

EUROPEAN QUALIFYING EXAMINATION 1996

PAPER A CHEMISTRY

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INSTRUCTIONS TO CANDIDATES

You are to assume that you have received the annexed letter from your client including a description of an invention for which he wishes you to obtain a European patent together with references to the most pertinent prior art known to your client.

You should accept the facts given in the paper and base your answers upon such facts. Whether and to what extent these facts are used is your responsibility.

You should not use any special knowledge you may have of the subject-matter of the invention, but are to assume that the prior art given is in fact exhaustive.

Your task is to draft an independent claim (or claims) offering the applicant the broadest protection possible while at the same time having a good chance of succeeding before the EPO. In drafting your claim(s) you should bear in mind the need for inventive step over the prior art indicated, the requirements of the Convention, in particular as to the form of claims, and the recommendations made in the Guidelines for Examination in the EPO. Dependent claims should also be drafted so as to enable you to fall back upon them should the independent claim(s) fail and should be kept to a reasonable number.

You are also expected to draft an introduction, i.e. that part of the description which precedes the examples or the explanation of the drawings. The introduction should be sufficient to provide support for the independent claim(s). In particular, you should consider the advisability of mentioning advantages of the invention in the introduction.

You are expected to draft claims and an introduction for one European patent application only. This application should meet the requirements of the Convention as to unity. If you would in practise seek to protect further inventions by filing one or more separate applications, you should, in a note, clearly identify the subject-matter of the independent claim of such separate application(s). However, it is not necessary to draft the wording of the independent claim for the or each separate application.

In addition to your chosen solution, you may - but this is not mandatory - give, in a note, the reasons for your choice of solution, for example, why you selected a particular form of claim, a particular feature for an independent claim, a particular piece of prior art as starting point or why you rejected or preferred some piece of prior art. Any such note should however be brief.

It is assumed that you have studied the examination paper in the language in which you have given your answer. If this is not so, please indicate on the front page of your answer in which language you have studied the examination paper. This always applies to candidates who - after having filed such a request when enrolling for the examination - give their answer in a language other than German, English or French.

CLIENT'S LETTER

Dear Sir/Madam,

We are a small company developing and producing visual aids. Increasing importance has been attached recently to visual aids which, for aesthetic as well as partly for medical reasons, are applied directly to the cornea. Such aids are usually referred to as contact lenses.

We have begun to take a particular interest in this specialised field of products, and we should now like to see the results of our research and development work protected by a European patent. We therefore ask you to take the necessary steps to achieve this.

Our specialised products, which we are constantly developing further, have a good reputation in this particular field and are marketed by a large number of customers throughout Europe. To keep our customers abreast of developments, once a year we stage an international customers' conference which is organised by our advertising department. The next such conference is scheduled for Monday of next week. It is here that we will be unveiling our latest developments, to which the products described below belong. Customers expressing an interest in these products will be provided with samples immediately.

Various types of contact lens have already been described and we refer in this connection to the attached **Document I** which addresses the important questions in this field very well.

Our invention concerns itself exclusively with polymers for "hard" contact lenses. Increasing prominence has been given to wearing comfort, including the requirement that the wearers encounter no problems when wearing the lenses for lengthy periods. To achieve this wearing comfort, the combination of the following lens properties is necessary: Firstly, a high level of specific oxygen permeability in conjunction with freedom from any allergic reactions or from irritations of the eye should be mentioned. The lenses should also be as scratch-resistant as possible so as to prevent shortening of their service life due to deterioration of optical qualities or wearing comfort. Hard lenses are more fragile than soft ones. Mechanical strength is therefore a particular requirement. Fragile lenses are no longer accepted in the market. Finally, lenses should have a hydrophilic surface (i.e. a good water-wettability) and retain this property throughout their service life. Needless to say, it is essential that the polymer used in their production be glass-clear and streak-free.

The first materials used in the production of contact lenses were polymethyl methacrylate and, later, polymers of substituted alkyl methacrylates such as 2-hydroxyethyl methacrylate (**HEMA**). The latter monomers result, in general, in soft lenses which swell strongly in water.

The incorporation of fluoroalkyl (meth)acrylates and/or silicone macromers into such polymers heralded the breakthrough in achieving higher specific oxygen permeabilities, although this had the disadvantage of reducing lens hydrophilicity. Wearing comfort likewise suffered, as in many cases did the mechanical strength of the lenses. Polysiloxanes which contain polymerisable ethylenically unsaturated groups are also referred to as silicone, siloxane and polysiloxane macromers.

We have now discovered that the disadvantages of the prior art can be avoided by copolymerising certain siloxane group-containing monomers with certain copolymerisable comonomers in certain quantitative proportions (components **(A)** to **(D)** defined below). It will be noted that the compounds we use are in principle all known as such; we even recently found that silicone compounds which conform to the definition of the component **(A')** below are commercially available.

In wording the application you should bear in mind that even small amounts of unsuitable monomers cause a deterioration in the optical quality of the polymers and sometimes in their other properties, even to the point of rendering them unusable. The application should therefore be worded with the greatest of care so as not to include unsuitable polymers. We once suffered the misfortune of seeing a patent of ours revoked in opposition proceedings because the claims had been worded too broadly. It is an experience we are anxious not to repeat.

Component (A) consists mainly or totally of siloxane group-containing monomers, hereinafter referred to as reactive siloxanes (A'). To avoid any misunderstanding, please note that the term "monomer" as used here is intended to cover all compounds which can be (co)polymerised, i.e. including ethylenically unsaturated oligomers.

The structure of the reactive siloxanes (A') we use corresponds to formula (1) in **Document I**. Please note that our process does not require the presence of separate polymer blocks in the siloxane either. Whereas the number of siloxane units (= degree of polymerisation) in the silicone macromers used in **Document I** totals between 500 and 1000, the siloxane compounds we use have a degree of polymerisation of up to 150, preferably 100 to 150. This type of compound with such a limited degree of polymerisation is often described as an oligomer. In the reactive siloxanes (A') of formula (1) which we use, the R groups possess independently of one another the meanings C₁ to C₄ alkyl and/or phenyl. Here it is generally found that the hydrophilicity decreases as the number of C atoms in the R groups increases, i.e. that hydrophobicity already increases significantly when going from C₁ to C₄. The short-chained groups such as methyl and ethyl, and in particular methyl, are therefore preferred. The choice of these groups R also influences the optical properties.

The number of R¹-X- groups in which an ethylenically unsaturated group R¹ is bonded to a silicon atom of the reactive siloxane by a urethane group X is at least 1 in our invention. Their number should not however exceed 25 % of the total number of all the silicon-bonded organic groups (R and R¹-X-). As the examples below show, products with particularly good swelling and mechanical strength characteristics are obtained if these unsaturated groups account for between 5 and 10 % of all these groups R and R¹-X-. For the preparation of these reactive siloxanes reference has only to be made to our example 1 and to **Document I**.

These reactive siloxanes are polymerised with comonomers the major proportion of which are methacrylic acid alkyl esters (= alkyl methacrylates) (B). Because of the properties required in the polymer, only the C₁ to C₅ alkyl methacrylates are used. Of these the ethyl, and particularly the methyl ester, are preferred, as the polymers obtained are softer the longer the alkyl group of the methacrylic acid ester and the higher the proportion of these longer-chained alkyl esters.

Also polymerised as further key components are hydroxy group-containing alkyl acrylates and/or methacrylates (C) in order to increase hydrophilicity. Methacrylic esters and acrylic esters of alkane diols, which contain a free hydroxy group are to be mentioned in this connection. Preferably hydroxyethyl or hydroxypropyl methacrylates are used.

The desired high mechanical strength is most easily obtained by using cross-linked polymers. If therefore the reactive siloxanes are not already providing sufficient cross-linkage through several ethylenically unsaturated R¹-X- groups, further polyethylenically unsaturated monomers are also added to the reaction mixture as cross-linking agents (D). The only compounds suitable for use as such cross-linking agents are compounds having at least two polymerisable ethylenically unsaturated groups, such as neopentylglycol diacrylate or dimethacrylate, to name but two. Increasing cross-linkage while leaving the monomer composition otherwise unchanged makes the polymer harder and reduces its swelling capacity.

To obtain polymers that meet our requirements the monomers are copolymerised in the following proportions: component (A) in amounts of 15 to 40 % by weight, the alkyl methacrylates (B) in amounts of 40 to 80 % by weight, the hydroxy group-containing (meth)acrylates (C) in amounts of 2 to 10 % by weight and the cross-linking agents (D) in amounts of up to 10 % by weight. Of crucial importance for the polymer thus obtained is that the degree of cross-linking is such that the polymer does not swell in water by more than 10 vol. %, so as to ensure that the polymer, and the contact lens obtained from it, has sufficient dimensional stability. On the other hand, the Shore-D hardness should not exceed 85. This figure is a simple indication of the limit value for the required mechanical strength.

In component (A), a part of the reactive siloxanes (A') can be replaced by fluoroalkyl methacrylates (A'') of which the fluoroalkyl groups contain 2 to 10 C atoms. The amount of these fluorinated monomers should not exceed 10 % by weight of the total amount of the components (A) to (D). The longer the fluoroalkyl group, and the higher the total amount of this fluorinated monomer (A'') and of the reactive siloxane (A'), the less hydrophilic is the polymer. Under no circumstances, therefore, should the total amount of this component (A), i.e. (A')+(A''), exceed 40 % by weight, as hydrophilicity will otherwise fall below an acceptable limit value. This limit value is defined by the contact angle (see **Document I**) which must be at least 100°.

The monomers are admixed in the above proportions and 0.001 to 0.5 % by weight of initiator (E) is added. No other substances, e.g. solvents, are added to the mixture. The monomer mixture must already be glass-clear and streak-free. Numerous tests have shown that monomer mixtures that are not streak-free always produce polymers which are unsuitable for us because of their unsatisfactory optical properties.

To prevent bubbles of entrapped gas being formed in the mixture, this is briefly placed in a vacuum prior to starting the polymerisation. After degassing, polymerisation under inert gas is then started either thermally (using peroxide group-containing radical-forming initiators) or photochemically (by means of photo-initiators). The polymers can be regarded as being identical, irrespective of the method used for initiating the reaction. The degree of polymerisation of the polymers is kept in the required range by using the above-stated amount of initiator and ensuring that the reaction temperature does not rise beyond 60° C.

Usually polymerisation for the production of contact lenses is performed in a mould with a space approximately the same shape as the lens, so that lens blanks are produced directly. This ensures good reaction heat dissipation and further reduces the likelihood of the formation of streaks. To reduce this still further, polymerisation is preferably started photochemically. This obviates the need for external heat and it prevents the reaction mixture overheating.

Furthermore this method of polymerisation in the mould simplifies subsequent processing and avoids excessive material loss. The blanks are then machined to achieve their exact shape, following which the surfaces are polished. The more dimensionally stable the polymer is, the simpler these stages in processing are. These stages are common knowledge among skilled practitioners.

The following examples are intended to explain the invention to you in greater detail. We refer you to the description in the attached **Document I** for further details of the methods of measurement used.

Example 1

As described in the **Document I**, a reactive siloxane with three polymerisable methacrylate groups bonded to siloxane groups was made from a dimethyl siloxane oligomer having a degree of polymerisation of 100 which contained three hydroxyethyl groups per molecule, diisocyanate and hydroxyethyl methacrylate (**HEMA**).

Examples 2-7

The reactive siloxane produced in example 1 was copolymerised with the monomers listed in table 1 into 0.1 mm thick films following addition of 0.2 % by weight of a UV photo-initiator commercially available as "UVInit A" by irradiation with UV light between plates of quartz glass which have been treated so as to be non-sticking. Measurements of the specific oxygen permeability (**O₂-DK**) were carried out on these films. Using the same method, 1 mm thick sheets were made from each monomer mixture and used to determine their water wettability.

In a similar way, and as described in **Document I**, samples for hardness measurements were also made and examined.

Water swelling was determined by measuring the increase in volume of samples after standing for 48 hours in distilled water at 20° C. The samples were produced by the method described for the hardness measurement. The value for Shore-D hardness should never be less than 70. Below this limit the polymers are too soft. The results are summarised in table 1.

Examples 8-10

In a manner analogous to example 1, a reactive siloxane was produced which had a degree of polymerisation of 100 and contained polymerisable methacrylate groups, their number being 10 % of all the organic groups bonded to siloxane groups. This reactive siloxane was used to repeat examples 2, 3 and 4. The results are shown in table 1.

Tests with various commercially available photo-initiators or monomer-soluble peroxide group-containing radical-forming initiators consistently produced polymers with negligibly small amounts of residual monomers.

Incidentally these polymers can also be used for other applications for which good transparency and water wettability are essential, such as for containers or for optical lenses.

Table 1

Ex.	Comonomers (wt.%, balance to 100%: reactive siloxane)	Appearance	O ₂ -DK	Contact angle	Shore-D hardness	Swelling (Vol.%)
2	MMA (60) HEMA (4)	clear	34	110°	73	6.9
3	MMA (66) HEMA (4)	clear	28	117°	75	7.4
4	MMA (73) HEMA (4)	clear	17	123°	80	8.7
5*	MMA (87) HEMA (4)	clear	7.5	124°	83	9.5
6	MMA (60) NPDA (4) HEMA (4)	clear	25	117°	77	5.9
7	MMA (60) FPMA (4) HEMA (4)	clear	33	101°	70	7.5
8	MMA (60) HEMA (4)	clear	34	110°	79	5.2
9	MMA (66) HEMA (4)	clear	28	118°	81	5.6
10	MMA (73) HEMA (4)	clear	16	123°	83	5.9

MMA = methyl methacrylate

FPMA = hexafluoroisopropyl methacrylate

HEMA = 2-hydroxyethyl methacrylate

NPDA = neopentylglycol diacrylate

"clear" means glass-clear in each case

* Comparison test

We hope that the above data are sufficient for you to formulate the application and hereby instruct you to file the application with the Patent Office prior to our customer conference.

Yours faithfully

Perspicacious plc

DOCUMENT I (State of the Art)

The present invention relates to glass-clear, strong, cross-linked polymers, obtained by the copolymerisation of (A) a linear or branched polysiloxane macromer containing at least two terminal or side-chain polymerisable vinyl groups attached to the polysiloxane by way of a urethane group and (B) a vinyl and optionally a divinyl monomer, 85 to 100 % of the monomers being water-insoluble. These polymers, which must of course be streak-free, are useful in the preparation of soft or hard contact lenses, particularly hard lenses.

Contact lenses fall into two main categories, normally called "hard" and "soft", but which are better distinguished by the mode in which they are fitted to the eye. Hard lenses are rather loosely fitted to facilitate tear-liquid exchange between lens and cornea. This they do by their "rocking-chair" motion, by which they continuously pump tear liquid out from the space between lens and eye surface. Such tear-liquid exchange is the only way by which the extremely important oxygen is supplied to the cornea of the wearers of conventional hard contact lenses made from polymethyl methacrylate (PMMA). Hard PMMA lenses are, at least initially, uncomfortable and irritating for the wearer because the blinking eyelid hits a hard edge. They are nevertheless popular because they can be made with great precision by machining (or lathing) and polishing. This is especially important for the production of lenses of asymmetrical design for the correction of astigmatism. Another advantage of hard lenses is that they are very easy to keep clean.

Soft contact lenses on the other hand adhere closely to the cornea and are therefore much more comfortable for the wearer. Since they allow only limited tear liquid exchange they have to possess a specific oxygen permeability high enough to prevent damage to the eye even if they are worn only for a period of hours. In all commercially available soft lenses (made, for example, from hydrophilic hydroxyethyl methacrylate) this O_2 permeability is a function of their water content. In addition, water acts as a plasticiser, which gives the lens its softness and the necessary hydrophilicity which allows it to swim on the cornea rather than to stick to it. Sticking to the cornea is the main problem with hydrophobic soft lenses, such as the known silicone-rubber lenses. Although soft hydrophilic lenses offer higher comfort, optical precision is open to question since precise shaping is not possible because of the softness of the material and because certain distortions due to water swelling are unavoidable. Because they tend to adjust to the cornea, soft lenses are not suitable for the correction of astigmatism. Added to this is the inconvenience of lens-care procedures with standard soft lenses.

The object of an embodiment of this invention is to provide a silicone-containing lens the surface of which is permanently hydrophilic. It is a further embodiment of this invention to provide silicone-containing polymeric materials which range from "soft" to "hard" (using contact-lens terminology) but which do not exhibit the above-described drawbacks.

The polysiloxane macromer corresponds to the general formula (1), wherein the $-(R^1-X)Si(R)-O-$ and $-[Si(R)_2-O]-$ groups need not be in the form of separate polymer blocks, but may, for example, be spread more or less statistically, e.g. evenly, throughout the molecule:



wherein R = methyl, ethyl, propyl or butyl, R^1 = an ethylenically unsaturated group, in particular $CH_2=C(R^2)-CO-O-$, $R^2 = H$ or CH_3 , $X = -R^3-O-CO-NH-R^5-NH-CO-O-R^4-$, each of R^3 and R^4 = a linear or branched (divalent) alkylene residue and R^5 a linear or cyclic alkylene residue, and $m \geq 2$, $n > 0$ and $500 \leq (m + n) \leq 1000$.

The siloxane macromers are obtained in a two-step reaction from free hydroxy group-containing polysiloxane, diisocyanate and e.g. hydroxyethyl (meth)acrylate as follows:

- (i) polysiloxane-OH + OCN-R⁵-NCO → siloxane-O-CO-NH-R⁵-NCO
(ii) polysiloxane-O-CO-NH-R⁵-NCO + HO-C₂H₄-O-CO-C(R²)=CH₂ →
polysiloxane-O-CO-NH-R⁵-NH-CO-O-C₂H₄-O-CO-C(R²)=CH₂

Styrenes or C₁- to C₁₂-alkyl, C₆- to C₁₂-cycloalkyl or C₆- to C₁₂-aralkyl acrylates or methacrylates can be used as comonomers. The longer-chained esters are better suited for soft lenses. Small amounts of divinyl compounds or hydroxyalkyl, as well as C₂- to C₁₀-fluoroalkyl acrylates and/or methacrylates, such as hydroxyethyl methacrylate and hexafluoroisopropyl methacrylate, can also be used.

The polymers obtained were tested as follows.

Specific oxygen permeability (O₂-DK) was determined by measuring the permeability for dissolved oxygen at 35° C using a polarographic electrode in an air-saturated aqueous environment and is expressed in "Barrer" units: 10⁻¹¹ ml·cm/(cm²·s·mmHg) (=7.50·10⁻¹⁴ ml·cm/(cm²·s·Pa)). Below a value of 15 the specific O₂ permeability is hardly viewed as satisfactory.

Water wettability was determined by immersing at 36° C a 1 mm thick sample sheet in water saturated with n-octane. An n-octane droplet was allowed to rise to the lower surface of the sheet and the **contact angle** of the droplet was measured. In this measurement high numbers signify high wettability (hydrophilicity).

Hardness was determined using a **Shore-D** durometer on polished surfaces of a button cut from the centre of a polymer blank (cf. DIN 53 505, ASTM D-2240, ISO 868).

It is of course common knowledge that quantitative figures for polymers and oligomers only represent average properties according to a statistical Gauss distribution.

Example 1

A reactor fitted with a stirrer was filled under inert gas with 30 mols of polydimethyl siloxane which contained three hydroxyethyl groups and which had a degree of polymerisation of 500.

94.5 mols of hexane diisocyanate (a commercial alkylene diisocyanate) were then added together with 25g dibutyltin dilaurate as catalyst. After stirring for 5 hours at 50° C the conversion was practically complete.

25 mols of this intermediate product were reacted with 76 mols of hydroxyethyl methacrylate (**HEMA**) under inert gas at room temperature until no more isocyanate groups (-NCO) were present. The resulting product consisting of polysiloxane having methacrylate groups had a purity of more than 99.5 %. This product is referred to below as siloxane macromer.

Examples 2-4

The siloxane macromer prepared according to example 1 was copolymerised with the monomers listed in table 1 into 0.1 mm thick films, following the addition of 0.2 wt.% "UVInit" initiator, by irradiation with UV-light between quartz glass plates which had been treated so as to be non-sticky. These films were used to measure specific oxygen permeability. In the same manner 1 mm thick sheets made from each monomer mixture were used for determining water wettability.

In the same manner, buttons of 15 mm diameter and 10 mm height were polymerised in cylindrical polypropylene moulds. The cylindrical buttons were then cut in half and the cut surfaces polished for the measurement of hardness.

The results are summarised in the following table 1:

Ex.	Comonomers (wt. %, balance to 100 %: siloxane macromer)	Appear- ance	O ₂ - DK	Contact angle	Shore-D hardness
2	MMA (64) HEMA (4)	clear	29	96°	68
3	CHMA (66) HEMA (4)	clear	28	94°	66
4	MMA (60) FPMA (4) HEMA (4)	clear	32	100°	64
5	MMA (50) NPDA (16) HEMA (4)	clear	28	90°	68
6	CHMA (50) NPDA (16) HEMA (4)	clear	27.5	88°	67
7	MMA (72) HEMA (4)	clear	17	98°	76
8	MMA (86) HEMA (4)	clear	7.8	103°	80

MMA = methyl methacrylate

CHMA = cyclohexyl methacrylate

FPMA = hexafluoroisopropyl methacrylate

HEMA = 2-hydroxyethyl methacrylate

NPDA = neopentylglycol diacrylate

"clear" means glass-clear in each case