings that cannot be seen under BF settings. Number of dark field glistening per visual spot was also reported in Table 2.

TABLE 2

Example	% Extractables	EWC (35 °C) (wt. %)	Refractive Index (35 °C)	Clarity	Dark Field Glistening
A	3.17 ± 0.5	2.7	-	Hazy	-
B	2.0 ± 0.3	1.5	1.524	Clear	<30
C	2.7 ± 0.1	2.1	1.506	Clear	<10
D	4.2 ± 0.1	2.2	1.507	Clear	<10
E	1.7 ± 0.1	2.2	1.506	Clear	<5
F	2.9 ± 0.2	2.3	1.509	Clear	<15
G	2.5 ± 0.1	2.5	1.507	Clear	<5
H	2.5 ± 0.1	2.1	1.509	Clear	<5
I	2.5 ± 0.1	2.2	1.508	Clear	<5
J	4.6 ± 0.2	2.1	1.512	Clear	-

EXAMPLE 3

Tack Measurements

Select test samples from Example A – J were tested for tack using a modified Instron test method which measures polymer to metal (stainless steel) and polymer to polymer. Tack values greater than 52 N were considered to have very high tack and could not be accurately measured using the chosen load cell.

Tack values between 40 – 52 N were considered to have high tack. Tack values between 30 – 40 N were considered to have moderate tack. Tack values between 20 – 30 N were considered to have low tack.

The polymer to metal tack testing was conducted on an Instron mechanical tester using a custom fixture for measuring the metal-polymer tack or adhesion. The fixture includes a highly polished stainless steel circular stationary pin of 8 mm in diameter that is affixed to the stationary portion of the load frame. The upper (moveable) section of the load frame crosshead is attached to a circular metal platform with a hole in the center. The moveable crosshead is lowered until the bottom pin appears through the hole in the center of the upper fixture and the crosshead movement is stopped when the pin is slightly above the metal platform. The polymer sample is then placed on the protruding pin. A fresh 10mm diameter disk is press cut from the polymer sample and is placed on the top of the protruding pin. A 300 gram weight is placed on top of the sample, pressing the sample to the pin with a uniform load. One minute after placing the weight on the sample, the Instron mechanical tester is started with a separation rate of 5 mm/min. Data is collected at a rate of 5 points/sec until the sample is pulled up off of the pin. The maximum force is recorded.

Similarly polymer to polymer tack testing was also carried out. In brief, two 6 mm diameter PMMA posts were employed at the stationary and the moveable section of the load frame crosshead. Samples were cut into 6 mm diameter disks and glued on to the PMMA posts using an epoxy adhesive. The applied adhesive was allowed to dry for about 15 hours before testing. One post of the test sample was placed in the bottom grip and one in the top grip. The upper and lower posts were brought together and posts were aligned so that samples were in full contact with each other. A 300 gram weight was placed on the top post and pressed with a uniform load against the sample glued to the bottom post. One minute after placing the weight on the sample, the Instron mechanical tester is started with a separation rate of 1 mm/min. Data is collected at a rate of 0.15 point/sec until the sample is pulled up off of the pin.

The maximum force is recorded. The maximum force was recorded about 7 N for AcrySof Material (SM9.2) by this test. Therefore, tack value around 7N or less should be considered to have low polymer to polymer tack.

Pre-extraction, post-extraction and post-plasma treated samples were tested for polymer to metal tack and polymer to polymer tack. Results are summarized in Table 3. Sample J contained no PDMS-1000-DMA. As shown in Table 3, addition of 2% PDMS-1000-DMA results in decreased polymer to metal and polymer to polymer tack. Most of the polymer to metal tack values are below 20 N and very low (well below 7N) polymer to polymer tack values were measured for these samples.

TABLE 3

sample	Polymer to Metal Tack (N)			Polymer to Polymer Tack (N)		
	Pre-Extraction	Post-Extraction	Post-Plasma	Pre-extraction	Post-Extraction	Post-Plasma
A	26.2 ± 3.1	-	-	-	-	-
B	33 ± 3.1	-	-	-	-	-
C	15 ± 0.7	14 ± 1.8	16.6 ± 1.8	-	-	1.4 ± 0.4
D	14 ± 1.9	15.4 ± 2	21.6 ± 3.2	-	-	-
E	19 ± 2.6	20 ± 1.1	15 ± 0.4	-	-	-
F	10 ± 0.7	12.2 ± 1.8	-	-	-	0.7 ± 0.3
G	10 ± 0.8	13.1 ± 4.8	-	-	-	0.4 ± 0.1
H	16 ±1.5	14.3 ± 1.6	5.1±2.2	3.4 ± 1.8	3 ± 0.2	1.6± 0.7
I	18.2 ± 5.8	21.6 ± 4.0	6.6 ± 1.7	4.1 ± 0.5	3.2 ± 1.4	1.5 ± 0.5
J	26.3 ± 3.2	19.4 ± 2.4	-	5.0 ± 0.6	5.2 ±2.1	-

EXAMPLE 4

Tensile Testing

The tensile properties of extracted test samples from Example A – I were measured using an Instron tensilometer and results are shown in Table 4.

TABLE 4

Example (N ≥ 3)	Stress at Break (MPa)	Strain at Break (%)	Young's Modulus (MPa)	25% Secant Modulus (MPa)	100% Secant Modulus (MPa)
A	8.9 ± 0.9	139 ± 6.8	62.7 ± 5.3	13.7 ± 1.1	6.1 ± 0.3
B	4.5 ± 0.3	198 ± 9.8	22 ± 2.2	3.1 ± 0.2	1.8 ± 0.1
C	5.9 ± 0.6	167 ± 4.6	12.1 ± 0.7	3.6 ± 0.2	2.7 ± 0.2
D	6.4 ± 0.4	183 ± 6.7	12.0 ± 0.7	3.7 ± 0.1	2.7 ± 0.06
E	5.9 ± 0.4	152 ± 4.9	11.2 ± 0.6	3.99 ± 0.15	3.2 ± 0.11
F	5.9 ± 0.7	167 ± 9	11 ± 0.7	3.6 ± 0.3	2.7 ± 0.2
G	5.4 ± 0.2	144 ± 2.8	12 ± 0.9	3.9 ± 0.1	3.1 ± 0.1
H	5.8 ± 0.9	145 ± 11.8	11.9 ± 1.0	4.7 ± 0.2	3.6 ± 0.15
I	5.6 ± 0.4	145 ± 7.7	11.9 ± 1.0	4.4 ± 0.2	3.4 ± 0.2
J	6.4 ± 0.7	185 ± 10	11.5 ± 0.7	4.7 ± 0.5	3.0 ± 0.3

EXAMPLE 5

Surface Scatter Measurements

Light scattering of IOL surfaces is a well known phenomenon which eye care physicians can detect in implanted eyes with the aid of a slit lamp microscope. Scheimpflug photography is one method commonly used to quantify the amount of scattered light. In short, a Scheimpflug camera is used to capture an image of an implanted IOL. The scattered light intensity, measured in CCT values, can be subsequently quantified using the available software. To date, best in class competitor IOLs have shown CCT values of less than 30 in samples of lenses that have been accelerated aged for 10 years. In this study, 21 diopter single piece IOLs were made from formulations. The IOLs were first aged under accelerated conditions in saline solution (BSS) at 90°C. The lenses were rinsed

in deionized water to remove the salts and then dried. Surface scatter measurements were carried out on samples previously equilibrated in BSS saline solution at ambient temperature for 20 hours. As shown in Table 5, samples aged for 3 and 5 years showed low surface scatter counts, between 0 – 30 CCT. Ten year data will be available by June 2011, respectively.

TABLE 5

Sample (N = 3)	SS (CCT) (t=10 yr) (hydrated)
B	33.7 ± 6.9
C	5.8 ± 2.2
D	13.1 ± 7.3
E	19.2 ± 7.5 (t= 3 yr)
F	9.8 ± 3.8
G	11.9 ± 5.7
H	15.7 ± 1.4
I	10.9 ± 2.9

EXAMPLE 6

Delivery Evaluation of Lenses

Lenses cast in 40 Diopter molds from select formulations were delivered through Monarch III D cartridges using H4 handpieces (with and without soft tip) and Viscoat viscoelastic. Lens delivery was carried out at 18 °C and 23 °C with no dwell time. Post delivery evaluations included cartridge tip stress levels, optic and haptic damage and optic and haptic unfolding times are reported in Table 6. In general, stress level values of 5 typically signify high level of cartridge damage. Stress level values of 3-4 signify some but expectable levels of

cartridge damage. Values between 0 – 2 indicates little to no damage. As shown in Table 6, stress level values were low and no significant cartridge damage was observed at either 18 or 23°C. Furthermore, the nozzle stress values were less than those reported for 27.0 diopter Acrysof (SN60WF) lenses using similar cartridges and conditions. Delivery force measurements, where values below 15 N are also considered acceptable. In general, all the lens optics unfolded quickly, within 4 seconds of delivery at 18 and 23 °C and passed post-delivery cosmetic inspection. In addition, haptics did not stick to the optic region upon delivery. However, longer haptic unfolding times were measured for the formulations with lower level of crosslinker (1.5 wt %) as compared to formulations having higher levels of crosslinker (1.75 and 2.0 wt %)

TABLE 6

Formulation (N = 3)	Injection Force (N)		Nozzle Stress Level (0 – 5)		Optic Unfolding time (s)	Haptic Unfolding time (s)
	18°C	23°C	18°C	23°C		
B	7.9 ± 0.4	5.9± 0.4	<4	<3	<4	<10
C	Hand inj. w/normal force		<4	<3	<4	>300
D	Hand inj. w/normal force		<4	<3	<6	<4
G	Hand inj. w/normal force		<4	<3	<4	<4
	11.1 ± 0.3	8.6 ± 0.3				

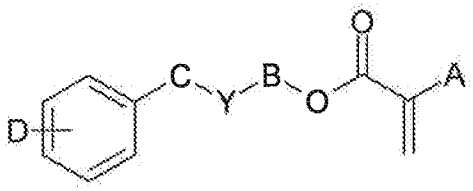
The invention having now been fully described, it should be understood that it may be embodied in other specific forms or variations without departing from its spirit or essential characteristics. Accordingly, the embodiments

described above are to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are intended to be embraced therein.

We claim:

1. A copolymeric ophthalmic device material formed by polymerizing a mixture comprising

a) 30 – 60 % (w/w) or more of an aryl acrylic hydrophobic monomer of formula (I)



(I)

wherein:

A is H;

B is $(CH_2)_m$, $S(CH_2)_u$, $O(CH_2)_v$, or $[O(CH_2)_2]_n$;

u is 1 – 4;

v is 1 – 4;

C is $(CH_2)_w$;

m is 1 – 6;

n is 1 – 10;

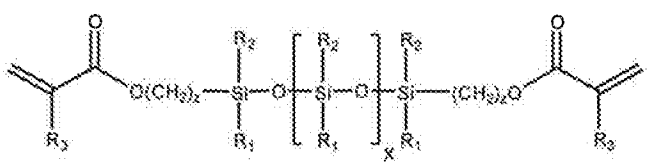
Y is nothing, O, S, or NR, provided that if Y is O, S, or NR, then B is $(CH_2)_m$;

R is H, CH_3, C_nH_{2n+1} (n=1-10), iso-OC_3H_7, C_6H_5, or $CH_2C_6H_5$;

w is 0 – 6, provided that m + w ≤8; and

D is H, C_1 – C_4 alkyl, C_1 – C_4 alkoxy, C_6H_5, $CH_2C_6H_5$, Br, F, Cl, or I;

b) 0.1 – 3.9 % (w/w) of a macromer of formula (II)



(II)

wherein

R_1 and R_2 are independently $-CH_3$, $-CH_2CH_3$, $-CH_2CH_2CH_2CH_3$, $CH_2CH_2CH_2CH_3$, $-C_6H_5$, $-CH_2C_6H_5$, $-CH_2CH_2C_6H_5$, $-CH_2CH_2CH_2C_6H_5$, or $-CH_2CH_2CH_2CH_2C_6H_5$;

R_3 is H, CH_3, or CH_2CH_3;

z is 2-11; and

x indicates the number of repeating units and determines the molecular weight of the macromer and is such that the macromer has a molecular weight of about 300 – about 3500;

c) 10 – 40 % (w/w) of 2-ethylhexyl acrylate or n-octyl acrylate;

d) 5 – 30% (w/w) of a hydrophilic monomer selected from the group consisting of: hydroxy(C_2 – C_4 alkyl)methacrylates, glycerol methacrylate, and *N*-vinyl pyrrolidone;

e) a cross-linking monomer; and

f) a reactive UV absorber;

wherein the copolymeric ophthalmic device material has an equilibrium water content at 35 °C of less than 4 %.

2. The copolymeric device material of Claim 1 wherein the aryl acrylic hydrophobic monomer is selected from the group consisting of: benzyl acrylate; 2-phenylethyl acrylate; 2-phenoxyethyl acrylate; 4-phenylbutyl acrylate; 5-phenylpentyl acrylate; 2-benzyloxyethyl acrylate; 3-benzyloxypropyl acrylate; 3-phenylpropyl acrylate; 3-phenoxypropyl acrylate; 2-(phenylthio)propyl acrylate; and 2-(phenylthio)ethyl acrylate.

3. The copolymeric device material of Claim 2 wherein the aryl acrylic hydrophobic monomer is selected from the group consisting of: 2-

phenylethyl acrylate; 2-phenoxyethyl acrylate; benzyl acrylate; and 2-(phenylthio)ethyl acrylate.

4. The copolymeric device material of Claim 1 wherein the mixture comprises 35 - 50 % (w/w) of the aryl acrylic hydrophobic monomer.

5. The copolymer device material of Claim 4 wherein the mixture comprises 40 - 50 % (w/w) of the aryl acrylic hydrophobic monomer.

6. The copolymeric device material of Claim 1 wherein the mixture comprises 1 – 3 % (w/w) of the macromer of formula (II).

7. The copolymeric device material of Claim 6 wherein the mixture comprises 1.5 – 2.5 % (w/w) of the macromer of formula (II).

8. The copolymeric device material of Claim 1 wherein the macromer of formula (II) has a molecular weight of 350 – 2,000.

9. The copolymeric device material of Claim 8 wherein the macromer of formula (II) has a molecular weight of 800 – 1,400.

10. The copolymeric device material of Claim 8 wherein the macromer of formula (II) has a molecular weight of 550 – 700.

11. The copolymeric device material of Claim 1 wherein the mixture comprises 15 – 35 % (w/w) of n-octyl acrylate.

12. The copolymeric device material of Claim 11 wherein the mixture comprises 17 - 32 % (w/w) of n-octyl acrylate.

13. The copolymeric device material of Claim 1 wherein the hydrophilic monomer is a hydroxy(C_2 – C_4 alkyl)methacrylate and the mixture comprises 10 – 25 % (w/w) of the hydrophilic monomer.

14. The copolymeric device material of Claim 13 wherein the hydrophilic monomer is 2-hydroxyethyl methacrylate and the mixture comprises 15 – 25 % (w/w) of the hydrophilic monomer.

15. The copolymeric device material of Claim 1 wherein the mixture comprises 0.5 – 10 % (w/w) of the cross-linking agent.

16. The copolymeric device material of Claim 15 wherein the mixture comprises 1 – 3 % (w/w) of the cross-linking agent and the cross-linking agent is selected from the group consisting of: ethylene glycol dimethacrylate; diethylene glycol dimethacrylate; allyl methacrylate; 1,3-propanediol dimethacrylate; 2,3-propanediol dimethacrylate; 1,6-hexanediol dimethacrylate; 1,4-butanediol dimethacrylate; triethylene glycol dimethacrylate; and their corresponding acrylates.

17. The copolymeric device material of Claim 16 wherein the cross-linking agent is selected from the group consisting of 1,4-butanediol dimethacrylate and triethylene glycol dimethacrylate.

18. The copolymeric device material of Claim 1 wherein the mixture further comprises a reactive blue-light absorbing compound.

19. An intraocular lens comprising the copolymeric device material of Claim 1.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/040246

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61L27/16 C08L33/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	US 5 331 073 A (WEINSCHENK III JOSEPH I [US] ET AL) 19 July 1994 (1994-07-19) column 2, line 19 - line 28 column 4, line 39 - column 5, line 7 column 5, line 32 - line 49 claims 1,8,14,18-20 -----	1-19
Y	US 7 585 900 B2 (CORDOVA DIANA M [US] ET AL) 8 September 2009 (2009-09-08) claims -----	1-19

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
15 August 2012	21/08/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Dudás, Eszter

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2012/040246

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