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<p>(54) Title: WETTABLE SILICONE HYDROGEL COMPOSITIONS AND METHODS</p>		
<p>(57) Abstract</p> <p>Improved silicone-containing hydrogels with enhanced wettability comprising a silicone-containing monomer, hydrophilic monomers, and an ethyleneically unsaturated dibasic carboxylic acid-containing or acid-anhydride-containing monomers are disclosed.</p>		

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WETTABLE SILICONE HYDROGEL COMPOSITIONS AND METHODS

BACKGROUND OF THE INVENTION

This is a continuation-in-part application of copending application, Ser. No. 07/758,047 filed September 12, 1991.

Field of the Invention

The present invention relates to improved polymeric silicone-containing hydrogel compositions useful for the production of biomedical devices, especially contact lenses.

Background

Hydrogels have been a desirable material for the preparation of biomedical devices, and have been known since at least Wichterle, et al U.S. Patent No. 3,220,960 which disclosed hydrogels comprising a hydrated polymer of a hydroxyalkyl acrylate or methacrylate crosslinked with a corresponding diester (poly 2-hydroxyethyl methacrylate, known as HEMA).

A hydrogel is a hydrated crosslinked polymeric system that contains water in an equilibrium state. The physical properties of hydrogels can vary widely and are mostly determined by their water content. Since hydrogels exhibit excellent biocompatibility, there has been extensive interest in the use of hydrogels for biomedical devices, especially contact lenses.

2

In the field of contact lenses, various factors combine to yield a material that has appropriate characteristics. Oxygen permeability, wettability, material strength and stability are but a few of the factors which must be carefully balanced to achieve a useable end-result contact lens. Since the cornea receives its oxygen supply exclusively from contact with the atmosphere, good oxygen permeability is a critical characteristic for any contact lens material.

It was discovered in the field that certain crosslinked polymeric materials could be hydrated and retain their water content. It was further found that the higher the water content within contact lenses made from these crosslinked hydrogel polymers, the greater was the oxygen permeability through the lens to the cornea.

High water-containing hydrogels have at times exhibited undesirable mechanical properties. For example, such hydrogels are not easily formed into hydrolytically stable lenses. Further such materials have at times exhibited tearing or other breakage as a result of poor tensile strength. What was needed was a highly oxygen permeable material that was durable and highly wettable. Wettability is important in that if

3

the lens is not sufficiently wettable, it does not remain lubricated and therefore cannot be worn comfortably on the eye. The optimal contact lens would have not only excellent oxygen permeability, but also excellent tear fluid wettability.

Silicone-containing materials were tried as viable contact lens materials and displayed very good oxygen permeability and durability. However, most silicone-containing materials are largely hydrophobic and therefore not sufficiently wettable. Further, it is believed that such hydrophobicity causes enhanced deposit problems, which may result in discomfort when wearing contact lenses made from these silicone-containing polymers.

Therefore, an optimal hydrogel material for biomedical devices, such as contact lenses, would have ideal rigidity, high oxygen permeability and a high degree of wettability.

SUMMARY OF THE INVENTION

In accordance with this invention, the surface wettability of hydrogels such as silicone-containing hydrogels, and more specifically urethane prepolymeric hydrogels and ethylenically terminated polysiloxane hydrogels, can be significantly enhanced by the addition

4

of at least one ethylenically unsaturated dibasic acid or corresponding anhydride monomer in the monomer mix. It is believed that these hydrophilic dibasic acid monomers react with the predominantly hydrophobic silicone-containing monomers and prepolymers to produce highly wettable hydrogels.

Further, in accordance with the instant invention, a method for making a wettable silicone-containing hydrogel composition is disclosed comprising the steps of a) combining an ethylenically unsaturated dibasic acid or acid anhydride and at least one silicone-containing prepolymer into a monomer mix and b) curing the monomer mix resulting from step a) to form a silicone-containing hydrogel composition.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to improved wettability of hydrogels, especially silicone-containing hydrogels with ideal rigidity suitable for biomedical applications such as contact lenses.

The silicone-containing hydrogels of the present invention display improved wettability as a result of the presence of an ethylenically unsaturated dibasic acid or corresponding acid anhydride in the monomer mix with the silicone-containing monomer or prepolymer.

5

Silicone hydrogels (i.e., hydrogels containing silicone) are usually prepared by polymerizing a mixture containing at least one silicone-containing monomer and at least one hydrophilic monomer. Either the silicone-containing monomer or the hydrophilic monomer may function as a crosslinking agent (a crosslinker being defined as a monomer having multiple polymerizable functionalities) or a separate crosslinker may be employed.

Any known silicone-containing monomer may be used in the process of this invention to form the silicone hydrogels of this invention, as will be apparent to one skilled in the art. The monomers added to the monomeric mixture may be monomers or prepolymers. A "prepolymer" is a reaction intermediate polymer of medium molecular weight having polymerizable groups. Thus it is understood that the terms "silicone-containing monomers" and "hydrophilic monomers" include prepolymers. Examples of such monomers may be found in United States Patent Nos. 4,136,250; 4,153,641; 4,740,533; 5,034,461; and 5,070,215.

Additional crosslinking agents which may be incorporated into the silicone-containing hydrogel of the present invention include polyvinyl, typically di-

6

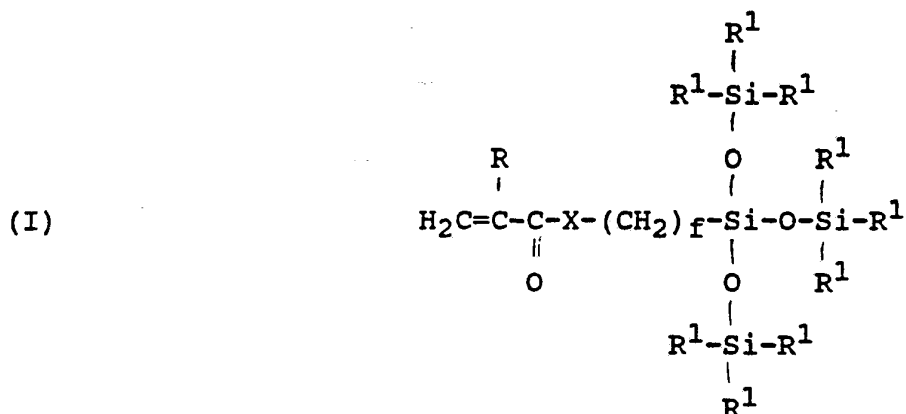
or tri-vinyl monomers, most commonly the di- or tri(meth)acrylates of dihydric ethylene glycol, triethylene glycol, butylene glycol, hexane-1,6-diol, thio-diethylene glycol-diacrylate and methacrylate; neopentyl glycol diacrylate; trimethylolpropane triacrylate and the like; N,N'-dihydroxyethylene-bisacrylamide and -bismethacrylamides; also diallyl compounds like diallyl phthalate and triallyl cyanurate; divinylbenzene; ethylene glycol divinyl ether; and the (meth)acrylate esters of polyols such as triethanolamine, glycerol, pentanerythritol, butylene glycol, mannitol, and sorbitol. Further, illustrations include N,N-methylene-bis-(meth)acrylamide, sulfonated divinylbenzene, and divinylsulfone. Also useful are the reaction products of hydroxyalkyl (meth)acrylates with unsaturated isocyanates, for example the reaction product of 2-hydroxyethyl methacrylate with 2-isocyanatoethyl methacrylate (IEM) as disclosed in U.S. Patent No. 4,954,587.

Other known crosslinking agents are polyether-bisurethane-dimethacrylates as described in U.S. Patent No. 4,192,827, and those crosslinkers obtained by reaction of polyethylene glycol, polypropylene glycol and polytetramethylene glycol with 2-isocyanatoethyl methacrylate (IEM) or m-isopropenyl- α,ω -dimethylbenzyl isocyanates (m-TMI), and polysiloxane-bisurethane-

7

dimethacrylates as described in U.S. Patent Nos. 4,486,577 and 4,605,712. Still other known crosslinking agents are the reaction products of polyvinyl alcohol, ethoxylated polyvinyl alcohol or of polyvinyl alcohol-co-ethylene with 0.1 to 10 mol % vinyl isocyanates like IEM or m-TMI.

One preferred class of suitable silicone-containing monomers contemplated by the present invention are bulky polysiloxanylalkyl (meth)acrylic monomers represented by the formula (I):



wherein:

X is O or NR;

each R is independently hydrogen or methyl; and

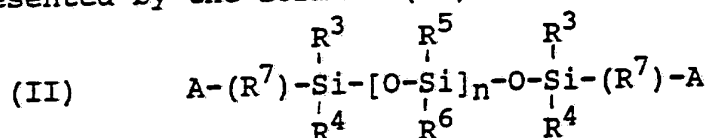
each R¹ is independently a lower alkyl or phenyl group; and

f is 1 or 3 to 10.

8

Such bulky monomers include methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy)methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi(trimethylsiloxy)methacryloxymethyl silane.

A further preferred class of silicone-containing monomers is a poly(organo-siloxane) prepolymer represented by the formula (II):



wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;

each R^3 - R^6 is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;

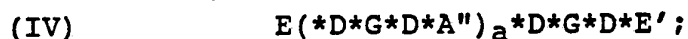
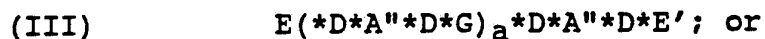
R^7 is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;

and

n is 0 or an integer greater than or equal to 1.

9

A further preferred class of silicone-containing monomers are the monomers having the following schematic representations:



where

D denotes an alkyl diradical, an alkyl cycloalkyl diradical, a cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 6 to 30 carbon atoms;

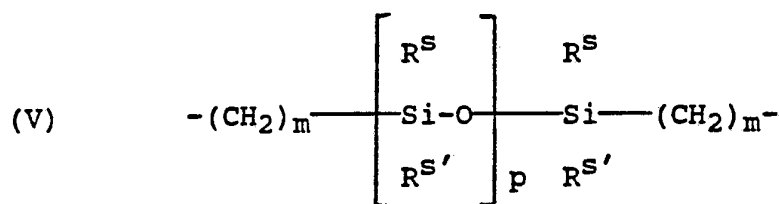
G denotes an alkyl diradical, a cycloalkyl diradical, an alkyl cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 1 to 40 carbon atoms and which may contain ether, thio or amine linkages in the main chain;

* denotes a urethane or ureido linkage;

a is at least 1;

A" denotes a divalent polymeric radical of formula

(V):



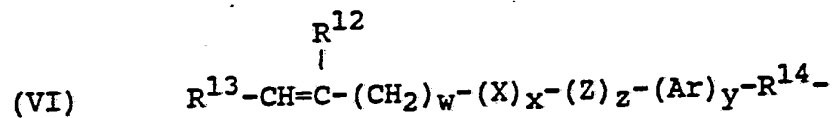
wherein: R^S and $R^{S'}$ independently denote an alkyl or fluoro-substituted alkyl group having 1 to 10 carbon atoms which may contain ether linkages between carbon atoms;

10

m is at least 1; and

p provides a moiety weight of 400 to 10,000;

E and E' independently denote a polymerizable unsaturated organic radical represented by formula (VI):



wherein: R¹⁴ denotes a divalent alkylene radical having 1 to 10 carbon atoms;

R¹² denotes H or CH₃;

R¹³ denotes H, a (C₁-C₆) alkyl radical or a -CO-Y-R¹⁵ group wherein Y is -O-, -S- or -NH- and R¹⁵ is a alkyl radical having 1 to 12 carbon atoms;

X is -CO- or -OCO-;

Z is -O- or -NH-;

Ar denotes an aromatic radical having 6 to 30 carbon atoms;

w is 0 to 6;

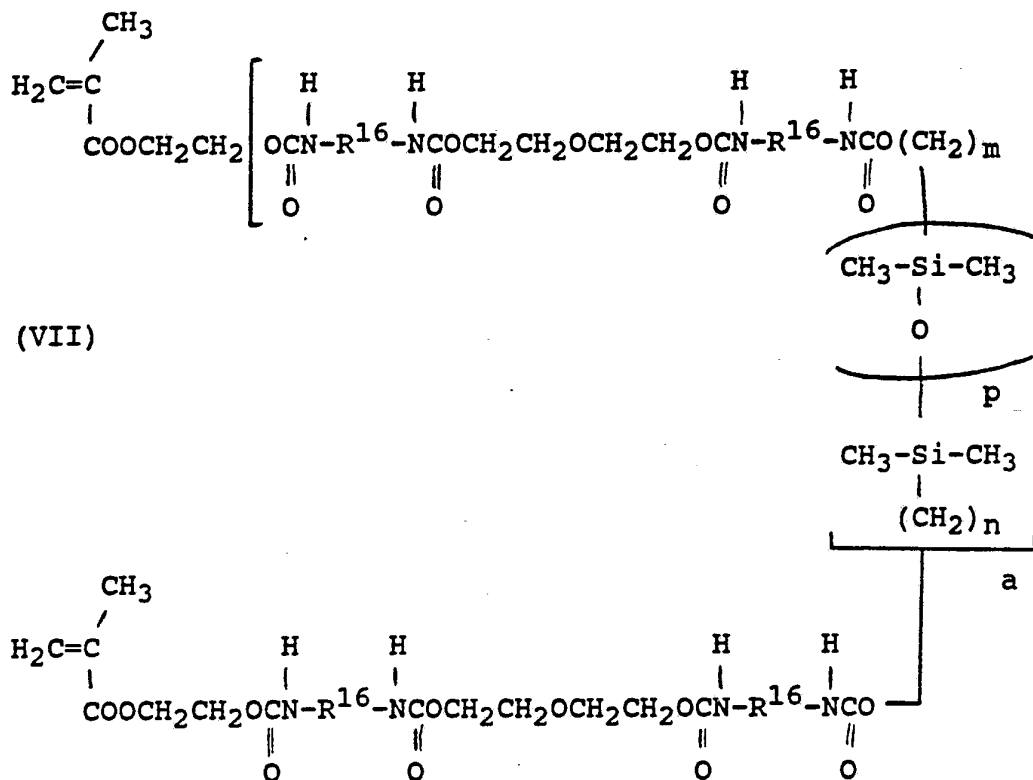
x is 0 or 1;

y is 0 or 1; and

z is 0 or 1.

A preferred urethane monomer is represented by formula (VII):

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wherein:

R¹⁶ is a diradical of a diisocyanate after removal of the isocyanate group, and is most preferably the diradical of isophorone diisocyanate, and m, p and a are the same as previously defined. Preferably, the sum of m and a is 3 or 4, and more preferably, a is 1 and m is 3 or 4. Preferably, p is at least 30.

It is contemplated that the wetttable silicone-containing hydrogels of the present invention, when used in contact lens applications, can produce a wide variety of types of hydrogel contact lenses. As is understood in the field, in general, hydrogel contact lenses should

/2

have oxygen permeabilities with DK values greater than $20 \times 10^{-11} \text{ cm}^3 \times \text{cm/sec} \times \text{cm}^2 \times \text{mmHg}$ (or DK units) and preferably greater than 60 DK. They should have a Young's modulus of elasticity in the range of 5 to 400 g/mm^2 , preferably greater than 20g/mm^2 as measured by ASTM test method D1938. Their water content should be between 10% to 80 %, and preferably between 20 to 60%. The contact angle, which is a measurement of the wettability of the lens, should be less than 80 degrees and should preferably be less than 40 degrees.

The present invention further provides articles of manufacture which can be used for biomedical devices, such as, surgical devices, heart valves, vessel substitutes, intrauterine devices, membranes and other films, diaphragms, catheters, mouth guards, denture liners, intraocular devices, and especially contact lenses.

The terms "shaped articles for use in biomedical applications" or "biomedical devices" mean the materials disclosed herein have physicochemical properties rendering them suitable for prolonged contact with living tissue, blood and the mucous membranes.

Further, notations such as "(meth)acrylate" or "(meth)acrylamide" are used herein to denote optional

13

methyl substitution. Thus, for example, methyl (meth)acrylate includes both methyl acrylate and methyl methacrylate, and N-alkyl (meth)acrylamide includes both N-alkyl acrylamide and N-alkyl methacrylamide.

The term "dibasic acid" is understood by those skilled in the field to describe compounds which contain groups, each of which supplies an hydrogen atom. The presence of two acid groups on these aforementioned dibasic acid compounds, and their anhydride forms where sterically possible, results in a reduction by one-half of the molar amount needed to be supplied to the reaction, as compared with conventional monobasic acids such as methacrylic acid. This is important because the hydrogel characteristics are drastically affected by even small increases in molar amounts of substituents used in the polymeric mix. For example, while a concentration of acid exceeding 10 weight percent might be desirable from a wettability standpoint, such a concentration may adversely affect other properties of the resulting hydrogel. The resulting polymeric film may have undesirable optical characteristics such as cloudiness, etc. When dibasic acids are used, only half the weight percent of the amount of monobasic acid need be used to obtain a comparable effect on the polymeric mixture.

14

The preferred range of dibasic acid concentration is about from 0.5 weight percent of the polymeric hydrogel mix to about 10 weight percent, and more preferably from about 2 weight percent to about 5 weight percent.

The resulting hydrogels of the present invention show great promise as a superior material for various biomedical devices such as surgical implants, blood vessels, artificial ureters, artificial breast tissue and membranes intended to come into contact with body fluid outside of the body, e.g., membranes for kidney dialysis and heart/lung machines and the like. It is known that blood, for example, is readily and rapidly damaged when it comes into contact with artificial surfaces. The design of a synthetic surface which is antithrombogenic and nonhemolytic to blood is necessary for prostheses and devices used with blood.

Further, although the exact mechanisms are not fully understood at the present time, these hydrophilic bifunctional or dibasic carboxylic acid monomers appear to reduce the deposition problems normally associated with, and believed to be caused by, the high hydrophobicity of the hydrophobic silicone-containing monomers.

15

Two preferred classes of silicone-containing monomers contemplated by the present invention are urethane-containing prepolymers, and ethylenically terminated polysiloxane containing monomers, such as, most preferably α,ω bis(methacryloxybutyl)polysiloxane (M_2D_{25}). The ethylenically unsaturated dibasic carboxylic acid containing monomer, (or the corresponding anhydride-containing monomer) of the present invention is preferably itaconic acid, maleic acid or their anhydrides, and fumaric acid, and most preferably are itaconic and maleic acid and their anhydrides.

The monomer mixes employed in this invention, can be readily cured to cast shapes by conventional methods such as UV polymerization, or thermal polymerization, or combinations thereof, as commonly used in polymerizing ethylenically unsaturated compounds. Representative free radical thermal polymerization initiators are organic peroxides, such as acetal peroxide, lauroyl peroxide, decanoyl peroxide, stearoyl peroxide, benzoyl peroxide. tertiarybutyl peroxyvalate, peroxydicarbonate, and the like, employed in a concentration of about 0.01 to 1 percent by weight of the total monomer mixture. Representative UV initiators are those known in the field such as, benzoin methyl ether, benzoin ethyl ether, Darocure 1173, 1164, 2273,

16

1116, 2959, 3331 (EM Industries) and Igracure 651 and 184 (Ciba-Geigy).

Polymerization of the crosslinker of this invention with other comonomers is generally performed in the presence of a diluent. The polymerization product will then be in the form of a gel. If the diluent is nonaqueous, the diluent must be removed from the gel and replaced with water through the use of extraction and hydration protocols well known to those skilled in the art.

It is also possible to perform the polymerization in the absence of diluent to produce a xerogel. These xerogels may then be hydrated to form the hydrogels as is well known in the art.

In addition to the above-mentioned polymerization initiators, the copolymer of the present invention may also include other monomers as will be apparent to one skilled in the art. For example, the monomer mix may include additional hydrophilic monomers such as N-vinyl pyrrolidone and N,N-dimethylacrylamide, colorants, or UV-absorbing and toughening agents such as those known in the contact lens art.

17

The polymers of this invention can be formed into contact lenses by spincasting processes (such as those disclosed in U.S. Pat. Nos. 3,408,429 and 3,496,254), cast molding processes (such as those disclosed in U.S. Pat. Nos. 4,084,459 and 4,197,266), or any other known method for making contact lenses. Polymerization may be conducted either in a spinning mold, or a stationary mold corresponding to a desired contact lens shape. The lens may be further subjected to mechanical finishing, as occasion demands. Polymerization may also be conducted in an appropriate mold or vessel to form buttons, plates or rods, which may then be processed (e.g., cut or polished via lathe or laser) to give a contact lens having a desired shape.

The hydrogels of the present invention are oxygen transporting, hydrolytically stable, biologically inert, and transparent. The monomers and prepolymers employed in accordance with this invention, are readily polymerized to form three dimensional networks which permit the transport of oxygen and are optically clear, strong and hydrophilic.

The relative softness or hardness of the contact lenses fabricated from the resulting polymer of this invention can be varied by decreasing or increasing the molecular weight of the polysiloxane prepolymer end-

18
capped with the activated unsaturated group or by varying the percent of the comonomer. Generally, as the ratio of polysiloxane units to end-cap units increases, the softness of the material increases.

Further, although the exact mechanisms are not fully understood at the present time, the hydrophilic ethylenically unsaturated dibasic acid monomers of the present invention significantly reduce the contact angle of the surface - a clear indication to those skilled in the field that enhanced wetting has occurred. The resulting dibasic acid- or anhydride-treated silicone-containing hydrogels were unexpectedly hydrolytically stable, within an acceptable range, while collecting only an acceptable level of deposits.

The resulting polymers and copolymers disclosed herein can be boiled and/or autoclaved in water without being damaged whereby sterilization may be achieved. Thus, an article formed from the disclosed polymers and copolymers may be used, for example, in surgery where an article is needed which is compatible with living tissue or with the mucous membranes.

The following examples serve only to further illustrate aspects of the present invention and should not be construed as limiting the invention.

19

EXAMPLE 1Preparation of Polyurethane Monomer Mix (Control)

A formulation containing the following was prepared: urethane prepolymer derived from isophorone diisocyanate, diethylene glycol, polysiloxanediol of molecular weight 3000 and 2-hydroxyethyl methacrylate, 35 parts; 3-methacryloxypropyl tris(trimethylsiloxy)silane, (TRIS), 35 parts; N,N-dimethyl acrylamide, 30 parts; n-hexanol, 40 parts; benzoin methyl ether, 0.2 part. The resulting clear mix was then UV cured into films or filtered through a 1.2 micron filter into a clean glass vial ready for lens casting.

EXAMPLE 2Preparation of Polyurethane Monomer Mix Containing a Dibasic Acid Monomer.

Monomer mix was prepared as in Example 1 with the addition of 2 parts of maleic, itaconic or fumaric acid to the monomer mix.

20

EXAMPLE 3Preparation of Polyurethane Monomer Mix Containing an Anhydride Monomer.

Monomer mix was prepared as in Example 1 with the addition of 2 parts of itaconic anhydride to the monomer mix.

EXAMPLE 4Preparation of M₂D_x Containing Monomer Mix

α,ω -Bis(methylacryloxybutyl)polysiloxane (M₂D₂₅) prepared from the reaction of 1,3-bis(4-methacryloxybutyl)disiloxane and 1,1,3,3,5,5-hexamethyltrisiloxane in molar ratio of 1:8.33 was mixed with TRIS, N,N-dimethyl acrylamide(DMA), a solvent (hexanol) and an initiator (Darocure-1173, EM Industries) in the following weight percent ratio:

M2D25	13
TRIS	47
DMA	40
n-hexanol	40
Darocure-1173	0.2

EXAMPLE 5M₂D_x mix with acid monomer

The monomer mixture of Example 4 was added with two parts of itaconic acid.

21

EXAMPLE 6Film Casting of Monomer Mixes

The resultant formulations from Examples 1 - 5 were placed between glass plates and cured under UV for 2 hours. After the films were released from the glass, they were extracted with ethanol for 16 hours and then boiled in water for 4 hours and placed in buffered saline at pH 7.4. The hydrogel films were then characterized for mechanical properties, oxygen permeability, contact angle and others.

EXAMPLE 7Comparison of Hydrogel Properties

The following comparative properties of the control polyurethane films combined with 2 parts of the ethylenically unsaturated dibasic carboxylic acids are noted below.

<u>Properties</u>	<u>Control</u>	<u>Itaconic Acid</u>	<u>Maleic Acid</u>
Water content %	24	34	36
Oxygen perm. (Dk)	100	81	89
Modulus g/mm ²	100	150	110
Tear strength	15	7	13

22

The formulations containing the dibasic carboxylic acid monomers gave higher water content, while the other physical properties were virtually unaffected.

EXAMPLE 8

Hydrolytic Stability Testing

The cured films, after being extracted with solvent (ethanol) and dried in vacuo, were cut into disks weighing 30 mg with a thickness of 250 microns. They were weighed while dry and were then submerged into buffered saline at pH 7.4 in 12 vials and sealed. After equilibration, the films were then placed in an oven at 80 degrees C. Three vials were taken out after 3, 5, 7 and 14 days and the dry weight and water contents were determined gravimetrically. The hydrolytic stabilities were reported as % weight loss after 14 day testing. Low weight losses are more desirable. Experimentally, it was determined that resultant hydrogels having a weight loss of 7% or less would be considered stable. The hydrolytic stability data of the control hydrogel film and those modified with two parts of dibasic acids are listed below.

	<u>Control</u>	<u>Itaconic Acid</u>	<u>Maleic Acid</u>	<u>Methacrylic Acid</u>
Hydrolytic 14 day weight loss %	0.9	3.5	3.8	11.5

23

These results show that the hydrogel films comprising 2 parts of itaconic acid and maleic acid were considered stable. By comparison, hydrogel films derived from a formulation containing methacrylic acid were not as hydrolytically stable.

EXAMPLE 9

Lysozyme Uptake Tests

The tests were accomplished by agitating hydrogel films of known weight, (usually 30-40 mg) in a vial containing a standard buffered saline (5 grams) with 500 ppm of lysozyme for a 7 day period. The amount of lysozyme remaining in the solution was determined by UV spectroscopy and the lysozyme uptake was reported as micrograms of lysozyme per milligram of hydrogel film, using poly(hydroxyethylmethacrylate) (HEMA) hydrogel films as references. The comparative lysozyme uptakes of control hydrogel films and those modified with 2 parts dibasic acid are listed below.

	<u>Control</u>	<u>Itaconic Acid</u>	<u>Maleic Acid</u>	<u>Methacrylic Acid</u>
Lysozyme Uptake	5	19	18	24

A high level of lysozyme uptake is not desirable in contact lenses. Such uptake decreases visual acuity and can result in adverse eye physiological side effects. While it is desirable to add ionic monomers into the

24

silicone-containing hydrogel to improve wettability, the lysozyme uptake level should remain at a low level.

EXAMPLE 10

Contact Angle Measurement

The contact angles of the surface of the films prepared from formulations in Examples 1 and 2 were measured by the captive bubble technique. The films were submerged in buffered saline solution and a bubble of air was attached to the undersurface of the film. The angle made by the intersection of the lens and bubble surfaces was measured using a goniometer. A lower contact angle represents a greater degree of hydrophilicity, or film surface wettability. The comparative contact angles of control hydrogel films and those modified with dibasic acids are listed below.

	<u>Control</u>	<u>Itaconic Acid</u>	<u>Maleic Acid</u>
Contact Angle	38	27	28

The results show that the ionic nature of the ethylenically unsaturated dibasic carboxylic acid containing compounds and their anhydrides improve wettability of the resulting silicone-containing hydrogels.

25

EXAMPLE 11Cast Moldings of Polyurethane Lenses

A polyurethane monomer mix of composition described in Examples 1 and 2 was filtered through a disposable filter of pore size 1.2 microns, into a clean vial. Through an applicator, under an inert nitrogen atmosphere, 60-90ul of the mix was injected onto a clean plastic mold (for the anterior surface of a lens) and then covered with a second plastic mold (forming the posterior surface of the lens). The molds are then compressed and cured for 90 minutes in the presence of ultraviolet light (4200 microwatts/cm²). The molds were opened mechanically and put in a beaker containing aqueous ethanol. The lenses were released from the mold within 10 to 50 minutes. The lenses were then extracted with ethanol for 48 hours, boiled in distilled water for 4 hours and inspected for cosmetic quality and dimension. Lenses passing inspection were thermally disinfected in phosphate-buffered saline prior to on-eye evaluation.

EXAMPLE 12Clinical Evaluations

The cast molded lenses described in Example 11 were evaluated on six subjects. In each test, a poly(HEMA) control lens was worn on eye one and the test lens on

26

the other eye. The lenses were analyzed after a minimum of one hour of wear, and optimally for 6 hours, for wettability and surface deposition. The wettability rating scale was 0-4 with 0 representing 2/3 of the anterior surface unwetted by the tear film and 4 representing complete wetting. The deposition scale was also 0-4 with 0 representing no surface deposit and 4 representing multiple deposits of 0.5mm diameter or larger. The results for the lenses of the control formulation made according to Example 1, was 2.0 for wetting and 1.6 for deposit after 1 hour of wear. For lenses comprising 2 parts of itaconic acid, the results showed a wettability rating of 3.0 and deposit rating of 0.3 after six hours of wear. This indicated that the lenses containing itaconic acid have superior wettability and deposit resistance characteristics resulting in a much higher rate of clinical acceptance.

Many other modifications and variations of the present invention are possible to the skilled practitioner in the field in light of the teachings herein. It is therefore understood that, within the scope of the claims, the present invention can be practiced other than as herein specifically described.

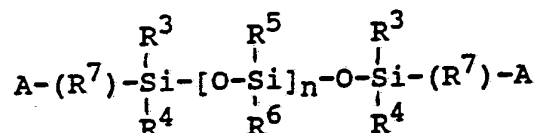
27

We Claim:

1. A method for making a wettable silicone-containing hydrogel composition comprising the steps of a) combining an ethylenically unsaturated dibasic acid or anhydride and at least one silicone-containing monomer into a monomer mix and b) curing the monomer mix resulting from step a) to form a silicone-containing hydrogel composition.
2. The method of Claim 1 wherein said silicone-containing monomer is a urethane-containing prepolymer.
3. The method of Claim 1 wherein said silicone-containing monomer is an ethylenically terminated polysiloxane-containing prepolymer.
4. The method of Claim 1 wherein said dibasic acid is selected from the group consisting of maleic acid, itaconic acid and fumaric acid.
5. The method of Claim 1 wherein said anhydride is selected from the group consisting of maleic anhydride and itaconic anhydride.

28

6. The method of Claim 1 wherein said silicone-containing monomer is a poly(organosiloxane) prepolymer represented by the formula:



wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;

each R^3 - R^6 is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;

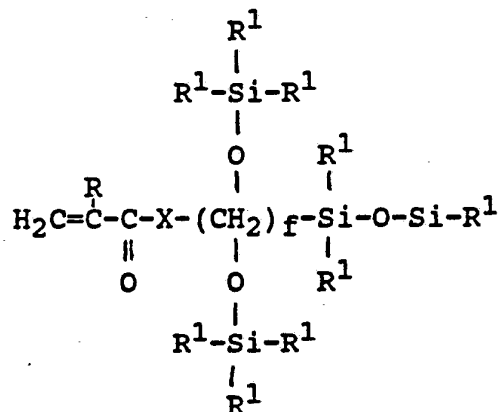
R^7 is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;

and

n is 0 or an integer greater than or equal to 1.

7. The method of Claim 1 wherein said silicone-containing monomer is a bulky polysiloxanylalkyl (meth)acrylic monomer having the formula:

29



wherein:

X is O or NR;

each R is independently hydrogen or methyl; and

each R¹ is independently a lower alkyl or phenyl group; and

f is 1 or 3 to 10.

8. The method of Claim 7 wherein said bulky polysiloxanyalkyl (meth)acrylate monomer is selected from the group consisting of methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy)methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi(trimethylsiloxy)methacryloxymethyl silane.

9. The method of Claim 1 wherein said silicone-containing monomer is a urethane-containing prepolymer having the following schematic representations:

30

$$E(*D*A"*D*G)_a *D*A"*D*E'; \text{ or}$$

$$E(*D*G*D*A")_a *D*G*D*E';$$

wherein

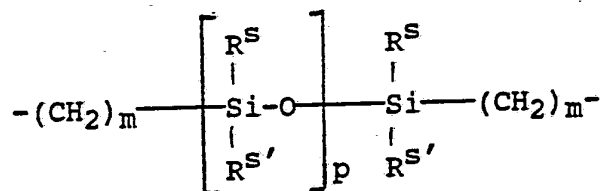
D denotes an alkyl diradical, an alkyl cycloalkyl diradical, a cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 6 to 30 carbon atoms;

G denotes an alkyl diradical, a cycloalkyl diradical, an alkyl cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 1 to 40 carbon atoms and which may contain ether, thio or amine linkages in the main chain;

* denotes a urethane or ureido linkage;

a is at least 1;

A denotes a divalent polymeric radical of formula :



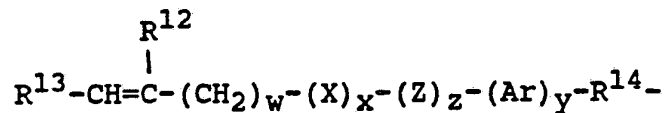
wherein: R^S and $R^{S'}$ independently denote an alkyl or fluoro-substituted alkyl group having 1 to 10 carbon atoms which may contain ether linkages between carbon atoms;

m is at least 1; and

p provides a moiety weight of 400 to 10,000;

31

E and E' independently denote a polymerizable unsaturated organic radical represented by formula:



wherein: R¹⁴ denotes a divalent alkylene radical having 1 to 10 carbon atoms;

R¹² denotes H or CH₃;

R¹³ denotes H, a (C₁-C₆) alkyl radical or a -CO-Y-R¹⁵ group wherein Y is -O-, -S- or -NH- and R¹⁵ is a alkyl radical having 1 to 12 carbon atoms;

X is -CO- or -OCO-;

Z is -O- or -NH-;

Ar denotes an aromatic radical having 6 to 30 carbon atoms;

w is 0 to 6;

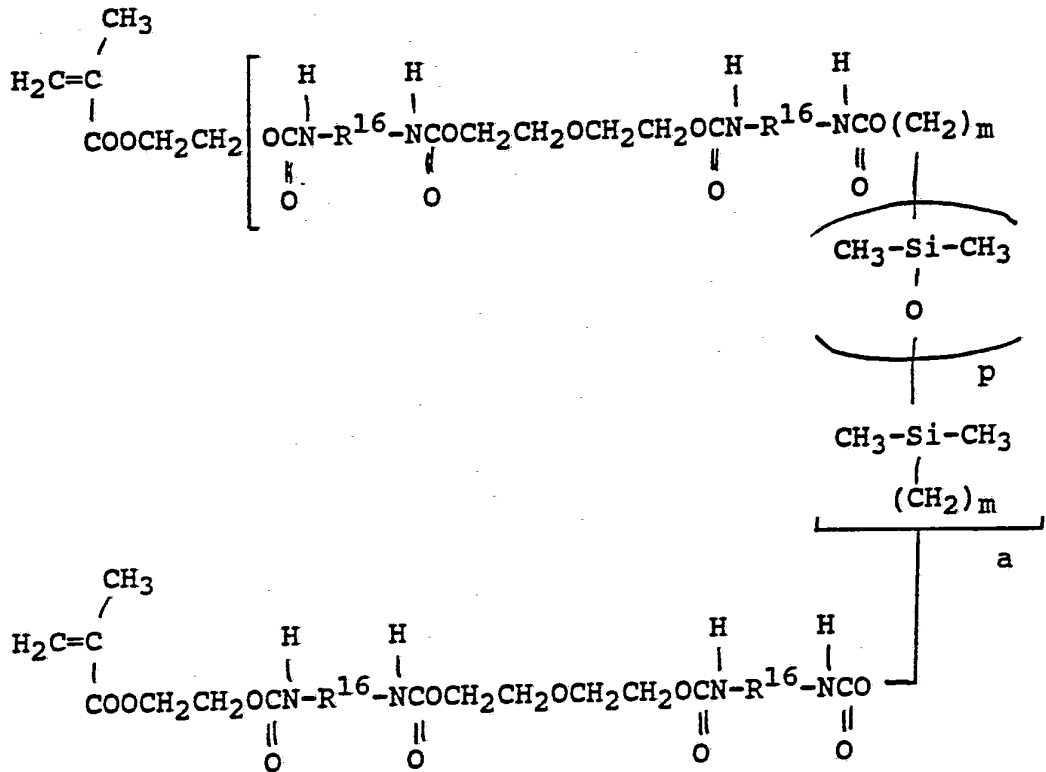
x is 0 or 1;

y is 0 or 1; and

z is 0 or 1.

10. The method of Claim 9 wherein said urethane-containing prepolymer is represented by formula:

32



wherein:

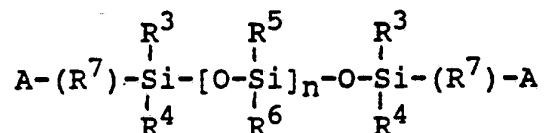
R¹⁶ is a diradical of a diisocyanate after removal of the isocyanate group and m, p and a are the same as previously defined.

11. A silicone-containing hydrogel composition comprising an ethylenically unsaturated dibasic acid or anhydride and a silicone-containing monomer.

12. The hydrogel of Claim 11 wherein said silicone-containing monomer is a urethane-containing prepolymer.

33

13. The hydrogel of Claim 11 wherein said silicone-containing monomer is an ethylenically terminated polysiloxane-containing prepolymer.
14. The hydrogel of Claim 11 wherein said dibasic acid is selected from the group consisting of maleic acid, itaconic acid and fumaric acid.
15. The hydrogel of Claim 11 wherein said anhydride is selected from the group consisting of maleic anhydride and itaconic anhydride.
16. The hydrogel of Claim 11 wherein said silicone-containing monomer is a poly(organosiloxane) prepolymer represented by the formula:



wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;

each R^3 - R^6 is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;

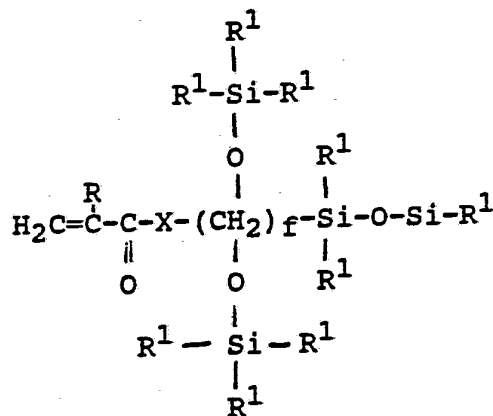
34

R^7 is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;

and

n is 0 or an integer greater than or equal to 1.

17. The hydrogel of Claim 11 wherein said silicone-containing monomer is a bulky polysiloxanylalkyl (meth)acrylic monomer having the formula:



wherein:

X is O or NR;

each R is independently hydrogen or methyl; and

each R^1 is independently a lower alkyl or phenyl group; and

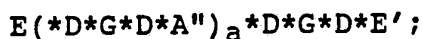
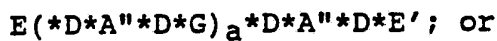
f is 1 or 3 to 10.

18. The hydrogel of Claim 17 wherein said bulky polysiloxanylalkyl (meth)acrylic monomer is selected from the group consisting of methacryloxypropyl

35

tris(trimethylsiloxy)silane,
 pentamethyldisiloxanylmethylmethacrylate,
 tris(trimethylsiloxy)methacryloxy propylsilane,
 phenyltetramethyldisiloxanylethyl acetate, and
 methyldi(trimethylsiloxy)methacryloxymethyl silane.

19. The hydrogel of Claim 11 wherein said silicone-containing monomer is a urethane-containing prepolymer having the following schematic representations:



wherein

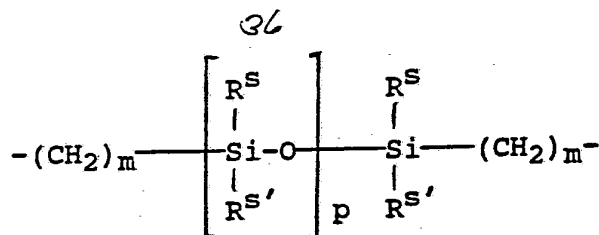
D denotes an alkyl diradical, an alkyl cycloalkyl diradical, a cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 6 to 30 carbon atoms;

G denotes an alkyl diradical, a cycloalkyl diradical, an alkyl cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 1 to 40 carbon atoms and which may contain ether, thio or amine linkages in the main chain;

* denotes a urethane or ureido linkage;

a is at least 1;

A" denotes a divalent polymeric radical of formula:

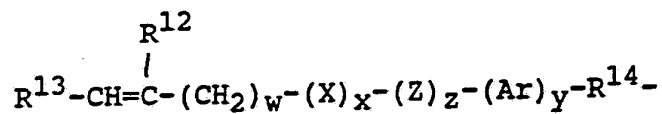


wherein: R^S and $R^{S'}$ independently denote an alkyl or fluoro-substituted alkyl group having 1 to 10 carbon atoms which may contain ether linkages between carbon atoms;

m is at least 1; and

p provides a moiety weight of 400 to 10,000;

E and E' independently denote a polymerizable unsaturated organic radical represented by formula:



wherein: R^{14} denotes a divalent alkylene radical having 1 to 10 carbon atoms;

R^{12} denotes H or CH_3 ;

R^{13} denotes H, a ($\text{C}_1\text{-C}_6$) alkyl radical or a -CO-Y-R^{15} group wherein Y is -O- , -S- or -NH- and R^{15} is a alkyl radical having 1 to 12 carbon atoms;

X is -CO- or -OCO- ;

Z is -O- or -NH- ;

Ar denotes an aromatic radical having 6 to 30 carbon atoms; w is 0 to 6;

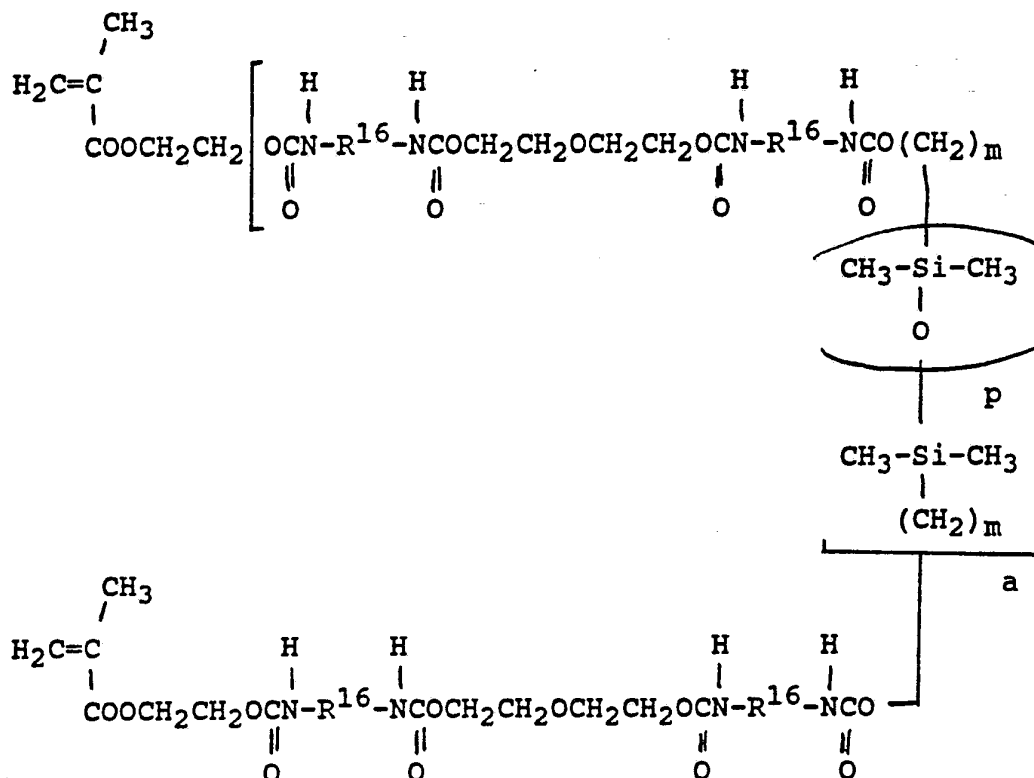
x is 0 or 1;

y is 0 or 1; and

z is 0 or 1.

37

20. The hydrogel of Claim 19 wherein said urethane-containing prepolymer is represented by formula:



wherein:

R^{16} is a diradical of a diisocyanate after removal of the isocyanate group and m, p and a are the same as previously defined.

21. The hydrogel of Claim 11 wherein said silicone-containing monomer is α,ω bis(methacryloxybutyl) polysiloxane, and said ethylenically unsaturated dibasic

38

carboxylic acid containing monomers and corresponding acid anhydride containing monomer is selected from the group consisting of itaconic acid and itaconic acid anhydride.

22. The hydrogel of Claim 11 wherein said silicone-containing monomer is α,ω bis(methacryloxybutyl) polysiloxane, and said ethylenically unsaturated dibasic carboxylic acid containing monomer and corresponding acid anhydride containing monomer is selected from the group consisting of maleic acid and maleic acid anhydride.

23. The hydrogel of Claim 11 wherein said silicone-containing monomer is α,ω bis(methacryloxybutyl) polysiloxane, and said ethylenically unsaturated dibasic carboxylic acid containing monomer is fumaric acid.

24. The hydrogel of Claim 11 wherein said silicone-containing monomer is a urethane-containing prepolymer, said ethylenically unsaturated dibasic carboxylic acid containing monomer and said corresponding acid anhydride containing monomer is selected from the group consisting of itaconic acid and itaconic acid anhydride.

25. The method of Claim 11 wherein said silicone-containing monomer is a urethane-containing prepolymer

39

and said ethylenically unsaturated dibasic carboxylic acid containing monomer and corresponding acid anhydride containing monomer is selected from the group consisting of maleic acid and maleic acid anhydride.

26. The method of Claim 11 wherein said silicone-containing monomer is a urethane-containing prepolymer and said ethylenically unsaturated dibasic carboxylic acid containing monomer is fumaric acid.

27. A biomedical device made from the hydrogel composition of Claim 11.

28. A contact lens made from the hydrogel composition of Claim 11.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 92/07322

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC5: C 08 G 77/20		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC5	C 08 G; C 08 L	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	EP, A2, 0291452 (CIBA-GEIGY AG) 17 November 1988, see claims 1-11, 18, 24 --	1-28
X	US, A, 4605712 (KARL F. MUELLER ET AL.) 12 August 1986, see claims 1-10, abstract --	1-28
X	US, A, 4486577 (KARL F. MUELLER ET AL.) 4 December 1984, see claims 1-5, abstract --	1-28
A	US, A, 4543398 (STEPHEN W. BANY ET AL.) 24 September 1985, see the whole document --	1-28
<p>* Special categories of cited documents:¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"Z" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
25th November 1992	07 DEC 1992	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	Barbro Nilsson	

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	US, A, 5034461 (YU-CHIN LAI ET AL.) 23 July 1991, see claims 1-14, abstract ----- -----	1-28

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.PCT/US 92/07322

SA 64254

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 30/10/92. The European Patent office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		AU-D- 1533088	03/11/88
		JP-A- 63297411	05/12/88
		US-A- 4837289	06/06/89
		US-A- 4923906	08/05/90
		ZA-A- 8803032	31/10/88
US-A- 4605712	12/08/86	AU-B- 585254	15/06/89
		AU-D- 4769785	10/04/86
		CA-A- 1238135	14/06/88
		DE-A- 3584868	23/01/92
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		CA-A- 2014211	07/12/90
		EP-A- 0401990	12/12/90
		JP-A- 3035014	15/02/91

For more details about this annex : see Official Journal of the European patent Office, No. 12/82