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(54) Title: METHOD OF MAKING SILICONE CONTAINING CONTACT LENS WITH REDUCED AMOUNT OF DILUENTS

(57) Abstract: The present invention relates to a method of manufacturing a contact lens including the steps of: (i) adding reactive components to a mold, wherein the reactive components comprise (a) at least one hydroxy-containing silicone component having a weight average molecular weight from about 200 to about 15,000 g/mole and (b) at least one mono-ether terminated, mono-methacrylate terminated polyethylene glycol having a weight average molecular weight from about 200 to about 10,000 g/mole; (ii) curing the reactive components within the mold to form the contact lens; and (iii) removing the contact lens from said mold.

# METHOD OF MAKING SILICONE CONTAINING CONTACT LENS WITH REDUCED AMOUNT OF DILUENTS

## Related Applications

This application claims priority to U.S. Provisional Patent Application No. 61/663,719, filed on June 25, 2012 entitled METHOD OF MAKING SILICONE CONTAINING CONTACT LENS WITH REDUCED AMOUNT OF DILUENTS, the contents of which are incorporated by reference.

## Field of the Invention

The present invention relates to the method of making silicone containing contact lens.

## Background of the Invention

Contact lenses have been used commercially to improve vision since the 1950s. The first contact lenses were made of hard materials. Although these lenses are still currently used, they are not suitable for all patients due to their poor initial comfort and their relatively low permeability to oxygen. Later developments in the field gave rise to soft contact lenses, based upon hydrogels, which are extremely popular today. Many users find soft lenses are more comfortable, and increased comfort levels can allow soft contact lens users to wear their lenses longer than users of hard contact lenses.

It is desirable to manufacture silicone-containing contact lens using reduced or no diluent systems, which can enable the cured polymer to be "dry released" from the mold parts, placed directly into the final package containing packing solution for equilibration. Typically, the zero diluent systems containing high levels of PVP tend to produce cured lenses that are very brittle. These lenses when released using mechanical force are susceptible to physical damage. Applicants have found the incorporation of at least one mono-ether terminated, mono-methacrylate terminated polyethylene glycol significantly lowers the level of brittleness in the cured lenses. Thus, the cured lenses are less liable to fracture when subjected to stress during the lens release process. The at least one mono-ether terminated, mono-methacrylate terminated polyethylene glycol also allows for

tuning the visco-elastic properties of the cured polymers for desirable mechanical lens release without the use of liquids.

## Summary of the Invention

In one aspect, the present invention relates to a method of manufacturing a contact lens, said method comprising the steps of:

(i) adding reactive components to form a reactive mixture, wherein said reactive components comprise (a) at least one hydroxy-containing silicone component having a weight average molecular weight from about 200 to about 15,000 g/mole and (b) at least one monofunctional polyethylene glycol having a weight average molecular weight from about 200 to about 10,000 g/mole; and less than about 15 wt% diluents;

(ii) curing said reactive components within said mold to form said contact lens comprising a polymer having a Tg (heating) of less than about 125C; and

(iii) dry removing said contact lens from said mold.

In another aspect, the present invention feature a contact lens manufactured according to the above method.

Other features and advantages of the present invention will be apparent from the detailed description of the invention and from the claims.

## Detailed Description of the Invention

It is believed that one skilled in the art can, based upon the description herein, utilize the present invention to its fullest extent. The following specific embodiments can be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. Also, all publications, patent applications, patents, and other references mentioned herein are incorporated by reference.

Definitions

As used herein "reactive mixture" refers to the mixture of components (both reactive and non-reactive) which are mixed together and subjected to polymerization conditions to form the silicone hydrogels and contact lenses of the present invention. The reactive mixture comprises reactive components such as monomers, macromers, prepolymers, cross-linkers, and initiators, and additives such as wetting agents, release agents, dyes, pigments, light absorbing compounds such as UV absorbers and photochromic compounds, any of which may be reactive or non-reactive but are capable of being retained within the resulting lens, as well as pharmaceutical and neutriceutical compounds, and any diluents. It will be appreciated that a wide range of additives may be added based upon the lens which is made, and its intended use.

Concentrations of components of the reactive mixture are given in weight % of all components in the reaction mixture, excluding any diluents. When diluents are used their concentrations are given as weight % based upon the amount of all components in the reaction mixture and the diluents.

As used herein "reactive groups" are groups that can undergo free radical and/or tionic polymerization.

As used herein, "polymerizable" means that the compound comprises at least one polymerizable functional group, such as acrylate, methacrylate, acrylamide, methacrylamide, N-vinyl lactam, N-vinylamide, and styryl functional groups. "Non-polymerizable" means that the compound does not comprise such a polymerizable functional group.

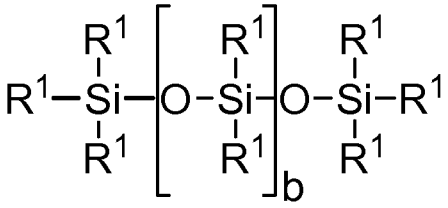
As used herein, "hydrophobic" means that the compound(s)/monomer(s) is insoluble in a mixture of 10 weight parts in 90 weight parts of water, and "hydrophilic" means that the compound(s)/monomer(s) is soluble in a mixture of 10 parts in 90 weight parts of water. The solubility of a substance is evaluated at 20 °C.

As used herein, the term "alkyl" refers to a hydrocarbon group of from 1 to 20 carbons, unless otherwise indicated.

Silicone Component

The reactive mixture contains at least one silicone-containing component comprising at least one hydroxy group ("hydroxy-containing silicone component") and having a weight average molecular weight from about 200 to about 15,000 g/mole, such as from about 300 to about 2,000 g/mole. A silicone-containing component (or silicone component) is one that contains at least one [—Si—O—Si] group, in a monomer, macromer or prepolymer. In one embodiment, the Si and attached O are present in the silicone-containing component in an amount greater than 20 weight percent, such as greater than 30 weight percent of the total molecular weight of the silicone-containing component. Useful hydroxy-containing silicone components include polymerizable functional groups such as acrylate, methacrylate, acrylamide, methacrylamide, N-vinyl lactam, N-vinylamide, and styryl functional groups. Examples of hydroxy-containing silicone components which are useful in this invention may be found in U.S. Patent Nos. 4,139,513; 4,139,692; 5,998,498; and 5,070,215.

Suitable hydroxyl-containing silicone components include compounds of Formula I



Formula I

wherein:

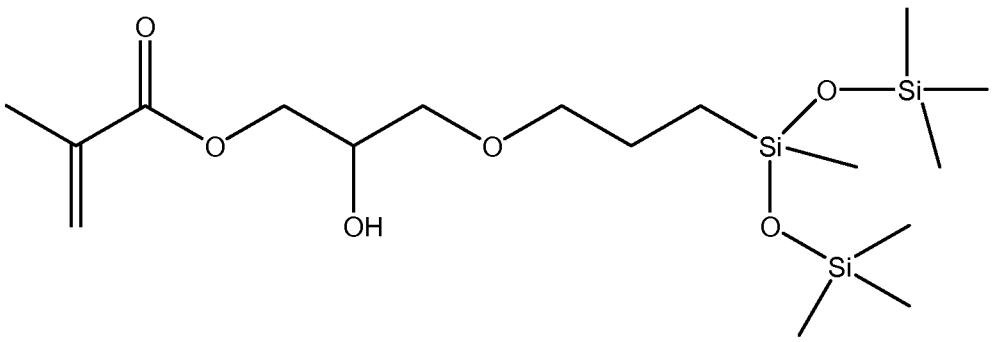
$R^1$ is independently selected from reactive groups, alkyl groups, or aryl groups, any of the foregoing which may further comprise functionality selected from hydroxy, amino, oxa, carboxy, alkyl carboxy, alkoxy, amido, carbamate, carbonate, halogen or combinations thereof; and siloxane chains comprising 1-100 Si-O repeat units which may further comprise functionality selected from alkyl, hydroxy, amino, oxa, carboxy, alkyl carboxy, alkoxy, amido, carbamate, halogen or combinations thereof;

where b = 0 to 500 (such as 0 to 100, such as 0 to 20), where it is understood that when b is other than 0, b is a distribution having a mode equal to a stated value; and

wherein at least one $R^1$ comprises a reactive group, and in some embodiments from one to three $R^1$ comprise reactive groups and at least one R group comprises one or more hydroxyl group.

Non-limiting examples of radical reactive groups include (meth)acrylates, styryls, vinyls, vinyl ethers, $C_{1-6}$alkyl(meth)acrylates, (meth)acrylamides, $C_{1-6}$alkyl(meth)acrylamides, N-vinyllactams, N-vinylamides, $C_{2-12}$alkenyls, $C_{2-12}$alkenylphenyls, $C_{2-12}$alkenylnaphthyls, $C_{2-6}$alkenylphenyl$C_{1-6}$alkyls, O-vinylcarbamates and O-vinylcarbonates. Non-limiting examples of cationic reactive groups include vinyl ethers or epoxide groups and mixtures thereof. In one embodiment the free radical reactive groups comprises (meth)acrylate, acryloxy, (meth)acrylamide, and mixtures thereof.

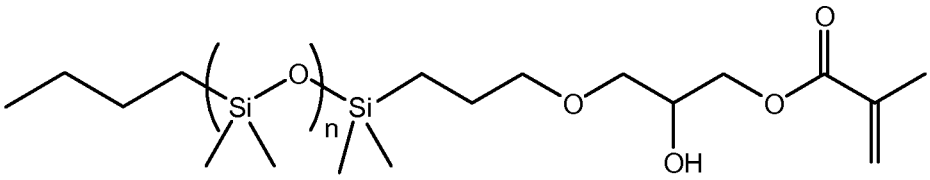
In one embodiment b is zero, one $R^1$ is a reactive group, and at least 3 $R^1$ are selected from monovalent alkyl groups having one to 16 carbon atoms, and in another embodiment from monovalent alkyl groups having one to 6 carbon atoms, in another embodiment one $R^1$ is a reactive group, two $R^1$ are trialkyl siloxanyl group and the remaining $R^1$ are methyl, ethyl or phenyl and in a further embodiment one $R^1$ is a reactive group, two $R^1$ are trialkyl siloxanyl groups and the remaining $R^1$ are methyl. Non-limiting examples of silicone components of this embodiment include propenoic acid,-2-methyl-,2-hydroxy-3-[3-[1,3,3,3-tetramethyl-1-[(trimethylsilyl)oxy]-1-disiloxanyl]propoxy]propyl ester ("SiGMA"; structure in Formula II),




Formula II

and 2-hydroxy-3-methacryloxypropyloxypropyl-tris(trimethylsiloxy)silane.

In another embodiment, b is 2 to 20, 3 to 20, 3-16, 3 to 15 or in some embodiments 3 to 10; at least one terminal $R^1$ comprises a reactive group and the remaining $R^1$ are selected from monovalent alkyl groups having 1 to 16 carbon atoms, and in another embodiment from monovalent alkyl groups having 1 to 6 carbon atoms. In yet another embodiment, b is 3 to 15, one terminal $R^1$ comprises a reactive group, the other terminal $R^1$ comprises a monovalent alkyl group having 1 to 6 carbon atoms and the remaining $R^1$ comprise monovalent alkyl group having 1 to 3 carbon atoms. Non-limiting examples of silicone components of this embodiment include (mono-(2-hydroxy-3-methacryloxypropyl)-propyl ether terminated polydimethylsiloxane (400 - 2000, or 400-1600 $M_w$) ("OH-mPDMS"; structure in Formula III).




Formula III

In one embodiment a mixture of hydroxyl-containing silicone components may be used to improve the compatibility of the reactive mixture.

In another embodiment, the hydroxyl-containing silicone component comprises a polydimethylsiloxane bis-methacrylate with pendent hydroxyl groups, such as compound C2, C4 or R2 described in US Patent Application No. 2004/0192872 or such as is described in Examples XXV, XXVIII, or XXXii in US Patent No. 4,259,467, polymerizable polysiloxanes with pendant hydrophilic groups such as those disclosed in US6867245. In some embodiments the pendant hydrophilic groups are hydroxyalkyl groups and polyalkylene ether groups or combinations thereof. The polymerizable polysiloxanes may also comprise fluorocarbon groups. An example is shown as structure B3.

Other silicone components suitable for use in this invention include those described as “C” Materials in WO 96/31792. Another class of suitable silicone-containing components includes silicone containing macromers made via GTP, such as

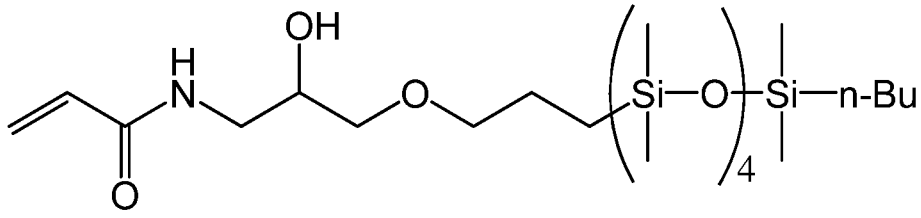
the hydroxyl-containing macromers disclosed in U.S. Pat Nos. 5,314,960, 5,371,147 and 6,367,929.

In one embodiment of the present invention where a modulus of less than about 120 psi is desired, the majority of the mass fraction of the silicone-containing components used in the lens formulation should contain only one polymerizable functional group ("monofunctional silicone containing component"). In this embodiment, to insure the desired balance of oxygen transmissibility and modulus it is preferred that all components having more than one polymerizable functional group ("multifunctional components") make up no more than 10 mmol/100 g of the reactive components, and preferably no more than 7 mmol/100 g of the reactive components.

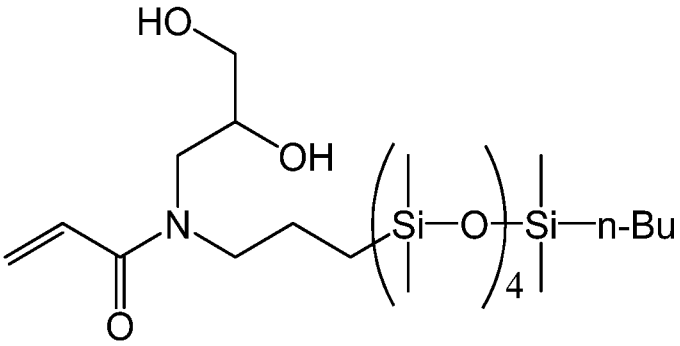
In one embodiment, the silicone component is selected from the group consisting of bis-3-acryloxy-2-hydroxypropyloxypropyl polydialkylsiloxane; mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-alkyl terminated polydialkylsiloxane; and mixtures thereof

In one embodiment, the silicone component is selected from bis-3-acryloxy-2-hydroxypropyloxypropyl polydialkylsiloxane; and mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane; and mixtures thereof.

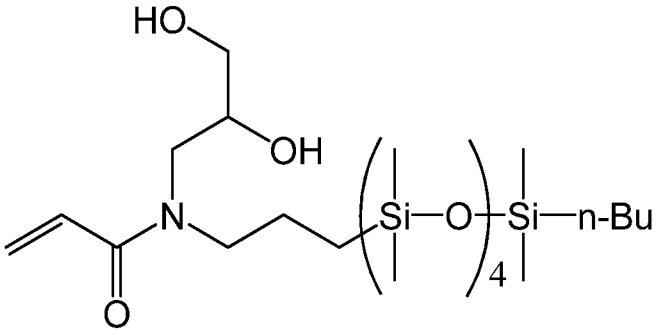
Examples of other silicone components include the following:



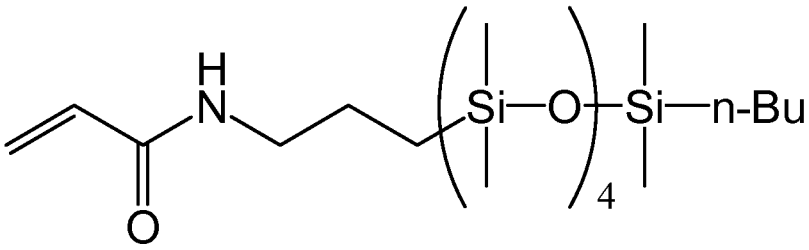

Formula IV



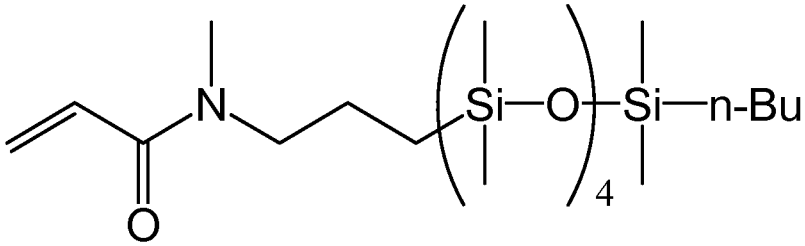

Formula V



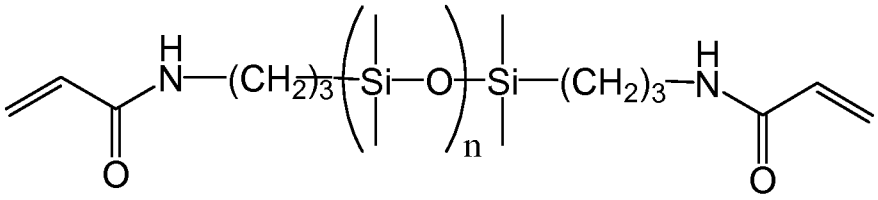

Formula VI



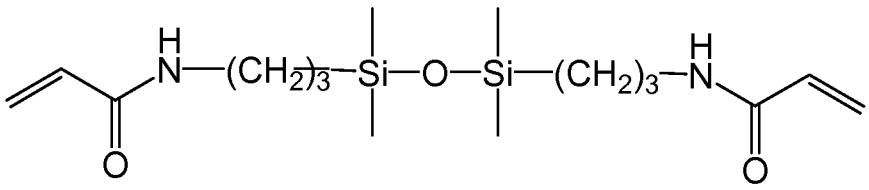

Formula VII




Formula VIII



Formula IX



Formula X

In one embodiment, the silicone component has an average molecular weight of from about 400 to about 4000 daltons.

The silicone containing component(s) may be present in amounts from about 10 to about 87 weight %, and in some embodiments from about 10 and about 80 and in other embodiments from about 20 and about 70 weight %, based upon all reactive components of the reactive mixture (e.g., excluding diluents).

Monofunctional Terminated Polyethylene Glycol

The reactive mixture also contains at least one monofunctional polyethylene glycol having a weight average molecular weight from about 200 to about 10,000 g/mole, such as from about 200 to about 2,000 g/mole. The monofunctional polyethylene glycol comprises only one polymerizable group and may be a mono-ether terminated, mono-(meth)acrylate or (meth)acrylamide terminated polyethylene glycol. Examples of mono-ether terminal groups include, but are not limited to, C1-C6 alkoxy groups, such as methoxy and ethoxy or alkoxy groups comprising up to 8 carbons. Examples of such mono-ether terminated, mono-methacrylate terminated polyethylene glycol include, but are not limited to, mPEG 475 (polyethyleneglycol (475 Mw) monomethylether monomethacrylate, available from Sigma-Aldrich, St. Louis, MO USA ("mPEG475").

The monofunctional polyethylene glycol(s) may be present in amounts from about 3 and about 30 weight%, from about 5 to about 30 weight%, and in other embodiments

from about 10 and about 30 weight %, based upon all reactive components of the reactive mixture (e.g., excluding diluents if any).

The monofunctional polyethylene glycol(s) provide the resulting cured, prehydrated polymers with glass transition temperature upon heating, Tg, of less than about 125C, or between about 115 and about 125C. This provides desirable dry release characteristics, and particularly a resistance to fracturing. The properties of the hydrated lens are substantially unchanged from reactive mixtures which do not comprise at least one monofunctional polyethylene glycol.

Other Hydrophilic Components

In one embodiment, the reactive mixture/lens may also include at least one other hydrophilic component. In one embodiment, these hydrophilic components can be any of the hydrophilic monomers known to be useful to make hydrogels.

One class of suitable hydrophilic monomers includes acrylic- or vinyl-containing monomers. Such hydrophilic monomers may themselves be used as crosslinking agents, however, where hydrophilic monomers having more than one polymerizable functional group are used, their concentration should be limited as discussed above to provide a contact lens having the desired modulus.

The term "vinyl-type" or "vinyl-containing" monomers refer to monomers containing the vinyl grouping ($Y\text{-}CH{=}CH_2$) and that are capable of polymerizing, where Y is not a carbonyl (C=O) group.

Hydrophilic vinyl-containing monomers which may be incorporated into the reactive mixtures/hydrogels/lenses of the present invention include, but are not limited to, monomers such as N-vinyl amides, N-vinyl lactams (e.g. N-vinylpyrrolidone or NVP), N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-ethyl formamide, N-vinyl formamide, with NVP being preferred.

"Acrylic-type" or "acrylic-containing" monomers are those monomers containing the acrylic group: ($CH_2{=}CRCOX$) wherein R is H or $CH_3$, and X is O or N, which are also known to polymerize readily, such as N,N-dimethyl acrylamide (DMA), acrylamide, 2-hydroxyethyl methacrylate (HEMA), glycerol methacrylate, 2-hydroxyethyl

methacrylamide, polyethyleneglycol monomethacrylate, methacrylic acid, mixtures thereof and the like.

Other hydrophilic monomers that can be employed in the invention include, but are not limited to, polyoxyethylene alcohols having one or more of the terminal hydroxyl groups replaced with a functional group containing a polymerizable double bond. Examples include polyethylene glycol, ethoxylated alkyl glucoside, and ethoxylated bisphenol A reacted with one or more molar equivalents of an end-capping group such as isocyanatoethyl methacrylate ("IEM"), methacrylic anhydride, methacryloyl chloride, vinylbenzoyl chloride, or the like, to produce a polyethylene polyol having one or more terminal polymerizable olefinic groups bonded to the polyethylene alcohol through linking moieties such as carbamate or ester groups.

Still further examples are the hydrophilic vinyl carbonate or vinyl carbamate monomers disclosed in U.S. Patents No. 5,070,215 and the hydrophilic oxazolone monomers disclosed in U.S. Patents No. 4,910,277. Other suitable hydrophilic monomers will be apparent to one skilled in the art.

In one embodiment the other hydrophilic component comprises at least one hydrophilic monomer such as DMA, HEMA, glycerol methacrylate, 2-hydroxyethyl methacrylamide, NVP, N-vinyl-N-methyl acrylamide, polyethyleneglycol monomethacrylate, and combinations thereof. In another embodiment, the other hydrophilic monomers comprise at least one of DMA, HEMA, NVP and N-vinyl-N-methyl acrylamide and mixtures thereof. In another embodiment, the other hydrophilic monomer comprises DMA and/or HEMA.

The other hydrophilic component(s) (e.g., DMA or HEMA) may be present in a wide range of amounts, depending upon the specific balance of properties desired. In one embodiment, the amount of the hydrophilic component is up to about 60 weight %, such as from about 5 and about 40 weight %, from about 10 to about 40 weight%, from about 13 to about 40 weight%, or from about 13 to about 30 weight%, based upon the weight of the reactive components. In one embodiment, the weight ratio of (i) said hydrophilic components (e.g., DMA or HEMA) and (ii) said at least one at least one mono-methacrylate terminated polyethylene glycol is from about 25:75 to about 75:25.

In another embodiment the amount of (meth)acrylamide monomers is less than about 10 weight% or between about 3 and about 10 weight% of all components in the reaction mixture, excluding any diluents. Examples of (meth)acrylamide monomers include, DMA, acrylamide, N-vinyl-N-methyl acrylamide, N-vinylacrylamide, mixtures thereof and the like.

The amount of hydroxyl alkyl monomers, may be between about 10 and about 20 weight % of all components in the reaction mixture, excluding any diluents. Examples of hydroxyl alkyl monomers include HEMA, 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylamide, 2-hydroxypropyl methacrylamide, 2-hydroxypropyl methacrylate, 2-hydroxybutyl methacrylamide, 2-hydroxybutyl methacrylate, mixtures thereof and the like,

Polymerization Initiator

One or more polymerization initiators may be included in the reaction mixture. Examples of polymerization initiators include, but are not limited to, compounds such as lauryl peroxide, benzoyl peroxide, isopropyl percarbonate, azobisisobutyronitrile, and the like, that generate free radicals at moderately elevated temperatures, and photoinitiator systems such as aromatic alpha-hydroxy ketones, alkoxyoxybenzoins, acetophenones, acylphosphine oxides, bisacylphosphine oxides, and a tertiary amine plus a diketone, mixtures thereof and the like. Illustrative examples of photoinitiators are 1-hydroxycyclohexyl phenyl ketone, 2-hydroxy-2-methyl-1-phenyl-propan-1-one, bis(2,6-dimethoxybenzoyl)-2,4-4-trimethylpentyl phosphine oxide (DMBAPO), bis(2,4,6-trimethylbenzoyl)-phenyl phosphineoxide (IRGACURE® 819), 2,4,6-trimethylbenzyldiphenyl phosphine oxide and 2,4,6-trimethylbenzoyl diphenylphosphine oxide, benzoin methyl ester and a combination of camphorquinone and ethyl 4-(N,N-dimethylamino)benzoate. Commercially available visible light initiator systems include, but are not limited to, IRGACURE® 819, IRGACURE®1700, IRGACURE®1800, IRGACURE®1850 (all from Ciba Specialty Chemicals) and Lucirin TPO initiator (available from BASF). Commercially available UV photoinitiators include Darocur 1173 and Darocur 2959 (Ciba Specialty Chemicals). These and other photoinitators which may be used are disclosed in Volume III, Photoinitiators for Free Radical Cationic

& Anionic Photopolymerization, 2nd Edition by J.V. Crivello& K. Dietliker; edited by G. Bradley; John Wiley and Sons; New York; 1998.

The polymerization initiator is used in the reaction mixture in effective amounts to initiate photopolymerization of the reaction mixture, such as from about 0.1 to about 2 weight %. Polymerization of the reaction mixture can be initiated using the appropriate choice of heat or visible or ultraviolet light or other means depending on the polymerization initiator used. Alternatively, initiation can be conducted without a photoinitiator using, for example, e-beam. However, when a photoinitiator is used, the preferred initiators are bisacylphosphine oxides, such as bis(2,4,6-trimethylbenzoyl)-phenyl phosphine oxide (IRGACURE® 819) or a combination of 1-hydroxycyclohexyl phenyl ketone and DMBAPO, and in another embodiment the method of polymerization initiation is via visible light activation.

Internal Wetting Agent

In one embodiment, the reaction mixture includes one or more internal wetting agents. Internal wetting agents may include, but are not limited to, high molecular weight, hydrophilic polymers such as those described in US Patent Nos. 6,367,929; 6,822,016; 7786185; PCT Patent Application Nos. WO03/22321 and WO03/22322, or reactive, hydrophilic polymers such as those described in US Patent No. 7,249,848. Examples of internal wetting agents include, but are not limited to, polyamides such as poly(N-vinyl pyrrolidone), poly(dimethyl acrylamide) and poly (N-vinyl-N-methyl acetamide), polyN-vinyl acetamide, polyacrylamide and copolymers thereof. Suitable comonomers include acrylic acid, methacrylic acid, 2-hydroxyethyl methacrylate, reactive polyethylene glycol monomers, combinations thereof and the like.

The internal wetting agent(s) may be present in a wide range of amounts, depending upon the specific parameter desired. In one embodiment, the amount of the wetting agent(s) is up to about 50 weight %, up to about 30 weight%, such as from about 5 and about 40 weight %, from about 5 and about 30 weight %, such as from about 6 to about 40 weight % or from about 6 to about 25 weight % based upon all % of all components in the reaction mixture, excluding any diluents.

Other Components

Other components that can be present in the reaction mixture used to form the contact lenses of this invention include, but are not limited to, ultra-violet absorbing compounds, medicinal agents, antimicrobial compounds, copolymerizable and nonpolymerizable dyes, copolymerizable and non-copolymerizable photochromic compounds, ionic monomers or components, surfactants, release agents, reactive tints, pigments, combinations thereof and the like. In one embodiment, the sum of additional components may be up to about 20 wt%.

Diluents

In one embodiment, the reactive components (e.g., silicone-containing components, hydrophilic monomers, wetting agents, and/or other components) are mixed together either with or without a diluent to form the reaction mixture. In one embodiment, the reactive mixture comprises less than about twenty percent (e.g., such as less than about ten percent, less than about five percent, or less than about one percent) by weight, of one or more diluents, or comprises no diluents.

In one embodiment where a diluent is used, the diluent has a polarity sufficiently low to solubilize the non-polar components in the reactive mixture at reaction conditions. One way to characterize the polarity of the diluents of the present invention is via the Hansen solubility parameter, $\delta p$. In certain embodiments, the $\delta p$ is less than about 10, and preferably less than about 6. Suitable diluents are further disclosed in US Patent Application No. 20100280146 and US Patent No. 6,020,445.

In another embodiment the selected diluents are ophthalmically compatible, at least in small concentrations. Thus, in one embodiment the diluent is ophthalmically compatible in concentrations of up to 5 weight % in the packing solution and in some embodiments, up to 1% by weight of the packing solution.

Classes of suitable diluents include, without limitation, alcohols having 2 to 20 carbons, amides having 10 to 20 carbon atoms derived from primary amines, ethers, polyethers, ketones having 3 to 10 carbon atoms, and carboxylic acids having 8 to 20 carbon atoms. As the number of carbons increase, the number of polar moieties may also be increased to provide the desired level of water miscibility. In some embodiments,

primary and tertiary alcohols are preferred. Preferred classes include alcohols having 4 to 20 carbons and carboxylic acids having 10 to 20 carbon atoms.

In one embodiment, the diluents are selected from 1,2-octanediol, t-amyl alcohol, 3-methyl-3-pentanol, decanoic acid, 3,7-dimethyl-3-octanol, tripropylene glycol methyl ether (TPME), 1, 2-propanediol, glycerol, polyethylene glycol having molecular weights between about 200 and about 30,000, methyl glucose ethers, such as Glucam polymers, butoxyethyl acetate, mixtures thereof and the like.

In one embodiment, the diluents are selected from diluents that have some degree of solubility in water. In some embodiments at least about three percent of the diluent is miscible water. Examples of water soluble diluents include, but are not limited to, 1-octanol, 1-pentanol, 1-hexanol, 2-hexanol, 2-octanol, 3-methyl-3-pentanol, 2-pentanol, t-amyl alcohol, *tert*-butanol, 2-butanol, 1-butanol, 2-methyl-2-pentanol, 2-ethyl-1-butanol, ethanol, 3,3-dimethyl-2-butanol, decanoic acid, octanoic acid, dodecanoic acid, 1-ethoxy-2- propanol, 1-tert-butoxy-2-propanol, EH-5 (commercially available from Ethox Chemicals), 2,3,6,7-tetrahydroxy-2,3,6,7-tetramethyl octane, 9-(1-methylethyl)-2,5,8,10,13,16-hexaoxaheptadecane, 3,5,7,9,11,13-hexamethoxy-1-tetradecanol, mixtures thereof and the like.

Suitable ranges for the components of the present invention are shown in the Table below.

| Component | Concentration (wt%) |
|---|---|
| Silicone component | 10-87, 10-80, 20-70 |
| PEG | 3-30 |
| Hydrophilic component | 5-40, 10-40, 13-40, 13-30 |
| Wetting agent | 0- 50; 5-40, 6- 40, 10-20 |
| Other | 0-20 |
| Diluent | $\leq$20, <15, $\leq$10, $\leq$5, $\leq$1, 0 |

It will be appreciated that the amount of the components in each embodiment will add up to 100. Also, the ranges may be combined in any combination.

Curing of Silicone Polymer/Hydrogel and Manufacture of Lens

The reactive mixture of the present invention may be cured via any known process for molding the reaction mixture in the production of contact lenses, including spincasting and static casting. Spincasting methods are disclosed in U.S. Patents Nos. 3,408,429 and 3,660,545, and static casting methods are disclosed in U.S. Patents Nos. 4,113,224 and 4,197,266. In one embodiment, the contact lenses of this invention are formed by the direct molding of the silicone hydrogels, which is economical, and enables precise control over the final shape of the hydrated lens. For this method, the reaction mixture is placed in a mold having the shape of the final desired silicone hydrogel and the reaction mixture is subjected to conditions whereby the monomers polymerize, to thereby produce a polymer in the approximate shape of the final desired product.

In one embodiment, the lenses are released, or deblocked from the mold dry. Dry release or deblocking is achieved without contacting the lenses with a fluid or liquid. Suitable methods of dry release include the rapidly cooling the lens and lens mold or application of mechanical force, such as tapping, twisting, or pressing the lens mold.

In one embodiment, after curing and deblocking, the lens is subjected to extraction to remove unreacted components and release the lens from the lens mold. The extraction may be done using conventional extraction fluids, such organic solvents, such as alcohols or may be extracted using aqueous solutions.

Aqueous solutions are solutions which comprise water. In one embodiment the aqueous solutions of the present invention comprise at least about 30 weight % water, in some embodiments at least about 50 weight % water, in some embodiments at least about 70% water and in others at least about 90 weight% water. Aqueous solutions may also include additional water soluble components such as release agents, wetting agents, slip agents, pharmaceutical and nutraceutical components, combinations thereof and the like. Release agents are compounds or mixtures of compounds which, when combined with water, decrease the time required to release a contact lens from a mold, as compared to the time required to release such a lens using an aqueous solution that does not comprise the release agent. In one embodiment the aqueous solutions comprise less than about 10 weight %, and in others less than about 5 weight % organic solvents such as isopropyl

alcohol, and in another embodiment are free from organic solvents. In these embodiments the aqueous solutions do not require special handling, such as purification, recycling or special disposal procedures.

In various embodiments, extraction can be accomplished, for example, via immersion of the lens in an aqueous solution or exposing the lens to a flow of an aqueous solution. In various embodiments, extraction can also include, for example, one or more of: heating the aqueous solution; stirring the aqueous solution; increasing the level of release aid in the aqueous solution to a level sufficient to cause release of the lens; mechanical or ultrasonic agitation of the lens; and incorporating at least one leach aid in the aqueous solution to a level sufficient to facilitate adequate removal of unreacted components from the lens. The foregoing may be conducted in batch or continuous processes, with or without the addition of heat, agitation or both.

Some embodiments can also include the application of physical agitation to facilitate leach and release. For example, the lens mold part to which a lens is adhered, can be vibrated or caused to move back and forth within an aqueous solution. Other embodiments may include ultrasonic waves through the aqueous solution.

In one embodiment, the lens is removed from the mold by a dry release process. In one embodiment of such a process, when then monomer mix has been cured to form a polymer the mold halves are separated by prying them apart. Typically the lens remains adhered to one surface of one mold half. That mold half is then flexed in order to force the lens to separate from the mold. Thus, the lens is removed from the mold without the use of any release solvent such as water or isopropanol. The released lens can then optionally be placed into a solvent for leaching or can be placed directly into a package containing a packaging solution such as buffered saline. Alternatively, the lens can be subjected to additional processing, such as plasma surface treatment, before it is hydrated.

The lenses may be sterilized by known means such as, but not limited to autoclaving.

Test Methods

Protein solution:

A tear like fluid ("TLF") was used for protein uptake measurements. The TLF was made from by solubilizing the components, in the amounts listed in the Table below in phosphate saline buffer supplemented by sodium bicarbonate at 1.37g/l.

Table: Tear Like Fluid (TLF) Composition

| Components | Composition (mg/ml) | Origin |
|---|---|---|
| Proteins and Glycoproteins | | |
| Lysozyme | 1.85 | Chicken egg white |
| Lactoferrin | 2.1 | Bovine colostrum |
| Gamma Globulins | 0.3 | Bovine plasma |
| Lipocalin | 1.3 | Milk lipocaline (β lactoglobulin) from bovine milk |
| Acid glycoprotein | 0.05 | Bovine plasma |
| Mucins | 0.15 | Bovine submaxillary glands |
| (Albumin, Fn[1], Vn[2] and others components present in tears at very low concentrations (ng) | 0.1% | Bovine serum |
| Lipids | | |
| Cholesteryl linoleate | 0.024 | |
| Linalyl acetate | 0.021 | |
| Triolein | 0.016 | |
| Oleic acid | 0.012 | |
| Undecylenic acid | 0.0032 | |
| Cholesterol | 0.0016 | |
| Glucose | 0.1 | |

[1]Fn: Fibronectin
[2]Vn: Vitronectin

Lipocalin uptake was measured as follows. The lipocalin solution contained B Lactoglobulin (Lipocalin) from bovine milk (Sigma, L3908) solubilized at a concentration of 2 mg/ml in phosphate saline buffer supplemented by Sodium bicarbonate at 1.37g/l and D-Glucose at 0.1 g/l. Three lenses for each sample were tested using each protein solution, and three were tested using PBS as a control solution. The test lenses were blotted on sterile gauze to remove packing solution and aseptically transferred, using sterile forceps, into sterile, 24 well cell culture plates (one lens per well) each well containing 2 ml of lysozyme solution. Each lens was fully immersed in the solution. 2 ml of the lysozyme solution was placed in a well without a contact lens as a control.

The plates containing the lenses and the control plates containing only protein solution and the lenses in the PBS, were sealed using parafilm to prevent evaporation and dehydration, placed onto an orbital shaker and incubated at 35°C, with agitation at 100 rpm for 72 hours. After the 72 hour incubation period the lenses were rinsed 3 to 5 times by dipping lenses into three (3) separate vials containing approximately 200 ml volume of PBS. The lenses were blotted on a paper towel to remove excess PBS solution and transferred into sterile conical tubes (1 lens per tube), each tube containing a volume of PBS determined based upon an estimate of lysozyme uptake expected based upon on each lens composition. The lysozyme concentration in each tube to be tested needs to be within the albumin standards range as described by the manufacturer (0.05 microgram to 30 micrograms). Samples known to uptake a level of lysozyme lower than 100 µg per lens were diluted 5 times. Samples known to uptake levels of lysozyme higher than 500 µg per lens (such as etafilcon A lenses) are diluted 20 times.

1 ml aliquot of PBS was used for samples 9, CE2 and the balafilcon lenses, and 20ml for etafilcon A lens. Each control lens was identically processed, except that the well plates contained PBS instead of either lysozyme or lipocalin solution.

Lysozyme and Lipocalin uptake was determined using on-lens bicinchoninic acid method using QP-BCA kit ( Sigma, QP-BCA) following the procedure described by the manufacturer (the standards prep is described in the kit) and is calculated by subtracting

the optical density measured on PBS soaked lenses ( background) from the optical density determined on lenses soaked in lysozyme solution.

Optical density was measured using a SynergyII Micro-plate reader capable for reading optical density at 562nm.

Mucin uptake was measured using the following solution and method. The mucin solution contained mucins from bovine submaxillary glands (Sigma, M3895-type 1-S) solubilized at a concentration of 2 mg/ml in phosphate saline buffer (Sigma, D8662) supplemented by sodium bicarbonate at 1.37g/l and D-Glucose at 0.1 g/l.

Three lenses for each example were tested using Mucin solution, and three were tested using PBS as a control solution. The test lenses were blotted on sterile gauze to remove packing solution and aseptically transferred, using sterile forceps, into sterile, 24 well cell culture plates (one lens per well) each well containing 2 ml of Mucin solution. Each lens was fully immersed in the solution. Control lenses were prepared using PBS as soak solution instead of lipocalin.

The plates containing the lenses immersed in Mucin as well as plates containing control lenses immersed in PBS were sealed using parafilm to prevent evaporation and dehydration, placed onto an orbital shaker and incubated at 35˚C, with agitation at 100 rpm for 72 hours. After the 72 hour incubation period the lenses were rinsed 3 to 5 times by dipping lenses into three (3) separate vials containing approximately 200 ml volume of PBS. The lenses were blotted on a paper towel to remove excess PBS solution and transferred into sterile 24 well plates each well containing 1 ml of PBS solution.

Mucin uptake was determined using on-lens bicinchoninic acid method using QP-BCA kit ( Sigma, QP-BCA) following the procedure described by the manufacturer (the standards prep is described in the kit) and is calculated by subtracting the optical density measured on PBS soaked lenses ( background) from the optical density determined on lenses soaked in Mucin solution. Optical density was measured using a SynergyII Micro-plate reader capable for reading optical density at 562nm.

Wettability is measured by measuring the dynamic contact angle or DCA, typically at 23 $\pm$3°C and a relative humidity of about 45 $\pm$5%, with borate buffered saline, using a Wilhelmy balance. The wetting force between the lens surface and borate buffered saline is measured using a Wilhelmy microbalance while the sample strip cut

from the center portion of the lens is being immersed into or pulled out of the saline at a rate of 100 microns/sec . The following equation is used

$$F = \gamma p \cos\theta \qquad \text{or} \qquad \theta = \cos^{-1}(F/\gamma p)$$

where F is the wetting force, $\gamma$ is the surface tension of the probe liquid, p is the perimeter of the sample at the meniscus and $\theta$ is the contact angle. Typically, two contact angles are obtained from a dynamic wetting experiment – advancing contact angle and receding contact angle. Advancing contact angle is obtained from the portion of the wetting experiment where the sample is being immersed into the probe liquid, and these are the values reported herein. Five lenses of each composition are measured and the average is reported.

Oxygen permeability (Dk) was determined by the polarographic method generally described in ISO 18369-4:2006, but with the following variations. The measurement is conducted at an environment containing 2.1% oxygen. This environment is created by equipping the test chamber with nitrogen and air inputs set at the appropriate ratio, for example 1800 ml/min of nitrogen and 200 ml/min of air. The t/Dk is calculated using the adjusted oxygen concentration. Borate buffered saline was used. The dark current was measured by using a pure humidified nitrogen environment instead of applying MMA lenses. The lenses were not blotted before measuring. Four lenses with uniform thickness in the measurement area were stacked instead of using lenses of varied thickness. The L/Dk of 4 samples with significantly different thickness values are measured and plotted against the thickness. The inverse of the regressed slope is the preliminary Dk of the sample. If the preliminary Dk of the sample is less than 90 barrer, then an edge correction of (1 + (5.88(CT in cm))) is applied to the preliminary L/Dk values. If the preliminary Dk of the sample is greater than 90 barrer, then an edge correction of (1 + (3.56(CT in cm))) is applied to the preliminary L/Dk values. The edge corrected L/Dk of the 4 samples are plotted against the thickness. The inverse of the regressed slope is the Dk of the sample. A curved sensor was used in place of a flat sensor. The resulting Dk value is reported in barrers.

Water Content

The water content was measured as follows: lenses to be tested are allowed to sit in packing solution for 24 hours. Each of three test lens are removed from packing

solution using a sponge tipped swab and placed on blotting wipes which have been dampened with packing solution. Both sides of the lens are contacted with the wipe. Using tweezers, the test lens are placed in a weighing pan and weighed. The two more sets of samples are prepared and weighed as above.pan is weighed three times and the average is the wet weight.

The dry weight is measured by placing the sample pans in a vacuum oven which has been preheated to 60°C for 30 minutes. Vacuum is applied until at least 0.4 inches Hg is attained. The vacuum valve and pump are turned off and the lenses are dried for four hours. The purge valve is opened and the oven is allowed reach atmospheric pressure. The pans are removed and weighed. The water content is calculated as follows:

Wet weight = combined wet weight of pan and lenses – weight of weighing pan
Dry weight = combined dry weight of pan and lens – weight of weighing pan

$$\% \text{ water content} = \frac{(\text{wet weight} - \text{dry weight})}{\text{wet weight}} \times 100$$

The average and standard deviation of the water content are calculated for the samples are reported.

Tensile modulus is measured by using the crosshead of a constant rate of movement type tensile testing machine equipped with a load cell that is lowered to the initial gauge height. A suitable testing machine includes an Instron model 1122. A dog-bone shaped sample having a 0.522 inch length, 0.276 inch "ear" width and 0.213 inch "neck" width is loaded into the grips and elongated at a constant rate of strain of 2 in/min. until it breaks. The initial gauge length of the sample (Lo) and sample length at break (Lf) are measured. Twelve specimens of each composition are measured and the average is reported. Tensile modulus is measured at the initial linear portion of the stress/strain curve. Percent elongation is = [(Lf – Lo)/Lo]x 100.

Glass transition temperature, Tg is defined as the peak (maximum) in tan δ. The glass transition Tg after the isothermal cure, the dynamic shear modulus (G'), loss modulus (G"), and tan δ were measured using DSC as a function of temperature

(frequency 1.0 Hz, auto-tension mode (tension=0), parallel plate (25.0 mm diameter), and shear stress 5.0 kPa), while the cured films were heated from 55°C to 150°C at 1°C/min.

Examples

These examples do not limit the invention. They are meant only to suggest a method of practicing the invention. Those knowledgeable in lenses as well as other specialties may find other methods of practicing the invention. The following abbreviations are used in the examples below:

| | |
|---|---|
| DMA | N,N-dimethylacrylamide |
| HEMA | 2-hydroxyethyl methacrylate |
| IRGACURE 819 | bis(2,4,6-trimethylbenzoyl)-phenylphosphineoxide |
| Norbloc | 2-(2'-hydroxy-5-methacrylyloxyethylphenyl)-2H-benzotriazole |
| OH-mPDMS | mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydimethylsiloxane (Mw 612 g/mole) |
| PVP | poly(N-vinyl pyrrolidone) (K values noted) |
| TEGDMA | tetraethyleneglycol dimethacrylate |
| acPDMS 1000 | bis-3-acryloxy-2-hydroxypropyloxypropyl polydimethylsiloxane (MW = 1000) |
| CGI1850 | 1:1 (wgt) blend of 1-hydroxycyclohexyl phenyl ketone and bis(2,6-dimethoxybenzoyl)-2,4-4-trimethylpentyl phosphine oxide |
| mPEG 475 | polyethyleneglycol (475 MW) monomethylether monomethacrylate |

Example 1: Formulations Containing mPEG 475 as Hydrophilic Component, with Various Ratios of K30 to K90

Components of the reactive monomer mixes of Table 1a were formulated in a zero diluent system. The blends were prepared in amber jars and rolled on a jar roller with periodic heating at 45 °C until complete solubilization was obtained. Reactive monomer mixes were degassed under vacuum followed by nitrogen backfill at 760 mmHg for 15 minutes. The lenses were photo-cured using the mold parts and cure

conditions shown in Table 1b. Lenses were cured with quartz plates placed on top of base curves to improve edge cut and centration. Pallets with reactive monomer mixtures loaded mold parts were placed on mirrored surface for cure.

The mold parts were mechanically separated, and the lenses remained predominantly in the zeonor front curve. The lenses were released from the front curves by applying a mechanical force on the outer surface of the plastic parts (i.e., tapping lightly on the front curve using a hammer) at room temperature.

Table 1a

| Component | Sample 1 | Sample 2 | Sample 3 | Sample 4 |
|---|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 | 40.00 |
| mPEG 475 | 10.00 | 17.00 | 19.00 | 21.00 |
| HEMA | 25.25 | 20.25 | 20.25 | 20.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 12.00 | 10.00 | 8.00 | 6.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 |

Table 1b

| | |
|---|---|
| Nitrogen Cure Box | |
| Oxygen Level | <0.5 % |
| Visible Light Intensity (TL03) | 5 – 6 mW/cm$^2$ |
| Temperature | 55 – 60 $^o$C |
| RRM Dose | 100 µL |
| Cure Time | 15 minutes |
| Mold Parts | |
| Front Curve | Zeonor |
| Base Curve | Polyproplyene |

The resulting "dry released" lenses were clear/non-phase separated after cure and appeared well plasticized with no evidence of physical damage. There was a noticeable level of difficulty in mechanical lens release (lens stuck to front curve), indicating a high level of plasticity or fluidity. The lenses were clear/non-phase separated in packing solution prior to autoclaving and were hazy/phase separated after autoclaving.

Example 2: Physical Properties

Water content, percent haze, modulus, and percent elongation were measured for the sterilized lenses from Sample 1. The data obtained are shown in Table 2, where a significant level of haze was observed.

Table 2

| % Water | % Haze (relative to CSI) | Mechanicals | |
|---|---|---|---|
| | | Modulus (psi) | % Elongation |
| 47.0 (0.2) | 152 (5) | 129.8 (6.3) | 322.1 (36.6) |

Example 3: Introduction of acPDMS 1000 for Formation of Non-phase Separated Autoclaved Lenses

The blends in Samples 3 and 4 (which previously produced phase separated lenses upon autoclaving) were re-formulated with acPDMS 1000 as a component of the cross-linker system, at the expense of HEMA. These blends are shown as Samples 5 and 6 in Table 3. Blends were treated as per Example 1. In addition, lenses were fabricated, de-molded and subjected to the aqueous process as per Example 1.

Table 3

| Component | Sample 5 | Sample 6 | Sample 7 |
|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 21.00 | 19.00 | 0.00 |
| DMA | 0.00 | 0.00 | 19.00 |
| HEMA | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 6.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 |

The resulting lenses were clear/non-phase separated after cure. Further, lenses from Samples 5 and 6 appeared to have a high level of plasticity while lenses from Sample 7 were very brittle. There was noticeable level of difficulty in mechanical lens release (lens stuck to FC) for Samples 5 and 6. The lenses were clear/non-phase separated in

packing solution prior to autoclaving and were clear/non-phase separated after autoclaving, indicating that acPDMS 1000 has a significant effect on reducing haze or phase separation.

Example 4: Physical Properties:

Sterilized lenses from Samples 5-7 were submitted for physical properties testing. Percent water content, percent haze, DCA advancing angle, Dk (edge corrected), modulus, and percent elongation were measured. The data obtained are shown in Table 4, where clear/non-phase separated lenses were obtained. In addition, all lenses were very wettable and characterized by low moduli.

Table 4

| Sample | % Water | % Haze (relative to CSI) | DCA Advancing angle | Dk (Edge Corrected) | Mechanicals | |
|---|---|---|---|---|---|---|
| | | | | | Modulus (psi) | % Elongation |
| 5 | 47.7 (0.0) | 15 (1) | [a]51 (14)<br>[b]50 (11)<br>[c]48 (6)<br>[d]62 (12) | 75 | 130.2 (5.8) | 159.9 (32.7) |
| 6 | 47.9 (0.1) | 21 (0) | [a]51 (7)<br>[b]50 (3)<br>[c]48 (3)<br>[d]51 (9) | NT | 123.4 (8.9) | 159.5 (31.2) |
| 7 | 45.5 (0.1) | NT | [a]51 (8) | 59 | 142.7 (7.2) | 226.8 (34.0) |

[a]Measured directly out of package
[b]3 hrs equilibration in DCA medium
[c]24 hrs equilibration in DCA medium
[d]48 hrs equilibration in DCA medium

Example 5: Adjustment of mPEG 475 to DMA Ratio for Optimal Lens Release

Using Sample 6 as the base formulation, DMA was added at 3%, 6% and 9% at the expense of mPEG 475, as shown in the Samples in Table 5. The intent was to tune the visco-elastic properties in the cured lenses, using low concentrations of DMA such that the mechanical lens release from the FC was acceptable, while obtaining optimal degree

of polymerization. Blends were treated as per Example 1. In addition, lenses were fabricated, de-molded and subjected to the aqueous process as per Example 1.

Table 5

| Component | Sample 8 | Sample 9 | Sample 10 |
|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 16.00 | 13.00 | 10.00 |
| DMA | 3.00 | 6.00 | 9.00 |
| HEMA | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 |

The resulting lenses were clear/non-phase separated after cure. There was a noticeable level of difficulty in mechanical lens release (lens stuck to FC) for Sample 8. Lenses for Samples 9 and 10 appeared to have acceptable level of plasticity and were mechanically released without difficulty.

Example 6: Physical Properties

Water content, percent haze, modulus, and percent elongation were measured for sterilized lenses from Samples 8 through 10. The data obtained are shown in Table 6.

Table 6

| Sample | % Water | % Haze (relative to CSI) | DCA Advancing angle | Dk | Mechanicals | |
|---|---|---|---|---|---|---|
| | | | | | Modulus (psi) | % Elongation |
| 8 | 46.4 (0.2) | 11 (1) | 55 (6) | 75 | 152.2 (9.2) | 129.6 (33.9) |
| 9 | 47.7 (0.3) | 19 (1) | NT | NT | 157.9 (8.6) | 149.7 (26.2) |
| 10 | 47.5 (0.2) | 20 (1) | NT | 64 | 151.9 (12.6) | 164.4 (41.8) |

Example 7: Lower Modulus

Blends containing a combination of K30 and K90 and various ratios of crosslinkers (acPDMS 1000: TEGDMA) were formulated as shown in Table 7 as per Example 1. In addition, lenses were fabricated and demolded as per Example 1. The "dry released" lenses were placed directly into individual lens vials containing 3 mL packing solution and subsequently sterilized.

Table 7

| Component | Sample 11 | Sample 12 | Sample 13 | Sample 14 | Sample 15 | Sample 16 | Sample 17 | Sample 18 |
|---|---|---|---|---|---|---|---|---|
| OH-mPDMS | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 10.00 | 13.00 | 13.00 | 13.00 | 13.00 | 13.00 | 14.00 | 14.00 |
| DMA | 11.00 | 8.00 | 8.25 | 8.50 | 6.00 | 8.00 | 7.00 | 7.00 |
| HEMA | 18.25 | 18.25 | 18.25 | 18.25 | 18.50 | 16.75 | 16.75 | 16.75 |
| TEGDMA | 0.50 | 0.50 | 0.25 | 0.00 | 0.25 | 0.00 | 0.00 | 0.00 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 | 10.00 | 12.00 | 12.00 | 12.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 10.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 |

The resulting lenses were clear/non-phase separated after cure, appeared to have acceptable level of plasticity, and released well from FC using mechanical force.

Example 8: Physical Properties

Water content, percent haze, modulus, and percent elongation were measured for sterilized lenses from Samples 11 through 18. The data obtained are shown in Table 8, where significantly lower moduli were obtained compared to the Samples in Table 6.

Table 8

| Sample | % Water | % Haze (relative to CSI) | DCA Advancing angle | Dk | Mechanicals | |
|---|---|---|---|---|---|---|
| | | | | | Modulus (psi) | % Elongation |
| 11 | 49.5 (0.2) | 10 (0) | NT | 60 | 133.9 (9.8) | 162.9 (24.7) |
| 12 | 49.5 (0.2) | 10 (1) | NT | 60 | 129.5 (7.4) | 127.7 (31.6) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 13 | 51.5 (0.3) | 16 (4) | NT | 63 | 113.0 (8.7) | 202.3 (27.5) |
| 14 | 52.3 (0.2) | 18 (0) | 61 (7) | 62 | 100.2 (8.7) | 204.7 (25.5) |
| 15 | 50.3 (0.2) | 9 (1) | NT | 62 | 127.4 (7.4) | 186.4 (45.4) |
| 16 | 54.5 (0.0) | 25 (1) | 51 (12) | 65 | 81.8 (4.9) | 261.9 (55.0) |
| 17 | 54.4 (0.2) | 22 (1) | 55 (11) | 63 | 83.0 (13.0) | 243.8 (42.8) |
| 18 | 54.3 (0.1) | 20 (2) | 52 (6) | 65 | 87.6 (5.1) | 258.7 (43.6) |

Example 9: PVP Release

Sterilized lenses from Samples 14 and 16 were tested for the release of PVP into packing solution (borate buffered saline solution). For each lot, 2 vials were opened and the lenses were transferred, using plastic tweezers, into a new vial containing 3 mL of fresh packing solution. The vial was capped and placed on a reciprocating shaker at medium speed and ambient conditions. After 1 hour, the lenses were transferred to new vial containing 3 mL of fresh packing solution and shaken for 2 hours. This procedure was repeated for the generation of samples at the time points shown in Table 9. The samples were analyzed for PVP by High Performance Liquid Chromatography with Electrospray Ionization Mass Spectrometry (HPLC/ESI MS).

Separation of PVP was achieved by reversed-phase chromatography using the following chromatographic conditions:

Column: Polymer Labs PLRP-S Polystyrene Di-vinyl benzene, 50 x 4.6mm x 5 μm, 100 A

Column Temperature: 50 °C

Injection Volume: 50 μL

Flow Rate: 1 mL/minute

Mobile Phase: Eluent A: Acetonitrile with 0.1% Trifluoroacetic acid

Eluent B: Water with 0.1% Trifluoroacetic acid

Eluent C: Isopropanol with 0.1% Trifluoroacetic acid

The mobile phase gradient for analysis was as follows:

| Time (mins) | %A | %B | %C |
|---|---|---|---|

| | | | |
|---|---|---|---|
| 0.0 | 22 | 78 | 0 |
| 1.0 | 22 | 78 | 0 |
| 11.0 | 70 | 30 | 0 |
| 11.1 | 50 | 0 | 50 |
| 14.0 | 50 | 0 | 50 |
| 14.1 | 22 | 78 | 0 |
| 17 | 22 | 78 | 0 |

Detection of PVP was achieved by ESI MS with 80% source Collision Induced Dissociation (CID), with monitoring ions with a mass to charge (m/z) of 86 (PVP). The data for cumulative release of PVP from Samples 14 and 16 are shown in Table 9, where release was demonstrated for up to 24 hours.

Table 9

| | **Sample 14** | **Sample 16** |
|---|---|---|
| **Time (hr)** | **Cumulative Release ug/Lens** | **Cumulative Release ug/Lens** |
| 1.00 | 76.02 | 18.63 |
| 2.00 | 79.11 | 21.18 |
| 4.50 | 89.29 | 32.65 |
| 6.00 | 92.93 | 36.60 |
| 8.50 | 99.10 | 45.87 |
| 12.00 | 107.84 | 57.67 |
| 24.00 | 139.17 | 100.53 |

Example 10: Optimization of mPEG 475:DMA Ratio for Desirable "Dry Release"

Blends containing a combination of K30 and K90 were formulated as shown in Table 10 as per Example 1. In addition, lenses were fabricated and "dry released" as per Example 1. The purpose of this study was to characterize the sensitivity of the cure and properties of the formulation to changes in the PEG:DMA ratio, in an attempt to optimize the properties with regards to processing.

The level of plasticity or fluidity increased with increasing levels of mPEG 475, which resulted in increasing level of difficulty with respect to mechanical release at room temperature. The highest level of difficulty was obtained with Sample 19 where about 60% of the lenses remained stuck to the zeonor front curve when the mechanical force

was applied. The level of brittleness increased with increasing levels of DMA, which resulted in significant improvement in the number of lenses obtained upon applying the mechanical force to the front curve. With Sample 26, 100% of the lenses release from the front curve when the mechanical force was applied at room temperature. However, a significant number of lenses were characterized with physical defects such as cracks or factures and edge chips likely due to the high degree of brittleness. The best yields, i.e. the highest number of lenses release with minimal number of physical defects, were obtained with Samples 22, 23, and 24.

Note that all of the dry release/mechanical release studies were conducted at room temperature, and temperature has a significant impact on the visco-elastic properties of the cured lenses. Therefore, temperature may be used to influence the release behavior of lenses.

Cooling the lenses with high levels of mPEG 475 (Samples 19, 20, and 21) to below room temperature, would tend to increase the viscosity and level of brittleness in the lenses, which would likely result in significant improvements in the yields obtained upon dry release/mechanical release.

While heating the lenses with high levels of DMA (Samples 25 and 26) to above room temperature, would tend to decrease the viscosity and level of brittleness in the lenses, which would likely result in significant improvements in the physical defects and hence improve the yields obtained upon dry release/mechanical release.

Table 10a

| Component | Sample 19 | Sample 20 | Sample 21 | Sample 22 | Sample 23 | Sample 24 | Sample 25 | Sample 26 |
|---|---|---|---|---|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 19.00 | 18.00 | 16.00 | 13.00 | 10.00 | 6.00 | 3.00 | 0.00 |
| DMA | 0.00 | 1.00 | 3.00 | 6.00 | 9.00 | 13.00 | 16.00 | 19.00 |
| HEMA | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.0 | 2.0 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.0 | 10.00 | 10.00 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.0 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 |

The Tg(heating)of the lenses of Samples 19-26 was measured and the results are shown in Table 10b.

Table 10b

| Sample # | mPEG475 (wt%) | DMA (wt%) | $Tg_{heating\ (C)}$ |
|---|---|---|---|
| 19 | 19 | 0 | 116 |
| 20 | 18 | 1 | 116 |
| 21 | 16 | 3 | 114 |
| 22 | 13 | 6 | 118 |
| 23 | 10 | 9 | 124 |
| 24 | 6 | 13 | 127 |
| 25 | 3 | 16 | 129 |
| 26 | 0 | 19 | 135 |

Example 11: Effect of Ratio of PVP K30:K90 on Lens Properties

Blends containing a combination of K30 and K90 were formulated as shown in Table 11 as per Example 1. In addition, lenses were fabricated and demolded as per Example 1. The "dry released" lenses were transferred directly into 1 mL polypropylene blister packages containing 995 μL packing solution (with 50 ppm methylcellulose) heat sealed with propylene lined aluminum foil and subsequently sterilized by autoclaving. The purpose of this study was to examine the impact of the K30:K90 ratio on the physical properties, parameters, biometrics profile and leachable monomers of the lenses.

Table 11

| **Component** | **Sample 27** | **Sample 28** | **Sample 29** | **Sample 30** |
|---|---|---|---|---|
| OH-mPDMS | 38.00 | 38.00 | 38.00 | 38.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 13.00 | 13.00 | 13.00 | 13.00 |
| DMA | 8.00 | 8.00 | 8.00 | 8.00 |
| HEMA | 16.73 | 16.73 | 16.73 | 16.73 |
| Blue HEMA | 0.02 | 0.02 | 0.02 | 0.02 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 12.00 | 10.00 | 8.00 | 6.00 |
| PVP K30 | 8.00 | 10.00 | 12.00 | 14.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 |

Example 12: Lens Physical Properties

Lenses from Example 11 were tested for physical properties. As demonstrated for Samples 25 through 28 in Table 12, comparable lens properties were obtained for the ratios of K90:K30 examined. Percent water content, percent haze, DCA advancing angle, Dk (edge corrected), modulus, and percent elongation were measure using the methods set forth in US Patent No. 8,168,720. All the lenses were very clear and wettable with low moduli, and the overall properties of the lenses are suitable for good clinical performance. In addition, the refractive indices of the lenses were measured on five consecutive days, after the sterilized lenses were stored at room temperature for about 1 week. The data in Table 12 show that the refractive indices of all of the lenses remained essentially constant from day 1 through day 5, suggesting that the lenses have attained equilibrium very quickly.

Table 12

| **Property** | **Sample 27** | **Sample 28** | **Sample 29** | **Sample 30** |
|---|---|---|---|---|
| Water Content, % | 54.8 (0.3) | 54.4 (0.1) | 54.3 (0.1) | 53.9 (0.3) |
| Haze, % of CSI | 15 (1) | 17 (0) | 17 (0) | 18 (0) |
| Refractive Index, Day 1 | 1.4013 | 1.4026 | 1.4034 | 1.4038 |
| Refractive Index, Day 2 | 1.4016 | 1.4022 | 1.4033 | 1.4037 |
| Refractive Index, Day 3 | 1.4015 | 1.4026 | 1.4040 | 1.4045 |
| Refractive Index, Day 4 | 1.4024 | 1.4030 | 1.4033 | 1.4043 |
| Refractive Index, Day 5 | 1.4019 | 1.4033 | 1.4038 | 1.4040 |
| Sessile Drop | 74.00 (3.61) | 70.67 (7.51) | 66.33 (4.51) | 71.33 (4.16) |
| Dk (edge corr.) | 63.0 | 67.9 | 68.6 | 66.8 |
| Modulus, psi | 75.9 (6.1) | 77.7 (3.2) | 89.2 (5.9) | 71.1 (3.8) |
| Elongation, % | 187.9 (67.1) | 207.3 (66.0) | 214.5 (52.2) | 210.8 (76.7) |

The wettability of lenses were be determined using a sessile drop technique measured using KRUSS DSA-100 TM instrument at room temperature and using DI water as probe solution. The lenses to be tested (3-5/sample) were rinsed in DI water to remove carry

over from packing solution. Each test lens was placed on blotting lint free wipes which were dampened with packing solution. Both sides of the lens were contacted with the wipe to remove surface water without drying the lens. To ensure proper flattening, lenses were placed "bowl side down" on the convex surface on contact lens plastic moulds. The plastic mould and the lens were placed in the sessile drop instrument holder, ensuring proper central syringe alignment and that the syringe corresponds to the assigned liquid. A 3 to 4 microliters of DI water drop was formed on the syringe tip using DSA 100-Drop Shape Analysis software ensuring the liquid drop was hanging away from the lens. The drop was released smoothly on the lens surface by moving the needle down. The needle was withdrawn away immediately after dispensing the drop. The liquid drop was allowed to equilibrate on the lens for 5 to 10 seconds and the contact angle was computed based on the contact angle measured between the drop image and the lens surface.

Example 13: Effect of Ratio of PVP K30:K90 on Lens Biometrics Profile

Lenses from Example 11 were tested for uptake of protein, mucin and lipocalin. Total protein uptake was measure using method described above.

The data obtained are shown in Table 13, where negligible differences were obtained. In addition, the levels obtained are consistent with lenses of good clinical performance.

Table 13

| Property | Sample 27 | Sample 28 | Sample 29 | Sample 30 |
|---|---|---|---|---|
| Total Protein Uptake (µg/Lens) | 7.85 (0.63) | 7.71 (0.25) | 7.75 (0.32) | 7.70 (0.40) |
| Mucin Uptake (µg/Lens) | 5.26 (0.08) | 5.26 (0.12) | 5.23 (0.02) | 5.15 (0.04) |
| Lipocalin Uptake (µg/Lens) | 3.71 (0.18) | 3.49 (0.15) | 3.75 (0.31) | 3.70 (0.40) |

Example 14: Effect of Ratio of PVP K30:K90 on Leachable Levels

Lenses from Example 11 were tested for leachable monomers by reversed-phase HPLC-UV. The data for Samples 27 through 30 are shown in Table 14, where the levels of leachable monomers were below the limit of quantization.

Ten blister packages were opened and lenses were transferred to lint-free blotting paper. Lenses were briefly blotted and transferred to a glass scintillation vial. Five (5) mL of methanol was added and the vial was sonicated at room temperature of 30 minutes. Samples were prepared in triplicate and the extracts were analyzed by HPLC-UV using the following conditions:

| | |
|---|---|
| Column: | Agilent Eclipse Plus C18, 75 x 4.6mm x 1.8μm |
| Column Temperature: | 25 °C |
| Injection volume: | 10 μL |
| Flow rate: | 1 mL/minute |
| Mobile Phase: | Eluent A: Water with 0.05% o-phosphoric acid |
| | Eluent B: Acetonitrile with 0.05% o-phosphoric acid |
| | Eluent C: Isopropanol with 0.1% Trifluoroacetic acid |

The mobile phase gradient for analysis of DMA, HEMA, mPEG 475 and Norbloc was as follows:

| Time (mins) | %A | %B | %C |
|---|---|---|---|
| 0.0 | 97 | 3 | 0 |
| 4.0 | 97 | 3 | 0 |
| 20 | 0 | 100 | 0 |
| 30 | 0 | 100 | 0 |
| 31 | 97 | 3 | 0 |
| 35 | 97 | 3 | 0 |

The mobile phase gradient for analysis of OH-mPDMS was as follows:

| Time (mins) | %A | %B | %C |
|---|---|---|---|
| 0.0 | 0 | 90 | 10 |
| 5 | 0 | 90 | 10 |
| 8 | 0 | 30 | 70 |
| 11 | 0 | 30 | 70 |
| 12 | 0 | 90 | 10 |
| 17 | 0 | 90 | 10 |

The results are depicted in Table 14.

Table 14

| Component | Sample 27 | Sample 28 | Sample 29 | Sample 30 |
|---|---|---|---|---|
| DMA | < 3 μg/g | < 3 μg/g | < 3 μg/g | < 3 μg/g |
| HEMA | < 3 μg/g | < 3 μg/g | < 3 μg/g | < 3 μg/g |
| mPEG 475 | < 78 μg/g | < 78 μg/g | < 78 μg/g | < 78 μg/g |
| Norbloc | < 3 μg/g | < 3 μg/g | < 3 μg/g | < 3 μg/g |
| OH-mPDMS (n=4) | < 78 μg/g | < 78 μg/g | < 78 μg/g | < 78 μg/g |

It is understood that while the invention has been described in conjunction with the detailed description thereof, that the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the claims.

What is claimed is:

Claims

1. A method of manufacturing a contact lens, said method comprising the steps of:

(i) adding reactive components to form a reactive mixture, wherein said reactive components comprise (a) at least one hydroxy-containing silicone component having a weight average molecular weight from about 200 to about 15,000 g/mole and (b) at least one monofunctional polyethylene glycol having a weight average molecular weight from about 200 to about 10,000 g/mole; and less than about 15 wt% diluents;

(ii) curing said reactive components within said mold to form said contact lens comprising a polymer having a Tg (heating) of less than about 125C; and

(iii) dry removing said contact lens from said mold.

2. The method of claim 1, wherein said at least one mono-methacrylate terminated polyethylene glycol is a mono-ether terminated, mono-methacrylate terminated polyethylene glycol.

3. The method of claim 2, wherein said at least one at least one mono-methacrylate terminated polyethylene glycol is mPEG 475.

4. The method of claim 1, wherein said reactive components comprises less than five percent, by weight, of one or more diluents.

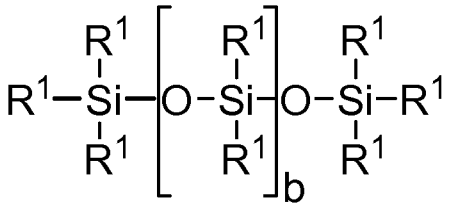
5. The method of claim 3, wherein said reactive components comprises less than five percent, by weight, of one or more diluents.

6. The method of claim 1, wherein said polymer comprises a Tg (heating) of between about 115 and about 125C. .

7. The method of claim 1, wherein said reactive mixture comprises from about 10 to about 20 weight % of at least one hydoxyalkyl containing monomer.

8. The method of claim 5, wherein said reactive mixture comprises less than about 10 20 weight % (meth)acrylamide containing monomers.

9. The method of claim 1, wherein at least one at least one hydroxy-containing silicone component is selected from compounds of Formula I:



Formula I

wherein:

$R^1$ is independently selected from reactive groups, monovalent alkyl groups, or monovalent aryl groups, any of the foregoing which may further comprise functionality selected from hydroxy, amino, oxa, carboxy, alkyl carboxy, alkoxy, amido, carbamate, carbonate, halogen or combinations thereof; and monovalent siloxane chains comprising 1-100 Si-O repeat units which may further comprise functionality selected from alkyl, hydroxy, amino, oxa, carboxy, alkyl carboxy, alkoxy, amido, carbamate, halogen or combinations thereof;

where b = 0 to 500, where it is understood that when b is other than 0, b is a distribution having a mode equal to a stated value; and

wherein at least one $R^1$ comprises a hydroxy group.

10. The method of claim 1 wherein said at least one hydroxy-containing silicone component is selected from the group consisting of bis-3-acryloxy-2-hydroxypropyloxypropyl polydialkylsiloxane; and mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-alkyl terminated polydialkylsiloxane; and mixtures thereof.

11. The method of claim 1 wherein said at least one hydroxy-containing silicone component is selected from monomethacrylate terminated polydimethylsiloxanes; bis-3-acryloxy-2-hydroxypropyloxypropyl polydialkylsiloxane; and mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane; and mixtures thereof.

12. The method of claim 1, wherein said at least one hydroxy-containing silicone component comprises mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane.

13. The method of claim 3, wherein said at least one hydroxy-containing silicone component comprises mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane.

14. The method of claim 5, wherein said at least one hydroxy-containing silicone component comprises mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane.

15. The method of claim 7, wherein said at least one hydroxy-containing silicone component comprises mono-(3-methacryloxy-2-hydroxypropyloxy)propyl terminated, mono-butyl terminated polydialkylsiloxane.

16. The method of claim 1, wherein said reactive components comprises DMA and the weight ratio of (i) said DMA and (ii) said at least one at least one mono-methacrylate terminated polyethylene glycol is from about 25:75 to about 75:25.

17. The method of claim 1, wherein said reactive components comprises from about 20 to about 70 percent, by weight, of said at least one mono-methacrylate terminated polyethylene glycol.

18. A contact lens manufactured by the method of claim 1.

19. A contact lens manufactured by the method of claim 14.

# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2013/045774

A. CLASSIFICATION OF SUBJECT MATTER
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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)
G02B B29D

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

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | US 2008/128930 A1 (FRIENDS G D; FRIENDS M L; LAI Y) 5 June 2008 (2008-06-05) contact lens is released from the mold in a dry state; claims 19, 22 Ease of demolding of contact lens depends on Tg of polymeric material; paragraph [0089] | 1-19 |
| | ----- | |
| A | EP 1 818 692 A2 (JOHSON & JOHNSON VISION CARE I [US] JOHNSON & JOHNSON VISION CARE [US]) 15 August 2007 (2007-08-15) no dry removing of contact lens; no reference to glass transition temperature; claims 9,14 | 1,2 |
| | ----- | |

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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| Date of the actual completion of the international search | Date of mailing of the international search report |
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|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Stabel, Andreas |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

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权利要求书2页 说明书24页

(54)发明名称

利用减少量的稀释剂制造含有机硅的接触镜片的方法

(57)摘要

本发明涉及一种制造接触镜片的方法,所述方法包括如下步骤:(i)将反应性组分添加到模具,其中所述反应性组分包含(a)至少一种含羟基的有机硅组分,所述含羟基的有机硅组分具有约200至约15,000g/mole的重均分子量;和(b)至少一种单醚封端的、单甲基丙烯酸酯封端的聚乙二醇,所述单醚封端的、单甲基丙烯酸酯封端的聚乙二醇具有约200至约10,000g/mole的重均分子量;(ii)在所述模具内固化所述反应性组分以形成所述接触镜片;以及(iii)从所述模具取出所述接触镜片。

CN 104395782 A

1. 一种制造接触镜片的方法，所述方法包括以下步骤：

(i) 添加反应性组分以形成反应性混合物，其中所述反应性组分包含 (a) 至少一种含羟基的有机硅组分，所述含羟基的有机硅组分具有约 200 至约 15,000g/mole 的重均分子量；和 (b) 至少一种单官能聚乙二醇，所述单官能聚乙二醇具有约 200 至约 10,000g/mole 的重均分子量；和小于约 15 重量 % 的稀释剂；

(ii) 在所述模具内固化所述反应性组分以形成所述接触镜片，所述接触镜片包含具有小于约 125C 的 Tg（加热）的聚合物；以及

(iii) 从所述模具干燥地取出所述接触镜片。

2. 根据权利要求 1 所述的方法，其中所述至少一种单甲基丙烯酸酯封端的聚乙二醇为单醚封端的、单甲基丙烯酸酯封端的聚乙二醇。

3. 根据权利要求 2 所述的方法，其中所述至少一种单甲基丙烯酸酯封端的聚乙二醇为 mPEG 475。

4. 根据权利要求 1 所述的方法，其中所述反应性组分包含按重量计小于百分之五的一种或多种稀释剂。

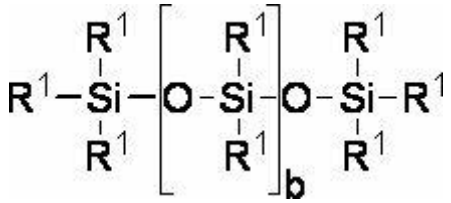
5. 根据权利要求 3 所述的方法，其中所述反应性组分包含按重量计小于百分之五的一种或多种稀释剂。

6. 根据权利要求 1 所述的方法，其中所述聚合物具有介于约 115 和约 125C 之间的 Tg（加热）。

7. 根据权利要求 1 所述的方法，其中所述反应性混合物包含约 10 重量 % 至约 20 重量 % 的至少一种含羟烷基单体。

8. 根据权利要求 5 所述的方法，其中所述反应性混合物包含小于约 10 重量 % 至 20 重量 % 的含（甲基）丙烯酰胺单体。

9. 根据权利要求 1 所述的方法，其中至少一种含羟基的有机硅组分选自式 I 的化合物：



式 I

其中：

$R^1$ 独立地选自反应性基团、一价烷基基团、或一价芳基基团，上述任何基团还可包含选自羟基、氨基、氧杂、羧基、烷基羧基、烷氧基、酰胺基、氨基甲酸酯基、碳酸酯基、卤素或它们的组合的官能团；并且一价硅氧烷链包含 1 至 100 个 Si-O 重复单元，所述重复单元还可以包含选自烷基、羟基、氨基、氧杂、羧基、烷基羧基、烷氧基、酰氨基、氨基甲酸酯基、卤素或它们的组合的官能团；

其中 b = 0 至 500，其中应当理解，当 b 不为 0 时，b 为具有等于指定值的众数的分布；

并且

其中至少一个 $R^1$ 包含羟基基团。

10. 根据权利要求 1 所述的方法，其中所述至少一种含羟基的有机硅组分选自双 -3- 丙烯酰氧基 -2- 羟丙基丙氧基聚二烷基硅氧烷；和单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单烷基封端的聚二烷基硅氧烷；以及它们的混合物。

11. 根据权利要求 1 所述的方法，其中所述至少一种含羟基的有机硅组分选自单甲基丙烯酸酯封端的聚二甲基硅氧烷；双 -3- 丙烯酰氧基 -2- 羟丙基丙氧基聚二烷基硅氧烷；和单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单 - 丁基封端的聚二烷基硅氧烷；以及它们的混合物。

12. 根据权利要求 1 所述的方法，其中所述至少一种含羟基的有机硅组分包括单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单丁基封端的聚二烷基硅氧烷。

13. 根据权利要求 3 所述的方法，其中所述至少一种含羟基的有机硅组分包括单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单丁基封端的聚二烷基硅氧烷。

14. 根据权利要求 5 所述的方法，其中所述至少一种含羟基的有机硅组分包括单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单丁基封端的聚二烷基硅氧烷。

15. 根据权利要求 7 所述的方法，其中所述至少一种含羟基的有机硅组分包括单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单丁基封端的聚二烷基硅氧烷。

16. 根据权利要求 1 所述的方法，其中所述反应性组分包含 DMA，并且 (i) 所述 DMA 与 (ii) 所述至少一种单甲基丙烯酸酯封端的聚乙二醇的重量比为约 25:75 至约 75:25。

17. 根据权利要求 1 所述的方法，其中所述反应性组分包含按重量计约 20% 至约 70% 的所述至少一种单甲基丙烯酸酯封端的聚乙二醇。

18. 一种接触镜片，所述接触镜片是通过权利要求 1 所述的方法制造的。

19. 一种接触镜片，所述接触镜片是通过权利要求 14 所述的方法来制造的。

# 利用减少量的稀释剂制造含有机硅的接触镜片的方法

[0001] 相关专利申请

[0002] 本专利申请要求 2012 年 6 月 25 日提交的名为“METHOD OF MAKING SILICONE CONTAINING CONTACT LENS WITH REDUCED AMOUNT OF DILUENTS”的美国临时专利申请号 61/663,719 的优先权，该临时专利申请的内容以引用方式并入本文。

## 技术领域

[0003] 本发明涉及制造含有机硅的接触镜片的方法。

## 背景技术

[0004] 自 20 世纪 50 年代起，接触镜片就已被商业化利用以改进视力。第一种接触镜片由硬质材料制得。尽管目前仍然使用这些镜片，但由于其较差的初始舒适度和相对较低的氧气透过性，这些镜片不适用于所有患者。该领域的后续发展产生了基于水凝胶的软性接触镜片，所述软性接触镜片在当今为极为流行。许多使用者发现软性镜片更舒适，增加的舒适水平可允许软性接触镜片使用者比硬质接触镜片的使用者佩戴镜片更长时间。

[0005] 希望使用减少的稀释剂体系或不使用稀释剂体系来制造含有机硅的接触镜片，由此可允许经固化的聚合物从模具部件“干燥地剥离”、直接放置到包含用于平衡的润湿溶液的最终包装内。通常，包含高含量 PVP 的零稀释剂体系趋于产生极其易碎的经固化的镜片。这些镜片在利用机械力进行剥离时易于受到物理损坏。申请人已发现，掺入至少一种单醚封端的、单甲基丙烯酸酯封端的聚乙二醇可显著降低经固化的镜片中的脆性水平。因此，经固化的镜片当在镜片剥离过程期间经受应力时不易断裂。所述至少一种单醚封端的、单甲基丙烯酸酯封端的聚乙二醇还允许在不使用液体的情况下调节经固化的聚合物的粘弹性性能，以实现所需的机械镜片剥离。

## 发明内容

[0006] 在一个方面，本发明涉及制造接触镜片的方法，所述方法包括以下步骤：

[0007] (i) 添加反应性组分以形成反应性混合物，其中所述反应性组分包含 (a) 至少一种含羟基的有机硅组分，所述含羟基的有机硅组分具有约 200 至约 15,000g/mole 的重均分子量；和 (b) 至少一种单官能聚乙二醇，所述单官能聚乙二醇具有约 200 至约 10,000g/mole 的重均分子量；和小于约 15 重量％的稀释剂；

[0008] (ii) 在所述模具内固化所述反应性组分以形成所述接触镜片，所述接触镜片包含具有小于约 125C 的 Tg( 加热 ) 的聚合物；以及

[0009] (iii) 从所述模具干燥地取出所述接触镜片。

[0010] 在另一方面，本发明的特征在于根据上述方法制造的接触镜片。

[0011] 通过本发明的具体实施方式和权利要求书，本发明的其他特征和优点将显而易见。

## 具体实施方式

[0012] 据信根据本文的描述，本领域的技术人员可最大限度地利用本发明。如下具体实施例可理解为仅是示例性的，并且无论如何都不会以任何方式限制本公开的其余部分。

[0013] 除非另有定义，否则本文使用的所有技术和科学术语都具有本发明所属技术领域普通技术人员公知的相同含义。另外，将本文提及的所有出版物、专利申请、专利及其它参考文献以引用方式并入本文。

[0014] 定义

[0015] 如本文所用，“反应性混合物”是指混合在一起并在聚合反应条件下形成本发明的有机硅水凝胶和接触镜片的组分（反应性和非反应性两者）的混合物。反应性混合物包含反应性组分，诸如，单体、大分子单体、预聚物、交联剂、和引发剂、以及添加剂（诸如润湿剂、剥离剂、染料、颜料）、吸光化合物（诸如紫外线吸收剂）和光致变色化合物，它们中的任何一种可以是反应性的，也可以是非反应性的，但能够保留在所得镜片内；以及药物和类药剂营养化合物、和任何稀释剂。应当理解，可基于所制得的镜片及其预期用途来添加宽泛范围的添加剂。

[0016] 反应性混合物的组分的浓度以除任何稀释剂之外的反应混合物中的所有组分的重量％给出。当使用稀释剂时，它们的浓度是基于在反应性混合物和稀释剂中的所有组分总量的量以重量％给出。

[0017] 如本文所用，“反应性基团”为可发生自由基和／或阳离子聚合的基团。

[0018] 如本文所用，“可聚合的”是指化合物包含至少一种可聚合的官能团，诸如丙烯酸酯、甲基丙烯酸酯、丙烯酰胺、甲基丙烯酰胺、N-乙烯基内酰胺、N-乙烯基酰胺和苯乙烯基官能团。“不可聚合的”是指化合物不包含此类可聚合的官能团。

[0019] 如本文所用，“疏水性”是指一种或多种化合物／单体在以10重量份置于90重量份的水的混合物中为不溶的，并且“亲水性”是指一种或多种化合物／单体在以10重量份置于90重量份的水的混合物中为可溶的。在20℃下评估物质的溶解度。

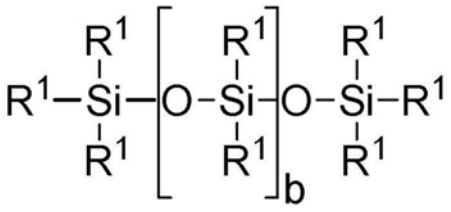
[0020] 如本文所用，除非另外指明，否则术语“烷基”是指1至20个碳原子的烃基。

[0021] 有机硅组分

[0022] 反应性混合物包含至少一种含有机硅的组分，所述含有机硅的组分包含至少一个羟基基团（“含羟基的有机硅组分”）并且具有约200至约15,000g/mole（诸如约300至约2,000g/mole）的重均分子量。含有机硅的组分（或有机硅组分）为在单体、大分子单体或预聚物中含有至少一个[-Si-O-Si]基团的组分。在一个实施例中，Si和附接的O以大于20重量％，诸如大于30重量％的含有机硅的组分的总分子量的量存在于含有机硅的组分中。可用的含羟基的有机硅组分包括可聚合官能团，诸如丙烯酸酯、甲基丙烯酸酯、丙烯酰胺、甲基丙烯酰胺、N-乙烯基内酰胺、N-乙烯基酰胺和苯乙烯基官能团。可用于本发明中的含羟基的有机硅组分的例子可见于美国专利4,139,513；4,139,692；5,998,498；和5,070,215中。

[0023] 合适的含羟基的有机硅组分包括式I的化合物

[0024]



式 I

[0025] 其中：

[0026] $R^1$ 独立地选自反应性基团、烷基基团、或芳基基团，上述任何基团还可包含选自羟基、氨基、氧杂、羧基、烷基羧基、烷氧基、酰胺基、氨基甲酸酯基、碳酸酯基、卤素或它们的组合的官能团；并且硅氧烷链包含 1 至 100 个 Si-O 重复单元，所述重复单元还可包含选自烷基、羟基、氨基、氧杂、羧基、烷基羧基、烷氧基、酰氨基、氨基甲酸酯基、卤素或它们的组合的官能团；

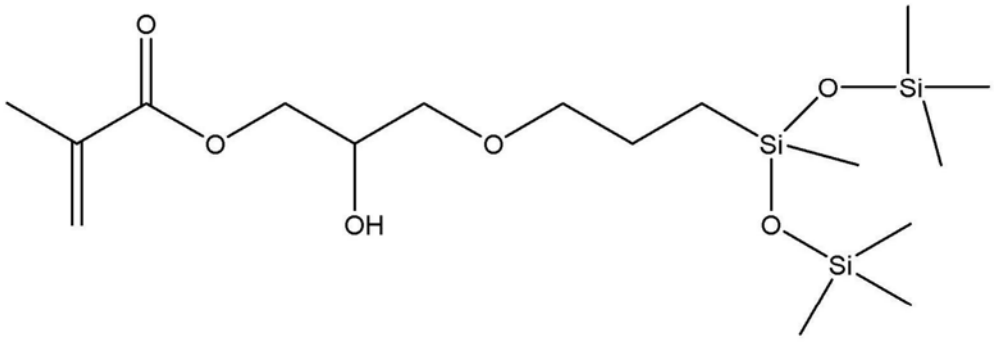
[0027] 其中 b ＝ 0 至 500（诸如 0 至 100，诸如 0 至 20），其中应当理解，当 b 不为 0 时，b 为具有等于指定值的众数 (mode) 的分布；并且

[0028] 其中至少一个 $R^1$ 包含反应性基团，并且在一些实施例中一至三个 $R^1$ 包含反应性基团，并且至少一个 R 基团包含一个或多个羟基基团。

[0029] 自由基反应性基团的非限制性例子包括（甲基）丙烯酸酯、苯乙烯基、乙烯基、乙烯基醚、$C_{1-6}$ 烷基（甲基）丙烯酸酯、（甲基）丙烯酰胺、$C_{1-6}$ 烷基（甲基）丙烯酰胺、N- 乙烯基内酰胺、N- 乙烯基酰胺、$C_{2-12}$ 烯基、$C_{2-12}$ 烯基苯基、$C_{2-12}$ 烯基萘基、$C_{2-6}$ 烯基苯基、$C_{1-6}$ 烷基、O- 乙烯基氨基甲酸酯、以及 O- 乙烯基碳酸酯。阳离子反应性基团的非限制性例子包括乙烯基醚或环氧基团以及它们的混合物。在一个实施例中，自由基反应性基团包括（甲基）丙烯酸酯、丙烯酰氧基、（甲基）丙烯酰胺、以及它们的混合物。

[0030] 在一个实施例中，b 为 0，一个 $R^1$ 为反应性基团，并且至少 3 个 $R^1$ 选自具有一至 16 个碳原子的一价烷基基团，并且在另一个实施例中选自具有一至 6 个碳原子的一价烷基基团，在另一个实施例中，一个 $R^1$ 为反应性基团，两个 $R^1$ 为三烷基硅氧烷基基团，剩余的 $R^1$ 为甲基、乙基或苯基，并且在另一个实施例中，一个 $R^1$ 为反应性基团，两个 $R^1$ 为三烷基硅氧烷基基团，剩余的 $R^1$ 为甲基。本实施例的有机硅组分的非限制性例子包括丙烯酸 -2- 甲基 -2- 羟基 -3-[3-[1,3,3,3- 四甲基 -1-[（三甲基甲硅烷基）氧基]-1- 二硅氧烷基] 丙氧基] 丙酯（“SiGMA”；式 II 中的结构），

[0031]

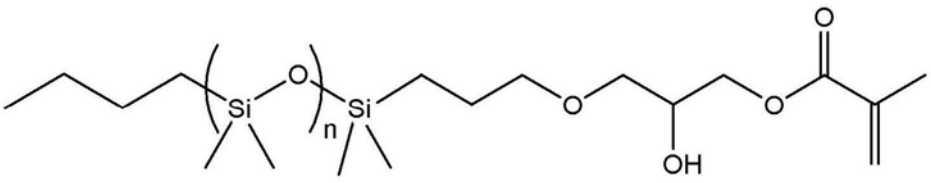


式 II

[0032] 和 2- 羟基 -3- 甲基丙烯酰氧基丙氧基丙基 - 三（三甲基甲硅烷氧基）硅烷。

[0033] 在另一个实施例中，b 为 2 至 20、3 至 20、3 至 16、3 至 15，或在一些实施例中为 3 至 10；至少一个末端 $R^1$ 包含反应性基团，并且剩余的 $R^1$ 选自具有 1 至 16 个碳原子的一价烷基基团，并且在另一个实施例中，选自具有 1 至 6 个碳原子的一价烷基基团。在另一个实施例中，b 为 3 至 15，一个末端 $R^1$ 包含反应性基团，另一个末端 $R^1$ 包含具有 1 至 6 个碳原子的一价烷基基团，剩余的 $R^1$ 包含具有 1 至 3 个碳原子的一价烷基基团。本实施例的有机硅组分的非限制性例子包括（单 -(2- 羟基 -3- 甲基丙烯酰氧基丙基）- 丙醚封端的聚二甲基硅氧烷 (400-2000、或者 400-1600$M_w$)(″ OH-mPDMS″ ；式 III 中的结构）。

[0034]




式 III

[0035] 在一个实施例中，含羟基的有机硅组分的混合物可用于改善反应性混合物的相容性。

[0036] 在另一个实施例中，含羟基的有机硅组分包括具有侧链羟基基团的聚二甲基硅氧烷双甲基丙烯酸酯（诸如，描述于美国专利申请 2004/0192872 中的化合物 C2、C4 或 R2，或描述于美国专利 4,259,467 的实例 XXV、XXVIII 或 XXXii 中的化合物）、具有侧链亲水性基团的可聚合的聚硅氧烷（例如，公开于 US6867245 中的那些）。在一些实施例中，侧链亲水性基团为羟烷基或聚亚烷基醚基团，或它们的组合。可聚合的聚硅氧烷也可包含氟碳基团。一个例子显示为结构 B3。

[0037] 适用于本发明的其他有机硅组分包括在 WO 96/31792 中描述为“C”材料的那些。另一类合适的含有机硅的组分包括通过 GTP 制备的含有机硅的大分子单体，诸如，美国专利 5,314,960、No.5,371,147 和 No.6,367,929 中所公开的含羟基大分子单体。

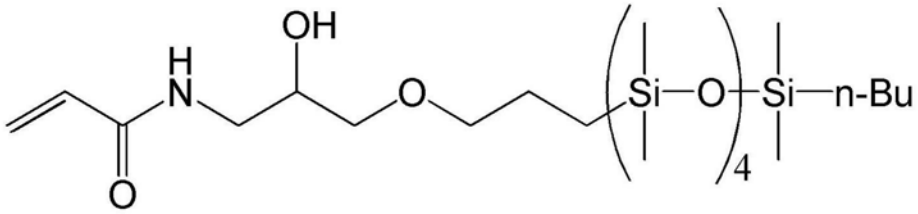
[0038] 在其中需要小于约 120psi 的模量的本发明的一个实施例中，镜片中所用的含有机硅的组分的质量分数的大部分应该仅含有一个可聚合的官能团（“单官能的含有机硅的组分”）。在该实施例中，为了确保氧气传递率和模量的所需平衡，优选的是所有具有多于一个可聚合的官能团的组分（“多官能组分”）构成反应性组分的不超过 10mmol/100g，优选构成反应性组分的不超过 7mmol/100g。

[0039] 在一个实施例中，有机硅组分选自双 -3- 丙烯酰氧基 -2- 羟丙基丙氧基聚二烷基硅氧烷；单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基）丙基封端的、单 - 烷基封端的聚二烷基硅氧烷；以及它们的混合物。

[0040] 在一个实施例中，有机硅组分选自双 -3- 丙烯酰氧基 -2- 羟丙基丙氧基聚二烷基硅氧烷；和单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基）丙基封端的、单 - 丁基封端的聚二烷基硅氧烷；以及它们的混合物。

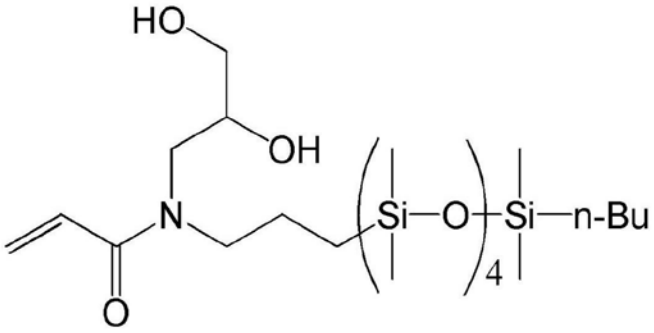
[0041] 其他有机硅组分的例子包括如下：

[0042]

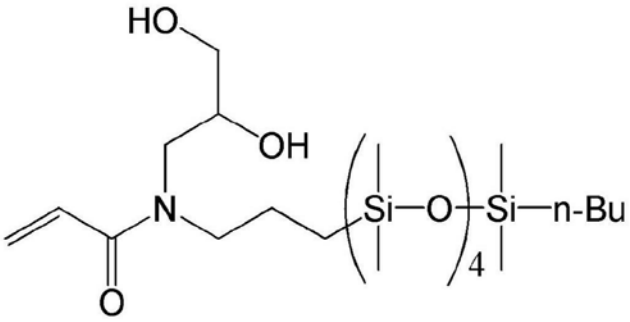



式 IV

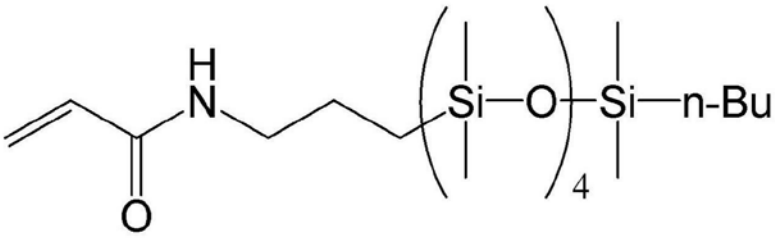
[0043]



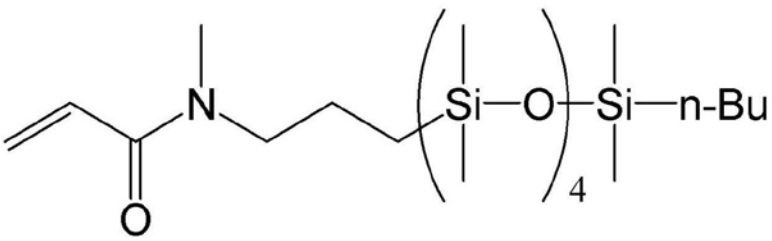
式 V



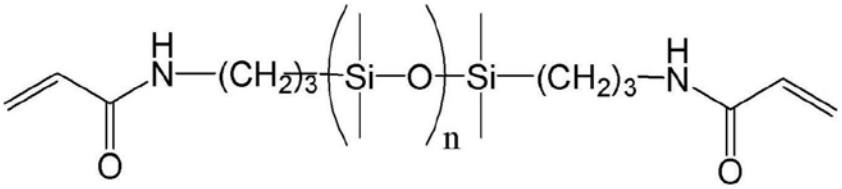
式 VI



式 VII

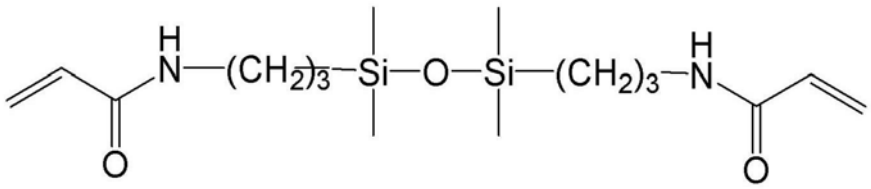


式 VIII



[0044]

式 IX



式 X

[0045] 在一个实施例中，有机硅组分具有约 400 至约 4000 道尔顿的平均分子量。

[0046] 基于反应性混合物的全部反应性组分（如，稀释剂除外）计，一种或多种含有机硅的组分可以约 10 至约 87 重量%，并且在一些实施例中约 10 重量%至约 80 重量%，并且在其他实施例中约 20 重量%至约 70 重量%的量存在。

[0047] 单官能的封端的聚乙二醇

[0048] 反应性混合物还包含至少一种单官能聚乙二醇，所述单官能聚乙二醇具有约 200 至约 10,000g/mole（诸如，约 200 至约 2,000g/mole）的重均分子量。单官能聚乙二醇包括仅一个聚合型基团，并且可为单醚封端的单 -（甲基）丙烯酸酯或（甲基）丙烯酸酯封端的聚乙二醇。单醚末端基团的例子包括但不限于 C1-C6 烷氧基基团，诸如甲氧基和乙氧基或包括至多 8 个碳原子的烷氧基基团。此类单醚封端的、单甲基丙烯酸酯封端的聚乙二醇的例子包括但不限于 mPEG 475（购自 Sigma-Aldrich(St.Louis,MO USA) 的聚乙二醇 (475Mw) 单甲醚单甲基丙烯酸酯（“mPEG475”））。

[0049] 基于反应性混合物的全部反应性组分（如，稀释剂（如果有的话）除外）计，一种或多种单官能聚乙二醇可以约 3 至约 30 重量%，约 5 至约 30 重量%，并且在其他实施例中约 10 至约 30 重量%的量存在。

[0050] 一种或多种单官能聚乙二醇提供所得的经固化的、预水合的聚合物，所述聚合物在加热时具有小于约 125C、或在介于约 115 和约 125C 之间的玻璃化转变温度 Tg。这提供所需的干燥剥离特性，并且具体地讲耐断裂性。水合镜片的性能基本上不因不包含至少一种单官能聚乙二醇的反应性混合物而改变。

[0051] 其他亲水性组分

[0052] 在一个实施例中，反应性混合物 / 镜片还可包含至少一种其他亲水性组分。在一个实施例中，这些亲水性组分可为已知可用于制备水凝胶的亲水性单体中的任何一种。

[0053] 一类合适的亲水性单体包括含丙烯酸基单体或含乙烯基单体。这种亲水性单体本身可用作交联剂，然而，当使用具有多于一种可聚合的官能团的亲水性单体时，它们的浓度应该如上所述限定，以提供具有所需模量的接触镜片。

[0054] 术语“乙烯基型”或“含乙烯基的”单体是指包含乙烯基基团 (Y-CH ＝ $CH_2$) 并且能够聚合的单体，其中 Y 不是羰基 (C ＝ O) 基团。

[0055] 可结合到本发明的反应性混合物 / 水凝胶 / 镜片中的亲水性含乙烯基单体包括但不限于诸如 N- 乙烯基酰胺、N- 乙烯基内酰胺（如 N- 乙烯基吡咯烷酮或 NVP）、N- 乙烯基 -N- 甲基乙酰胺、N- 乙烯基 -N- 乙基乙酰胺、N- 乙烯基 -N- 乙基甲酰胺、N- 乙烯基甲酰胺的单体，优选 NVP。

[0056] “丙烯酸型”或“含丙烯酸类”的单体为含有丙烯酸类基团的那些单体：($CH_2$ ＝

CRCOX)，其中 R 为 H 或 $CH_3$，并且 X 为 O 或 N，还已知这些单体容易聚合，诸如 N,N- 二甲基丙烯酰胺 (DMA)、丙烯酰胺、甲基丙烯酸 2- 羟乙酯 (HEMA)、甲基丙烯酸甘油酯、2- 羟乙基甲基丙烯酰胺、单甲基丙烯酸聚乙二醇酯、甲基丙烯酸、它们的混合物等等。

[0057] 可用于本发明中的其他亲水性单体包括但不限于末端羟基基团中的一个或多个被含有可聚合双键的官能团替代的聚氧乙烯醇。例子包括聚乙二醇、乙氧基化的烷基葡糖苷和乙氧基化的双酚 A，其与一摩尔或更多摩尔当量的封端基团（诸如甲基丙烯酸异氰根合乙酯（“IEM”）、甲基丙烯酸酸酐、甲基丙烯酰氯、乙烯基苯甲酰氯等）反应，生成聚乙烯多元醇，所述聚乙烯多元醇具有一个或多个通过连接基团（诸如氨基甲酸根或酯基基团）键合到聚乙烯醇上的末端可聚合烯属基团。

[0058] 另外的例子为公开于美国专利 5,070,215 中的亲水性乙烯基碳酸酯或乙烯基氨基甲酸酯单体，以及公开于美国专利 4,910,277 中的亲水性噁唑酮单体。其他合适的亲水性单体对于本领域技术人员而言是显而易见的。

[0059] 在一个实施例中，其他亲水性组分包括至少一种亲水性单体，诸如 DMA、HEMA、甲基丙烯酸甘油酯、2- 羟乙基甲基丙烯酰胺、NVP、N- 乙烯基 -N- 甲基丙烯酰胺、单甲基丙烯酸聚乙二醇酯、以及它们的组合。在另一个实施例中，其他亲水性单体包括 DMA、HEMA、NVP 和 N- 乙烯基 -N- 甲基丙烯酰胺以及它们的混合物中的至少一者。在另一个实施例中，其他亲水性单体包括 DMA 和 / 或 HEMA。

[0060] 根据所需的具体性能平衡，其他一种或多种亲水性组分（例如 DMA 或 HEMA）可以宽泛范围的量存在。在一个实施例中，基于反应性组分的重量计，亲水性组分的量为至多约 60 重量％，诸如约 5 至约 40 重量％、约 10 至约 40 重量％、约 13 至约 40 重量％、或约 13 至约 30 重量％。在一个实施例中，(i) 所述亲水性组分（例如 DMA 或 HEMA）与 (ii) 所述至少一种单甲基丙烯酸酯封端的聚乙二醇的重量比为约 25 ： 75 至约 75 ： 25。

[0061] 在另一个实施例中，（甲基）丙烯酰胺单体的量为反应性混合物中的所有组分（任何稀释剂除外）的小于约 10 重量％、或介于约 3 重量％和约 10 重量％之间。（甲基）丙烯酰胺单体的例子包括 DMA、丙烯酰胺、N- 乙烯基 -N- 甲基丙烯酰胺、N- 乙烯基丙烯酰胺、它们的混合物等等。

[0062] 羟烷基单体的量可为反应性混合物中所有组分（任何稀释剂除外）的介于约 10 重量％和约 20 重量％之间。羟烷基单体的例子包括 HEMA、丙烯酸 2- 羟乙酯、2- 羟乙基甲基丙烯酰胺、2- 羟丙基甲基丙烯酰胺、2- 甲基丙烯酸羟丙酯、2- 羟丁基甲基丙烯酰胺、2- 羟丁基甲基丙烯酸酯、它们的混合物等等。

[0063] 聚合引发剂

[0064] 一种或多种聚合引发剂可包含于反应混合物中。聚合引发剂的例子包括但不限于在适当高温下产生自由基的化合物（诸如月桂基过氧化物、过氧化苯甲酰、过碳酸异丙酯、偶氮二异丁腈等），和光引发剂体系（诸如芳族 α- 羟基酮、烷氧基氧基苯偶姻、苯乙酮、酰基氧化磷、双酰基氧化磷，和叔胺加上二酮、它们的混合物等）。光引发剂的示例性例子为 1- 羟基环己基苯基酮、2- 羟基 -2- 甲基 -1- 苯基 - 丙 -1- 酮、双 (2,6- 二甲氧基苯甲酰基 )-2,4-4- 三甲基戊基氧化膦 (DMBAPO)、双 (2,4,6- 三甲基苯甲酰基 )- 苯基氧化膦 (IRGACURE® 819)、2,4,6- 三甲基苄基二苯基氧化膦和 2,4,6- 三甲基苯甲酰基二苯基

氧化膦、苯偶姻甲酯，和荧醌与 4-(N,N- 二甲基氨基）苯甲酸乙酯的组合。可商购获得的可见光引发剂体系包括但不限于 IRGACURE® 819、IRGACURE® 1700、IRGACURE® 1800、IRGACURE® 1850（均得自 Ciba Specialty Chemicals），以及 Lucirin TPO 引发剂（得自 BASF）。可商购获得的 UV 光引发剂包括 Darocur 1173 和 Darocur 2959(Ciba Specialty Chemicals)。可使用的这些和其他光引发剂公开于由 G.Bradley 编辑的 J.V.Crivello&K.Dietliker 的 Photoinitiators for Free Radical Cationic&Anionic Photopolymerization，第 III 卷，第 2 版，John Wiley and Sons ;New York ;1998。

[0065] 聚合引发剂以引发反应混合物的光聚合的有效量（诸如约 0.1 至约 2 重量%）用于反应混合物中。可取决于所用的聚合引发剂，使用热或可见光或紫外光或其他方式的适当选择来引发反应混合物的聚合。另选地，引发可在没有使用光引发剂下进行，例如，e- 照射。然而，当使用光引发剂时，优选的引发剂为双酰基氧化膦，诸如双 (2,4,6- 三甲基苯甲酰基）- 苯基氧化膦（IRGACURE® 819）或 1- 羟基环己基苯基酮与 DMBAPO 的组合，并且在另一实施例中，聚合引发的方法是经由可见光活化。

[0066] 内部润湿剂

[0067] 在一个实施例中，反应混合物包含一种或多种内部润湿剂。内部润湿剂可包括但不限于高分子量亲水性聚合物（诸如描述于美国专利 6,367,929 ;6,822,016 ;7786185 ; PCT 专利申请 WO03/22321 和 WO03/22322 中的那些），或反应性亲水性聚合物（诸如描述于美国专利 7,249,848 中的那些）。内部润湿剂的例子包括但不限于聚酰胺，诸如，聚 (N- 乙烯基吡咯烷酮）、聚（二甲基丙烯酰胺）和聚 (N- 乙烯基 -N- 甲基乙酰胺））、聚 N- 乙烯基乙酰胺、聚丙烯酰胺以及它们的共聚物。合适的共聚单体包括丙烯酸、甲基丙烯酸、2- 甲基丙烯酸羟乙酯、反应性聚乙二醇单体、它们的组合等等。

[0068] 根据所需的具体参数，一种或多种内部润湿剂可以以宽泛范围的量存在。在一个实施例中，基于反应性混合物中的所有组分（任何稀释剂除外）的全部百分比计，一种或多种润湿剂的量为至多约 50 重量%、至多约 30 重量%，诸如约 5 重量%至约 40 重量%、约 5 重量%至约 30 重量%，诸如约 6 重量%至约 40 重量%或约 6 重量%至约 25 重量%。

[0069] 其他组分

[0070] 可存在于用于形成本发明的接触镜片的反应混合物中的其他组分包括但不限于紫外光吸收化合物、药剂、抗微生物化合物、共聚和非聚合的染料、可共聚和非聚合的光致变色化合物、离子单体或组分、表面活性剂、脱模剂、活性调色剂、颜料、它们的组合等等。在一个实施例中，另外的组分的总和可为至多约 20 重量%。

[0071] 稀释剂

[0072] 在一个实施例中，在存在或不存在稀释剂的情况下来将反应性组分（例如含有机硅的组分、亲水性单体、润湿剂和 / 或其他组分）混合在一起以形成反应混合物。在一个实施例中，反应性混合物包含小于约百分之二十（例如，诸如小于约百分之十、小于约百分之五、或小于约百分之一）的一种或多种稀释剂，或者不包含稀释剂。

[0073] 在使用稀释剂的一个实施例中，稀释剂具有足够低的极性以在反应条件下溶解反应混合物中的非极性组分。表征本发明的稀释剂的极性的一个方式为经由 Hansen 溶解度参数 δp。在某些实施例中，δp 小于约 10，优选小于约 6。合适的稀释剂进一步公开于美

国专利申请 20100280146 和美国专利 6,020,445 中。

[0074] 在另一个实施例中，选定的稀释剂为眼科相容性的（至少在低浓度下）。因此，在一个实施例中，稀释剂在具有润湿溶液的至多 5 重量％并且在一些实施例中润湿溶液的至多 1 重量％的浓度下为眼科相容性的。

[0075] 合适的稀释剂的类别包括但不限于具有 2 至 20 个碳原子的醇、衍生自伯胺的具有 10 至 20 个碳原子的酰胺、醚、聚醚、具有 3 至 10 个碳原子的酮、和具有 8 至 20 个碳原子的羧酸。随着碳数的增加，极性部分的数量也可增加，以提供所需水平的水溶混性。在一些实施例中，优选伯醇和叔醇。优选的类别包括具有 4 至 20 个碳原子的醇和具有 10 至 20 个碳原子的羧酸。

[0076] 在一个实施例中，稀释剂选自 1,2- 辛二醇、叔戊醇、3- 甲基 -3- 戊醇、癸酸、3,7- 二甲基 -3- 辛醇、三丙二醇甲醚 (TPME)、1,2- 丙二醇、丙三醇、具有介于约 200 和约 30,000 之间的分子量的聚乙二醇、甲基葡萄糖醚（诸如 Glucam 聚合物）、乙酸丁氧基乙酯、它们的混合物等等。

[0077] 在一个实施例中，稀释剂选自具有一定程度的水中溶解度的稀释剂。在一些实施例中，至少约百分之三的稀释剂可与水溶混。水溶性稀释剂的例子包括但不限于 1- 辛醇、1- 戊醇、1- 己醇、2- 己醇、2- 辛醇、3- 甲基 -3- 戊醇、2- 戊醇、叔戊醇、叔 - 丁醇、2- 丁醇、1- 丁醇、2- 甲基 -2- 戊醇、2- 乙基 -1- 丁醇、乙醇、3,3- 二甲基 -2- 丁醇、癸酸、辛酸、十二烷酸、1- 乙氧基 -2- 丙醇、1- 叔丁氧基 -2- 丙醇、EH-5（可购自 Ethox Chemicals）、2,3,6,7- 四羟基 -2,3,6,7- 四甲基辛烷、9-(1- 甲基乙基 )-2,5,8,10,13,16- 六氧杂十七烷、3,5,7,9,11,13- 六甲氧基 -1- 十四醇、它们的混合物等。

[0078] 用于本发明的组分的合适范围示于下表中。

[0079]

| 组分 | 浓度（重量％） |
|---|---|
| 有机硅组分 | 10-87,10-80,20-70 |
| PEG | 3-30 |
| 亲水性组分 | 5-40,10-40,13-40,13-30 |
| 润湿剂 | 0-50 ;5-40,6-40,10-20 |
| 其他 | 0-20 |
| 稀释剂 | ≤ 20,＜ 15,≤ 10,≤ 5,≤ 1,0 |

[0080] 应当理解，每个实施例中的组分的量将添加至多 100。另外，这些范围可以任何组合形式进行组合。

[0081] 有机硅聚合物 / 水凝胶的固化以及镜片的制造

[0082] 本发明的反应性混合物可经由在制造接触镜片中用于模塑反应混合物的任何已知的过程（包括旋模成型和静模铸造）进行固化。旋模成型方法公开于美国专利 3,408,429 和 3,660,545 中，静模铸造方法公开于美国专利 4,113,224 和 4,197,266 中。在一个实施

例中，本发明的接触镜片通过直接模塑有机硅水凝胶而形成，直接模制是经济的，并且能够精确控制水合镜片的最终形状。对于该方法，将反应混合物置于具有最终所需有机硅水凝胶的形状的模具中，使反应混合物经受使单体聚合的条件，由此产生具有最终所需产品的大概形状的聚合物。

[0083] 在一个实施例中，使镜片从模具干燥地剥离或脱粘。在使镜片不接触液体或流体的情况下，实现干燥剥离或脱粘。干燥剥离的合适方法包括快速冷却镜片以及镜片模塑或者施加机械力，诸如轻敲、扭转、或挤压镜片模具。

[0084] 在一个实施例中，固化和脱粘之后，对镜片进行提取，以去除未反应的组分并使镜片脱离镜片模具。可使用常规提取流体（如有机溶剂，如醇）进行提取，或者可使用水溶液提取。

[0085] 水溶液为包含水的溶液。在一个实施例中，本发明的水溶液包含至少约 30 重量％的水，在一些实施例中包含至少约 50 重量％的水，在一些实施例中至少约 70％的水，在其他实施例中至少约 90 重量％的水。水溶液也可包含另外的水溶性组分，诸如脱模剂、润湿剂、增滑剂、药物和类药剂营养品组分、它们的组合等。脱模剂为化合物或化合物的混合物，当其与水组合时，其相比于使用不包含脱模剂的水溶液使镜片脱离所需的时间，减少了接触镜片从模具中脱离所需的时间。在一个实施例中，水溶液包含小于约 10 重量％，在其他实施例中小于约 5 重量％的有机溶剂（诸如异丙醇），在另一个实施例中，水溶液不含有机溶剂。在这些实施例中，水溶液不需要特殊的处理，诸如纯化、再循环或特殊的处置工序。

[0086] 在各种实施例中，可例如经由将镜片浸入水溶液中，或使镜片暴露于水溶液流，从而实现提取。在各种实施例中，提取也可包括例如如下中的一种或多种 ：加热水溶液 ；搅拌水溶液 ；将水溶液中的脱模助剂的水平增加至足以使镜片脱离的水平 ；机械或超声搅拌镜片 ；以及将至少一种滤去助剂掺入水溶液中，直至足以促进从镜片中充分去除未反应的组分的水平。前述可在加入或不加入热、搅拌或上述两者的情况下，在间歇式或连续过程中进行。

[0087] 一些实施例也可包括施加物理搅拌以促进滤去和脱模。例如，可使附接镜片的镜片模具部件振动或使其在水溶液内前后移动。其他实施例可包括穿过水溶液的超声波。

[0088] 在一个实施例中，通过干燥剥离工艺来从模具取出镜片。在这种工艺的一个实施例中，当单体混合物随后已固化以形成聚合物时，通过撬开模具半部来使它们分离。通常，镜片保持附着到一个模具半部的一个表面。然后挠曲此模具半部以促使镜片与模具分离。因此，可在不使用任何剥离溶剂（诸如，水或异丙醇）的情况下从模具取出镜片。然后可将剥离的镜片任选地放置到用于浸沥的溶剂内或可直接放置到包含包装溶液（诸如，缓冲盐水）的包装内。另选地，镜片可在其水合之前经受附加的处理，诸如等离子体表面处理。

[0089] 镜片可通过已知方式（包括但不限于高压灭菌）杀菌。

[0090] 测试方法

[0091] 蛋白质溶液 ：

[0092] 将泪液状流体（“TLF”）用于蛋白质吸收率测量。通过将组分按照下表中列出的量溶解在由 1.37g/l 的碳酸氢钠补充的磷酸盐缓冲盐水溶液中来制备 TLF。

[0093]

表：泪液状流体(TLF)组合物

| 组分 | 组成(mg/ml) | 来源 |
|---|---|---|
| 蛋白质和糖蛋白 | | |
| 溶菌酶 | 1.85 | 鸡蛋清 |
| 乳铁蛋白 | 2.1 | 牛初乳 |
| γ球蛋白 | 0.3 | 牛血浆 |
| 脂质运载蛋白 | 1.3 | 得自牛乳的乳脂质运载蛋白（β乳球蛋白） |
| 酸性糖蛋白 | 0.05 | 牛血浆 |
| 粘蛋白 | 0.15 | 牛颌下腺 |
| （白蛋白、$Fn^1$、$Vn^2$、和以极低浓度(ng)存在于泪液中的其他组分 | 0.1% | 牛血清 |
| 脂质 | | |
| 胆甾醇基亚油酸酯 | 0.024 | |
| 乙酸里哪酯 | 0.021 | |
| 甘油三油酸酯 | 0.016 | |
| 油酸 | 0.012 | |
| 十一碳烯酸 | 0.0032 | |
| 胆固醇 | 0.0016 | |
| 葡萄糖 | 0.1 | |

[0094] 1 Fn :纤连蛋白

[0095] 2 Vn :玻连蛋白

[0096] 按如下方式来测量脂质运载蛋白吸收率。得自牛乳的包含 B 乳球蛋白（脂质运载蛋白）的脂质运载蛋白溶液 (Sigma，L3908) 以 2mg/mL 的浓度溶解于磷酸盐缓冲盐水溶液中，用 1.37g/l 的碳酸氢钠和 0.1g/l 的 D- 葡萄糖来补充。对于每个样品，使用每种蛋白溶液测试三个镜片，并使用 PBS 作为对照溶液测试三个镜片。测试镜片在无菌纱布上吸干以去除润湿溶液并无菌地转移至无菌的每个孔包含 2mL 的溶菌酶溶液的 24 个孔细胞培养板上（每个孔一个镜片）。每个镜片被完全浸入溶液中。将 2mL 的溶菌酶溶液放置在一个孔中而不接触镜片作为对照。

[0097] 包含镜片的板和仅包含蛋白质溶液并且镜片在 PBS 中的对照板利用石蜡膜进行密封以防止蒸发和脱水，放置在具有以 100rpm 搅拌的轨道式震荡器上并在 35℃下温育 72 小时。在 72 小时温育期后，镜片通过将镜片浸渍至三个 (3) 单独的包含约 200mL 体积 PBS 的小瓶中被冲洗 3 至 5 次。镜片在纸巾上吸干以去除过量的 PBS 溶液，并转移至无菌锥形管中（每根管 1 个镜片），包含一定体积的 PBS 的每根管基于期望的基于每个镜片组合物估计的溶菌酶吸收率测定。在每个管中欲被测量的溶菌酶浓度需要在如制造商所述的白蛋白标准物范围内 (0.05 微克至 30 微克）。已知吸收溶菌酶程度低于 100μg 每个镜片的样品被稀释 5 倍。已知溶菌酶吸收程度高于 500μg 每个镜片的样品（诸如依他菲康 A 镜片）被稀释 20 倍。

[0098] 将 PBS 的 1ml 等分试样用于样品 9、CE2、和 balafilcon 镜片，并且将 20ml 用于依

他菲康 A 镜片。对每个对照镜片进行同样的处理，不同的是孔板包含 PBS 而非溶菌酶或脂质运载蛋白溶液。

[0099] 溶菌酶或脂质运载蛋白吸收率使用镜片上的二喹啉甲酸法测定，所述方法使用 QP-BCA 试剂盒 (Sigma，QP-BCA)，遵循由制造商所述的步骤（标准物制备在试剂盒中有所描述），并且通过从在溶菌酶溶液中浸湿的镜片所测定的光密度减去在 PBS 中浸湿的镜片（背景）所测量的光密度进行计算。

[0100] 利用能够在 562nm 下读取光密度的 SynergyII 微酶标仪来测量光密度。

[0101] 粘蛋白吸收率使用下列溶液和方法测量。得自牛颌下腺，包含粘蛋白的粘蛋白溶液 (Sigma，M3895- 型 1-S) 以 2mg/mL 的浓度溶解于磷酸盐缓冲盐水溶液中 (Sigma，D8662)，用 1.37g/l 的碳酸氢钠和 0.1g/l 的 D- 葡萄糖来补充。

[0102] 对于每个例子的三个镜片使用粘蛋白溶液测试，并且使用 PBS 作为对照溶液测试三个。测试镜片在无菌纱布上吸干以去除润湿溶液并使用无菌镊子无菌地转移至无菌的每个孔包含 2mL 的粘蛋白溶液的 24 孔细胞培养板上（每个孔一个镜片）。每个镜片被完全浸入溶液中。对照镜片使用 PBS 作为浸泡溶液代替脂质运载蛋白来制备。

[0103] 包含浸入粘蛋白的镜片的板以及包含浸入在 PBS 中的对照镜片的板利用石蜡膜进行密封以防止蒸发和脱水，放置在具有以 100rpm 搅拌的轨道式震荡器上并在 35℃下温育 72 小时。在 72 小时温育期后，镜片通过将镜片浸渍至三个 (3) 单独的包含约 200mL 体积 PBS 的小瓶中被冲洗 3 至 5 次。镜片在纸巾上吸干以去除过量的 PBS 溶液并转移至每个孔包含 1mL 的 PBS 溶液的无菌 24 孔板中。

[0104] 粘蛋白吸收率使用镜片上的二喹啉甲酸法测定，所述方法使用 QP-BCA 试剂盒 (Sigma，QP-BCA)，遵循由制造商所述的步骤（标准物制备在试剂盒中有所描述），并且通过从在粘蛋白溶液中浸湿的镜片所测定的光密度减去在 PBS 中浸湿的镜片（背景）所测量的光密度计算。利用能够在 562nm 下读取光密度的 SynergyII 微酶标仪来测量光密度。

[0105] 通常在 23±3℃和约 45±5％的相对湿度下通过硼酸盐缓冲盐水并且利用 Wilhelmy 天平测量动态接触角或 DCA，由此来测量可湿润性。利用 Wilhelmy 微量天平测量镜片表面和硼酸盐缓冲盐水之间的润湿力，同时将从镜片的中央部分切割的样品条以 100 微米 / 秒的速率浸入到盐水溶液内或从盐水溶液拉出。使用下面的公式

[0106] $F = \gamma p \cos\theta$ 或 $\theta = \cos^{-1}(F/\gamma p)$

[0107] 其中 F 为润湿力，γ 为探测液体的表面张力，p 为弯月面处的样品周长，并且 θ 为接触角。通常，从动态润湿实验获得两个接触角 - 前进接触角和后退接触角。在样品被浸入探测液体的情况下从润湿实验的部分获得前进接触角，并且这些前进接触角为本文所记录的值。每个组成测量五个镜片，并记录平均值。

[0108] 通过 ISO 18369-4 :2006 中大体描述的、但具有以下变化的极谱法来测定透氧度 (Dk)。在含 2.1％氧的环境下进行测量。通过为测试室配备以合适比率设置的氮气和空气输入（例如，1800ml/min 的氮气和 200ml/min 的空气）来创造此环境。利用经调节的氧浓度来计算 t/Dk。使用硼酸盐缓冲盐水。通过使用加湿的纯氮气环境而不施加 MMA 镜片来测量暗电流。在测量之前未吸干镜片。在测量区域中堆叠四个具有均一厚度的镜片，而不是使用具有不同厚度的镜片。测量具有明显不同的厚度值的 4 个样品的 L/Dk，并将 L/Dk 相对于厚度作图。回归斜率的倒数为样品的初步 Dk。如果样品的初步 Dk 小于 90barrer，则

将 (1+(5.88(CT( 以 cm 计 )))) 的边缘校正应用到初步 L/Dk 值。如果样品的初步 Dk 大于 90barrer,则将 (1+(3.56(CT( 以 cm 计 )))) 的边缘校正应用到初步 L/Dk 值。将 4 个样品的经边缘校正的 L/Dk 相对于厚度作图。回归斜率的倒数为样品的 Dk。使用弧形传感器来代替平面传感器。所得的 Dk 值以 barrer 为单位进行记录。

[0109] 水含量

[0110] 按下述方式测量水含量 :使待测试的镜片位于润湿溶液中 24 小时。使用海绵端棉签从润湿溶液中取出三个测试镜片中的每一个,并将其置于吸收擦拭物上,所述吸收擦拭物已用润湿溶液润湿。使镜片的两侧均与擦拭物接触。使用镊子,将测试镜片置于称重盘中,并称重。按照上述方式制备并称重另外两组样品。将盘称重三次,并且平均值为湿重。

[0111] 通过将样品盘置于已预热至 60℃的真空烘箱中 30 分钟,从而测量干重。施加真空,直至达到至少 0.4 英寸 Hg。关闭真空阀和泵,干燥镜片 4 小时。打开放气阀,使烘箱达到大气压。移出盘并称重。如下计算水含量 :

[0112] 湿重 = 盘和镜片的组合湿重 - 称重盘的重量

[0113] 干重 = 盘和镜片的组合干重 - 称重盘的重量

[0114]

$$\%\text{水含量} = \frac{(\text{湿重} - \text{干重})}{\text{湿重}} \times 100$$

[0115] 计算样品的水含量的平均值和标准偏差并记录。

[0116] 通过使用降低至初始标距高度的配备负荷传感器的移动型拉伸试验机的恒定速率的十字头,测量拉伸模量。合适的试验机包括 Instron1122 型。将具有 0.522 英寸长、0.276 英寸“耳”宽和 0.213 英寸“颈”宽的狗骨形样品装载至夹持件中,并以 2in/min 的恒定速率拉长直至其破裂。测量样品的初始标距长度 (Lo) 和样品破裂长度 (Lf)。每个组成测量十二个试样,并记录平均值。在应力 / 应变曲线的初始线性部分处测量拉伸模量。伸长百分比为 = [(Lf-Lo)/Lo]×100。

[0117] 玻璃化转变温度 Tg 被限定为 tan δ 的峰值 ( 最大值 )。利用随温度而变化的 DSC( 频率 1.0Hz、自动张力模式 ( 张力 = 0)、平行板 (25.0mm 直径 )、和剪切应力 5.0kPa) 同时将经固化的膜从 55℃以 1℃ /min 的速率加热到 150℃来测量等温固化之后的玻璃化转变温度 Tg、动态剪切模量 (G’)、损耗模量 (G”)、和 tan δ 。

[0118] 实例

[0119] 这些实例不限制本发明。它们仅意在提出实施本发明的方法。具有丰富镜片知识的人和其他专家可能会找到其他实践本发明的方法。如下缩写在以下实例中使用 :

[0120] DMA N,N- 二甲基丙烯酰胺

[0121] HEMA 甲基丙烯酸 2- 羟乙酯

[0122] IRGACURE 819 双 (2,4,6- 三甲基苯甲酰基 )- 苯基氧化膦

[0123] Norbloc 2-(2’- 羟基 -5- 甲基丙烯酰氧基乙基苯基 )-2H- 苯并三唑

[0124] OH-mPDMS 单 -(3- 甲基丙烯酰氧基 -2- 羟基丙氧基 ) 丙基封端的、单 - 丁基封端的聚二甲基硅氧烷 (Mw 612g/mole)

[0125] PVP 聚 (N- 乙烯基吡咯烷酮 )( 所述 K 值 )

[0126] TEGDMA 四乙二醇二甲基丙烯酸酯

[0127] acPDMS 1000 双-3-丙烯酰氧基-2-羟丙基丙氧基聚二甲基硅氧烷(MW = 1000)

[0128] CGI1850 1-羟基环己基苯基酮和双(2,6-二甲氧基苯甲酰基)-2,4-4-三甲基戊基氧化膦的 1 : 1(wgt)共混物

[0129] mPEG 475 聚乙二醇(475MW)单甲醚单甲基丙烯酸酯

[0130] 实例 1:包含作为亲水性组分的 mPEG 475、以及各种比率的 K30 与 K90 的制剂

[0131] 将表 1 的反应性单体混合物的组分配制在零稀释剂体系中。在琥珀色广口瓶中制备共混物并且将此共混物在具有以 45℃周期性加热的广口瓶滚筒中进行滚动直到获得完全的溶解。在真空中对反应性单体混合物进行脱气,之后是利用 760mmHg 的氮气回填 15 分钟。利用表 1b 中所示的模具部件和固化条件来光固化镜片。利用放置在基底曲面上的石英板来固化镜片以改善边缘切割和向心性。将具有已加载反应性单体混合物的模具部件的托盘放置在镜像表面上以用于固化。

[0132] 机械地分离模具部件,并且镜片主要保持在 zeonor 前曲面中。通过在室温下将机械力施加到塑性部件的外表面上(即,利用锤子轻敲前曲面)来从前曲面剥离镜片。

[0133] 表 1a

[0134]

| 组分 | 样品 1 | 样品 2 | 样品 3 | 样品 4 |
|---|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 | 40.00 |
| mPEG 475 | 10.00 | 17.00 | 19.00 | 21.00 |
| HEMA | 25.25 | 20.25 | 20.25 | 20.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 12.00 | 10.00 | 8.00 | 6.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 |

[0135] 表 1b

[0136]

| | |
|---|---|
| 氮固化箱 | |
| 氧水平 | <0.5% |
| 可见光强度(TL03) | 5 - 6mW/cm$^2$ |
| 温度 | 55 - 60℃ |
| RRM 剂量 | 100μL |
| 固化时间 | 15 分钟 |
| 模具部件 | |
| 前曲面 | Zeonor |
| 基底曲面 | 聚丙烯 |

[0137] 所得的“干燥剥离”镜片在固化之后为透明的/非相分离的,并且看上去为适当塑化的且不具有物理损坏的迹象。在机械镜片剥离方面可存在显著地困难程度(镜片粘着到前曲面),这指示出高塑性或流动性水平。镜片在高压灭菌之前在润湿溶液中为透明的/非相分离的,并且在高压灭菌之后为模糊的/相分离的。

[0138] 实例 2:物理特性

[0139] 测量得自样品 1 的已灭菌镜片的水含量、雾度百分比、模量、和伸长百分比。获得

的数据示于表 2 中，其中可观察到显著的雾度水平。

[0140] 表 2

[0141]

| 水% | 雾度%（相对于 CSI） | 机械性能 | |
|---|---|---|---|
| | | 模量(psi) | 伸长率% |
| 47.0 (0.2) | 152 (5) | 129.8 (6.3) | 322.1 (36.6) |

[0142] 实例 3：引入 acPDMS 1000 以用于形成非相分离的高压消毒镜片

[0143] 在以减少 HEMA 为代价的情况下利用 acPDMS 1000 作为交联剂体系的组分来重新配制样品 3 和样品 4（这些样品先前在高压灭菌时产生相分离的镜片）中的共混物。这些共混物在表 3 中示为样品 5 和样品 6。根据实例 1 来处理共混物。此外，根据实例 1 来制造镜片、使镜片脱模、并使镜片经受水处理。

[0144] 表 3

[0145]

| 组分 | 样品 5 | 样品 6 | 样品 7 |
|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 21.00 | 19.00 | 0.00 |
| DMA | 0.00 | 0.00 | 19.00 |
| HEMA | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 6.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 |

[0146] 所得的镜片在固化之后为透明的 / 非相分离的。此外，得自样品 5 和 6 的镜片看上去具有高塑化水平，而得自样品 7 的镜片为极其易碎的。对于样品 5 和 6 而言，在机械镜片剥离方面存在显著的困难程度（镜片粘着到 FC）。镜片在高压灭菌之前在润湿溶液中为透明的 / 非相分离的，并且在高压灭菌之后为透明的 / 非相分离的，这指示 acPDMS 1000 在降低雾度或相分离方面具有显著作用。

[0147] 实例 4：物理特性

[0148] 使得自样品 5-7 的已灭菌镜片经受物理特性测试。测量水含量百分比、雾度百分比、DCA 前进角、Dk（边缘已校正）、模量、和伸长百分比。获得的数据示于表 4 中，其中获得了透明的 / 非相分离的镜片。此外，所有镜片为极其可润湿的并且具有低模量的特征。

[0149] 表 4

[0150]

| 样品 | 水% | 雾度%（相对于 CSI） | DCA 前进角 | Dk（边缘已校正） | 机械性能 | |
|---|---|---|---|---|---|---|
| | | | | | 模量(psi) | 伸长率% |
| 5 | 47.7 (0.0) | 15 (1) | [a]51 (14)<br>[b]50 (11) | 75 | 130.2 (5.8) | 159.9 (32.7) |

[0151]

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | [c]48 (6)<br>[d]62 (12) | | | |
| 6 | 47.9<br>(0.1) | 21 (0) | [a]51 (7)<br>[b]50 (3)<br>[c]48 (3)<br>[d]51 (9) | NT | 123.4 (8.9) | 159.5 (31.2) |
| 7 | 45.5<br>(0.1) | NT | [a]51 (8) | 59 | 142.7 (7.2) | 226.8 (34.0) |

[0152] a 从包装取出后直接测量

[0153] b 在 DCA 介质中平衡 3 小时

[0154] c 在 DCA 介质中平衡 24 小时

[0155] d 在 DCA 介质中平衡 48 小时

[0156] 实例 5 :调节 mPEG 475 相对 DMA 的比率以实现最佳镜片剥离

[0157] 利用样品 6 作为基础制剂,在以减少 mPEG 475 为代价的情况下添加 3%、6%和 9%的 DMA,如表 5 中的样品所示。目的是利用低浓度的 DMA 来调节经固化的镜片中的粘弹性性能,使得机械镜片从 FC 的剥离为可接受的,同时获得最佳的聚合度。根据实例 1 处理共混物。此外,根据实例 1 来制造镜片、使镜片脱模、并使镜片经受水处理。

[0158] 表 5 :

[0159]

| 组分 | 样品 8 | 样品 9 | 样品 10 |
|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 16.00 | 13.00 | 10.00 |
| DMA | 3.00 | 6.00 | 9.00 |
| HEMA | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 |

[0160] 所得的镜片在固化之后为透明的 / 非相分离的。对于样品 8 而言,在机械镜片剥离方面存在显著的困难程度 ( 镜片粘着到 FC)。样品 9 和 10 的镜片看上去具有可接受的塑化水平并且能够无困难地机械剥离。

[0161] 实例 6 :物理特性

[0162] 测量得自样品 8-10 的已灭菌镜片的水含量、雾度百分比、模量、和伸长百分比。获得的数据示于表 6 中。

[0163] 表 6 :

[0164]

| 样品 | 水% | 雾度%（相对于 CSI） | DCA 前进角 | Dk | 机械性能 | |
|---|---|---|---|---|---|---|
| | | | | | 模量(psi) | 伸长率% |
| 8 | 46.4 (0.2) | 11 (1) | 55 (6) | 75 | 152.2 (9.2) | 129.6 (33.9) |
| 9 | 47.7 (0.3) | 19 (1) | NT | NT | 157.9 (8.6) | 149.7 (26.2) |
| 10 | 47.5 (0.2) | 20 (1) | NT | 64 | 151.9 (12.6) | 164.4 (41.8) |

[0165] 实例 7 :较低模量

[0166] 根据实例 1 如表 7 中所示来配制包含 K30 和 K90 的组合以及各种比率的交联剂 (acPDMS 1000 :TEGDMA) 的共混物。此外，根据实例 1 来制造镜片并使其脱模。将“干燥剥离”镜片直接放置到含有 3mL 润湿溶液的单独镜片小瓶内，并且随后进行灭菌。

[0167] 表 7

[0168]

| 组分 | 样品 11 | 样品 12 | 样品 13 | 样品 14 | 样品 15 | 样品 16 | 样品 17 | 样品 18 |
|---|---|---|---|---|---|---|---|---|
| OH-mPDMS | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 | 38.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 10.00 | 13.00 | 13.00 | 13.00 | 13.00 | 13.00 | 14.00 | 14.00 |
| DMA | 11.00 | 8.00 | 8.25 | 8.50 | 6.00 | 8.00 | 7.00 | 7.00 |
| HEMA | 18.25 | 18.25 | 18.25 | 18.25 | 18.50 | 16.75 | 16.75 | 16.75 |
| TEGDMA | 0.50 | 0.50 | 0.25 | 0.00 | 0.25 | 0.00 | 0.00 | 0.00 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.00 | 10.00 | 12.00 | 12.00 | 12.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 | 10.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 |

[0169] 所得的镜片在固化之后为透明的 / 非相分离的，看上去具有可接受的塑化水平，并且能够利用机械力从 FC 适当地剥离。

[0170] 实例 8 :物理特性

[0171] 测量得自样品 11-18 的已灭菌镜片的水含量、雾度百分比、模量、和伸长百分比。获得的数据示于表 8 中，其中相对于表 6 中的样品获得了显著较低的模量。

[0172] 表 8

[0173]

| 样品 | 水% | 雾度%（相对于 CSI） | DCA 前进角 | Dk | 机械性能 | |
|---|---|---|---|---|---|---|
| | | | | | 模量(psi) | 伸长率% |
| 11 | 49.5 (0.2) | 10(0) | NT | 60 | 133.9 (9.8) | 162.9 (24.7) |
| 12 | 49.5 (0.2) | 10 (1) | NT | 60 | 129.5 (7.4) | 127.7 (31.6) |
| 13 | 51.5 (0.3) | 16 (4) | NT | 63 | 113.0 (8.7) | 202.3 (27.5) |
| 14 | 52.3 (0.2) | 18 (0) | 61 (7) | 62 | 100.2 (8.7) | 204.7 (25.5) |
| 15 | 50.3 (0.2) | 9 (1) | NT | 62 | 127.4 (7.4) | 186.4 (45.4) |
| 16 | 54.5 (0.0) | 25 (1) | 51 (12) | 65 | 81.8 (4.9) | 261.9 (55.0) |
| 17 | 54.4 (0.2) | 22 (1) | 55 (11) | 63 | 83.0 (13.0) | 243.8 (42.8) |
| 18 | 54.3 (0.1) | 20 (2) | 52 (6) | 65 | 87.6 (5.1) | 258.7 (43.6) |

[0174] 实例 9 :PVP 释放

[0175] 针对释放到润湿溶液（硼酸盐缓冲盐水溶液）内的 PVP 来测试得自样品 14 和样

品 16 的已灭菌镜片。对于每个试样，打开 2 个小瓶并且利用塑料镊子将镜片转移到含有 3mL 新鲜润湿溶液的新小瓶内。将小瓶封盖并且放置在中等速度和在环境条件下的往复式摇动器上。1 小时之后，将镜片转移到含有 3mL 新鲜润湿溶液的新小瓶内并且摇动 2 小时。对于所产生的样品，在表 9 所示的时间点重复此工序。通过高效液相色谱－电喷离子化质谱 (HPLC/ESI MS) 来分析样品的 PVP。

[0176] 通过反相色谱法利用下面的色谱分离条件实现 PVP 的分离：

[0177] 柱：Polymer Labs PLRP-S 聚苯乙烯二－乙烯基苯，50×46mm×5μm，100A

[0178] 柱温：50℃

[0179] 注入体积：50μL

[0180] 流速：1mL/ 分钟

[0181] 移动相：洗脱液 A：具有 0.1％三氟乙酸的乙腈

[0182] 洗脱液 B：具有 01％三氟乙酸的水

[0183] 洗脱液 C：具有 0.1％三氟乙酸的异丙醇

[0184] 用于分析的移动相梯度如下所示：

[0185]

| 时间（分钟） | %A | %B | %C |
|---|---|---|---|
| 0.0 | 22 | 78 | 0 |
| 1.0 | 22 | 78 | 0 |
| 11.0 | 70 | 30 | 0 |

[0186]

| | | | |
|---|---|---|---|
| 11.1 | 50 | 0 | 50 |
| 14.0 | 50 | 0 | 50 |
| 14.1 | 22 | 78 | 0 |
| 17 | 22 | 78 | 0 |

[0187] 通过具有 80％源碰撞诱导解离 (CID) 的 ESI MS 来实现 PVP 检测，其中监测具有 86 的质荷比 (m/z) 的离子 (PVP)。

[0188] 得自样品 14 和 16 的 PVP 的累积释放数据示于表 9 中，其中释放被证明持续至多 24 小时。

[0189] 表 9

[0190]

| | 样品 14 | 样品 16 |
|---|---|---|
| 时间 (hr) | 累积释放 ug/ 镜片 | 累积释放 ug/ 镜片 |
| 1.00 | 76.02 | 18.63 |
| 2.00 | 79.11 | 21.18 |
| 4.50 | 89.29 | 32.65 |
| 6.00 | 92.93 | 36.60 |

| | | |
|---|---|---|
| 8.50 | 99.10 | 45.87 |
| 12.00 | 107.84 | 57.67 |
| 24.00 | 139.17 | 100.53 |

[0191] 实例 10 :优化 mPEG 475 :DMA 比率以实现所需的“干燥剥离”

[0192] 根据实例 1 来配制包含 K30 和 K90 的组合的共混物，如表 10 所示。此外，根据实例 1 来制造并且“干燥剥离”镜片。本研究的目的在于表征所述制剂的固化和特性相对于 PEG ： DMA 比率变化的敏感度，由此试图相对于处理来优化特性。

[0193] 塑化水平或流动性水平随着 mPEG 475 水平的增加而增加，这导致在室温下对于机械剥离产生增加的困难程度。样品 19 具有最高的困难程度，其中当施加机械力时，镜片中的约 60％保持粘着到 zeonor 前曲面。脆性水平随着 DMA 水平的增加而增加，这导致在对前曲面施加机械力时显著改善所获得的镜片数。对于样品 26 而言，当在室温下施加机械力时镜片中的 100％均能从前曲面剥离。然而，大量的镜片被表征为具有可能因高脆性程度产生的物理缺陷，诸如裂缝或断裂和边缘缺口。样品 22、23 和 24 获得了最好产率，即，在具有最少数量的物理缺陷的情况下获得了最高数量的镜片剥离。

[0194] 需注意，所有的干燥剥离 / 机械剥离研究均在室温下进行，并且温度对于经固化的镜片的粘弹性性能具有显著的影响。因此，可使用温度来影响镜片的剥离性能。

[0195] 使具有高 mPEG 475 水平的镜片（样品 19、20 和 21）冷却到低于室温将趋于增加镜片的粘度和脆性水平，这将可能导致干燥剥离 / 机械剥离时所获得的产率得到显著改善。

[0196] 然而使具有高 DMA 水平的镜片（样品 25 和 26）加热到高于室温将趋于降低镜片的粘度和脆性水平，这将可能导致物理缺陷方面的显著改善并从而改善干燥剥离 / 机械剥离时所获得的产率。

[0197] 表 10a

[0198]

| 组分 | 样品 19 | 样品 20 | 样品 21 | 样品 22 | 样品 23 | 样品 24 | 样品 25 | 样品 26 |
|---|---|---|---|---|---|---|---|---|
| OH-mPDMS | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 | 40.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 19.00 | 18.00 | 16.00 | 13.00 | 10.00 | 6.00 | 3.00 | 0.00 |
| DMA | 0.00 | 1.00 | 3.00 | 6.00 | 9.00 | 13.00 | 16.00 | 19.00 |
| HEMA | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 | 18.25 |
| TEGDMA | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Norbloc | 2.0 | 2.0 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 10.00 | 10.00 | 10.0 | 10.00 | 10.00 | 10.00 | 10.00 | 10.00 |
| PVP K30 | 8.00 | 8.00 | 8.0 | 8.00 | 8.00 | 8.00 | 8.00 | 8.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 |

[0199] 测量样品 19-26 的镜片的 Tg（加热），并且结果示于表 10b 中。

[0200] 表 10b

[0201]

| 样品编号 | mPEG475（重量％） | DMA（重量％） | $Tg_{加热(C)}$ |
|---|---|---|---|
| 19 | 19 | 0 | 116 |
| 20 | 18 | 1 | 116 |
| 21 | 16 | 3 | 114 |
| 22 | 13 | 6 | 118 |
| 23 | 10 | 9 | 124 |
| 24 | 6 | 13 | 127 |
| 25 | 3 | 16 | 129 |
| 26 | 0 | 19 | 135 |

[0202] 实例 11 :PVP K30 ： K90 比率对镜片特性的影响

[0203] 根据实例 1 来配制包含 K30 和 K90 的组合的共混物，如表 11 所示。此外，根据实例 1 来制造镜片并使其脱模。将“干燥剥离”镜片直接转移到含有 995μL 润湿溶液（具有 50ppm 甲基纤维素）的利用丙烯内衬的铝箔热密封的 1mL 聚丙烯泡罩包装内并且随后通过高压灭菌进行灭菌。此研究的目的在于检查 K30 ： K90 比率对于镜片的物理特性、参数、生物统计学特性和可滤去单体的影响。

[0204] 表 11

[0205]

| 组分 | 样品 27 | 样品 28 | 样品 29 | 样品 30 |
|---|---|---|---|---|
| OH-mPDMS | 38.00 | 38.00 | 38.00 | 38.00 |
| acPDMS 1000 | 2.00 | 2.00 | 2.00 | 2.00 |
| mPEG 475 | 13.00 | 13.00 | 13.00 | 13.00 |
| DMA | 8.00 | 8.00 | 8.00 | 8.00 |
| HEMA | 16.73 | 16.73 | 16.73 | 16.73 |
| 蓝色 HEMA | 0.02 | 0.02 | 0.02 | 0.02 |
| Norbloc | 2.00 | 2.00 | 2.00 | 2.00 |
| PVP K90 | 12.00 | 10.00 | 8.00 | 6.00 |
| PVP K30 | 8.00 | 10.00 | 12.00 | 14.00 |
| IRGACURE 819 | 0.25 | 0.25 | 0.25 | 0.25 |

[0206] 实例 12 :镜片物理特性

[0207] 测试得自实例 11 的镜片的物理特性。如表 12 中的样品 25-28 所证明，对于所检查的 K90 ： K30 比率，获得了能与之相比的镜片特性。利用美国专利 8,168,720 中所示的方法来测量水含量百分比、雾度百分比、DCA 前进角、Dk（边缘已校正）、模量、和伸长百分比。全部镜片为极其透明的并且为可润湿的，具有低模量，并且镜片的总体特性适用于良好的临床性能。此外，在已灭菌镜片在室温下储存约 1 周之后，在接下来的五天连续测量镜片的折射率。表 12 中的数据显示，全部镜片的折射率从第 1 天至第 5 天基本上保持恒定，这

意味着镜片已非常快地取得了平衡。

[0208] 表 12

[0209]

| 性能 | 样品 27 | 样品 28 | 样品 29 | 样品 30 |
|---|---|---|---|---|
| 水含量，% | 54.8(0.3) | 54.4(0.1) | 54.3(0.1) | 53.9(0.3) |

[0210]

| | | | | |
|---|---|---|---|---|
| CSI 的雾度，% | 15(1) | 17(0) | 17(0) | 18(0) |
| 折射率,第 1 天 | 1.4013 | 1.4026 | 1.4034 | 1.4038 |
| 折射率,第 2 天 | 1.4016 | 1.4022 | 1.4033 | 1.4037 |
| 折射率,第 3 天 | 1.4015 | 1.4026 | 1.4040 | 1.4045 |
| 折射率,第 4 天 | 1.4024 | 1.4030 | 1.4033 | 1.4043 |
| 折射率,第 5 天 | 1.4019 | 1.4033 | 1.4038 | 1.4040 |
| 座滴法 | 74.00(3.61) | 70.67(7.51) | 66.33(4.51) | 71.33(4.16) |
| Dk(边缘已校正) | 63.0 | 67.9 | 68.6 | 66.8 |
| 模量,psi | 75.9(6.1) | 77.7(3.2) | 89.2(5.9) | 71.1(3.8) |
| 伸长率% | 187.9(67.1) | 207.3(66.0) | 214.5(52.2) | 210.8(76.7) |

[0211] 在室温下使用KRUSS DSA-100TM仪器,用去离子水作为探测溶液,通过座滴技术来测定镜片的可润湿性。在去离子水中冲洗待测试的镜片 (3-5/ 样品),以除去残留的润湿溶液。将每个测试镜片放置在用润湿溶液浸湿的不脱毛擦拭物上。使镜片的两个面均接触擦拭物,以除去表面水分,而不干燥镜片。为了确保适当的扁率,将镜片“碗面向下”地放置在接触镜片塑性模具上的凸形表面上。将塑性模具和镜片放置在座滴仪器夹持器上,以确保注射器正确的居中对齐并且确保注射器对应于指定的液体。利用 DSA 100-Drop Shape 分析软件在注射器顶端上形成 3 至 4 微升的去离子水液滴,以确保液滴远离镜片而悬挂。通过将针头向下移动使液滴平滑地释放到镜片表面上。在分配液滴之后立即撤回针。允许液滴在镜片上平衡 5 至 10 秒并且基于在液滴图像和镜片表面之间测得的接触角来计算接触角。

[0212] 实例 13 :PVP K30 ： K90 比率对镜片生物统计学特性的影响

[0213] 测试得自实例 11 的镜片的蛋白质吸收率、粘蛋白吸收率和脂质运载蛋白吸收率。利用上述方法测量总蛋白质吸收率。

[0214] 获得的数据示于表 13 中,其中获得了可忽略不计的差异。此外,获得的水平符合具有良好临床性能的镜片。

[0215] 表 13

[0216]

| 性能 | 样品 27 | 样品 28 | 样品 29 | 样品 30 |
|---|---|---|---|---|
| 总蛋白质吸收率（μg/ 镜片） | 7.85(0.63) | 7.71(0.25) | 7.75(0.32) | 7.70(0.40) |
| 粘蛋白吸收率（μg/ 镜片） | 5.26(0.08) | 5.26(0.12) | 5.23(0.02) | 5.15(0.04) |
| 脂质运载蛋白吸收率（μg/ 镜片） | 3.71(0.18) | 3.49(0.15) | 3.75(0.31) | 3.70(0.40) |

[0217] 实例 14 :PVP K30 ： K90 比率对可滤去水平的影响

[0218] 通过反相 HPLC-UV 来测试得自实例 11 的镜片的可滤去单体。样品 27 至 30 的数据示于表 14 中,其中可滤去单体的水平低于量化极限。

[0219] 打开十个泡罩包装并且将镜片转移到不脱毛吸收纸。将镜片短时间地吸干并且转移到玻璃闪烁小瓶内。添加五 (5)mL 甲醇并且将小瓶在室温下超声处理 30 分钟。样品被制备成一式三份并且通过 HPLC-UV 利用下述条件来分析提取物 :

[0220] 柱 :Agilent Eclipse Plus C18,75×4.6mm×1.8μm

[0221] 柱温 :25℃

[0222] 注入体积 :10μL

[0223] 流速 :1mL/ 分钟

[0224] 移动相 :洗脱液 A :具有 005％正磷酸的水

[0225] 洗脱液 B :具有 0.05％正磷酸的乙腈

[0226] 洗脱液 C :具有 0.1％三氟乙酸的异丙醇

[0227] 用于 DMA、HEMA、mPEG 475 和 Norbloc 的分析的移动相梯度如下所示 :

[0228]

| 时间（分钟） | %A | %B | %C |
|---|---|---|---|
| 0.0 | 97 | 3 | 0 |
| 4.0 | 97 | 3 | 0 |
| 20 | 0 | 100 | 0 |
| 30 | 0 | 100 | 0 |
| 31 | 97 | 3 | 0 |
| 35 | 97 | 3 | 0 |

[0229] 用于 OH-mPDMS 的分析的移动相梯度如下所示 :

[0230]

| 时间（分钟） | %A | %B | %C |
|---|---|---|---|
| 0.0 | 0 | 90 | 10 |
| 5 | 0 | 90 | 10 |
| 8 | 0 | 30 | 70 |
| 11 | 0 | 30 | 70 |
| 12 | 0 | 90 | 10 |
| 17 | 0 | 90 | 10 |

[0231] 结果示于表 14。

[0232] 表 14

[0233]

| 组分 | 样品 27 | 样品 28 | 样品 29 | 样品 30 |
|---|---|---|---|---|
| DMA | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g |
| HEMA | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g |
| mPEG475 | ＜ 78 μ g/g | ＜ 78 μ g/g | ＜ 78 μ g/g | ＜ 78 μ g/g |
| Norbloc | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g | ＜ 3 μ g/g |
| OH-mPDMS(n ＝ 4) | ＜ 78 μ g/g | ＜ 78 μ g/g | ＜ 78 μ g/g | ＜ 78 μ g/g |

[0234] 应当了解，虽然已结合本发明的具体实施方式描述了本发明，但是前述描述旨在说明而非限制由随附权利要求书所限定的本发明的范围。其他方面、优点和修改均在权利要求书范围内。