# United States Patent [19]

**Grucza**

[11] **3,807,398**

[45] **Apr. 30, 1974**


[54] **OCULAR IMPLANT**


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[52] **U.S. Cl.** ..... **128/260,** 128/268, 264/1

[51] **Int. Cl.** ..... **A61m 7/00,** A61j 1/00, B29d 11/00

[58] **Field of Search** ..... 128/260, 249, 268 X; 264/1



[56] **References Cited**

UNITED STATES PATENTS

| | | | |
|---|---|---|---|
| 3,700,761 | 10/1972 | O'Driscoll et al. | 264/1 |
| 3,496,254 | 2/1970 | Wichterle | 264/1 |
| 2,976,576 | 3/1961 | Wichterle et al. | 18/58 |
| 3,598,122 | 8/1971 | Zaffaroni | 128/268 |



*Primary Examiner*—Aldrich F. Medbery



[57] **ABSTRACT**

Improvements in the O'Driscoll et al U. S. Pat. No. 3,700,761 composition consisting of regulating critical proportions of PVP, HEMA, MA, EDMA, Water and the first and second stage initiators for producing hydrophilic lens blanks from which reproducible and predictable hydrated lenses are obtained with ratios of acceptance of 95 – 98 percent, to dimensional standards between the grinding dry and hydrated wet states and with ratios of resisting dimensional change in wet storage of upwards of ninety five percent. Compositions lying outside of the critical ranges of proportions provide lenses which are unpredictable (90 percent rejection) drift in size and do not provide reproducibility between dry and wet states and thereby create fitting problems. Critical ratios of MA to EDMA lying between 2.5/3.2 at 15 percent PVP content down to 1/1 at 28 percent PVP content provide reproducibility and predictability dry-to-wet and the optimum ratio is 1.5/0.7 at 20 percent PVP (reagents containing less than 1 percent water). Further improvement is made in the method of casting and cutting of U. S. Patent No. 3,700,761, in which there is used a disposable mold of Teflon, high-density polyethylene or of RTV Silicone material with break-away curved bottom which is discarded to provide a convex surface requiring no cutting thereby eliminating many cutting and grinding steps on the conventional hard-lens lathe. Water-soluble medicaments as in U.S. Pat. No. 3,700,761 can be added to precision-cut eye bandages by dissolving in $H_2O$ and adding a total of 5 percent $H_2O$ to HEMA or the medicament can be used in eye drops, the bandage with 5 percent added containing 65 percent $H_2O$ instead of 60 percent.


**3 Claims, 11 Drawing Figures**

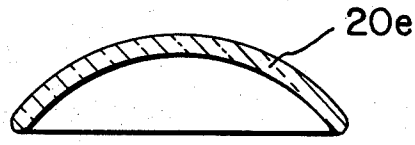


FIG. 1

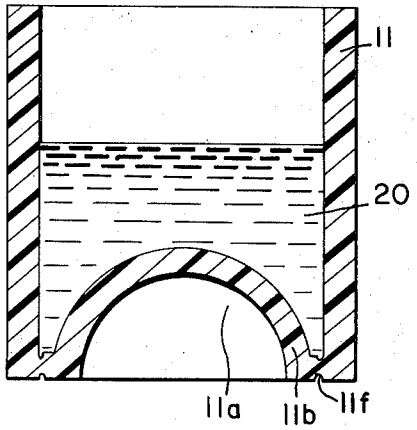



FIG. 2

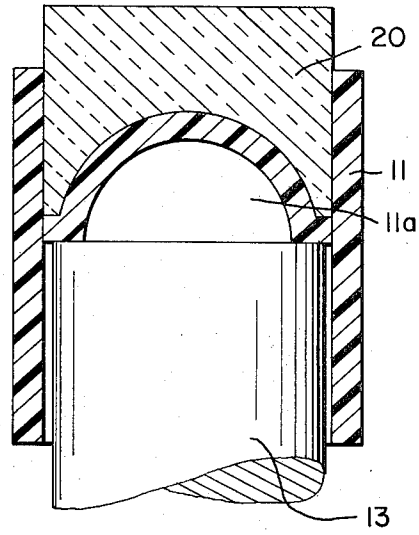



FIG. 3

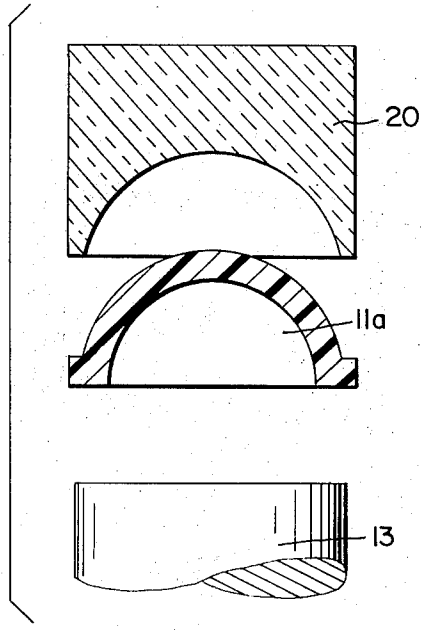



FIG. 4a

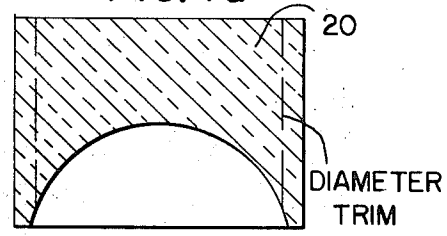



FIG. 4b

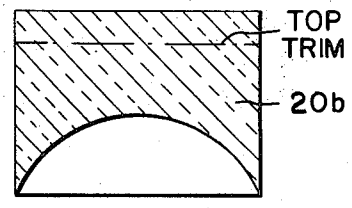



FIG. 4c

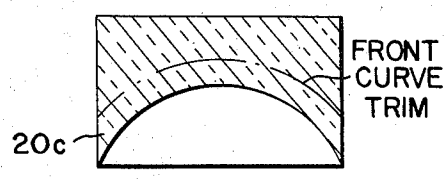



FIG. 4d

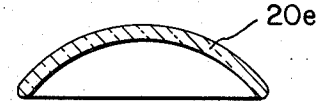


FIG. 5

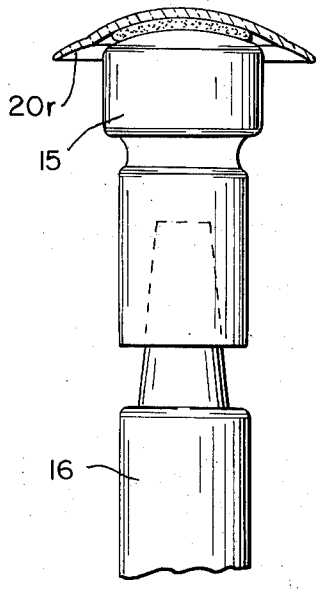



FIG. 6

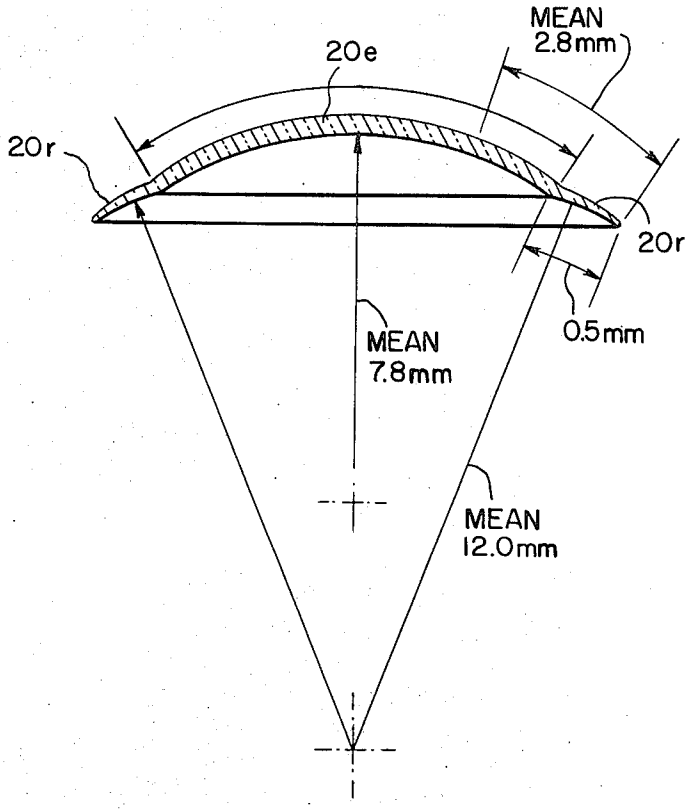



FIG. 7

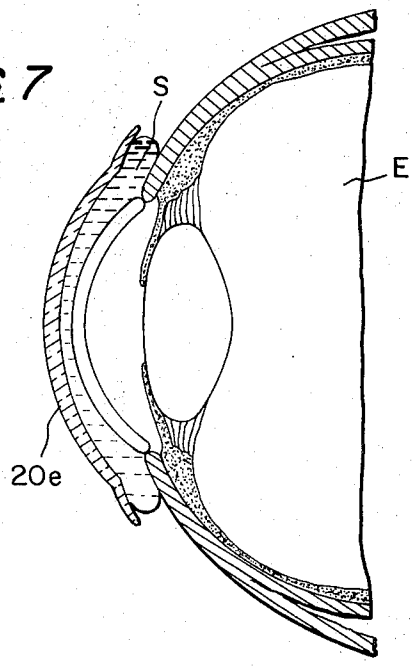
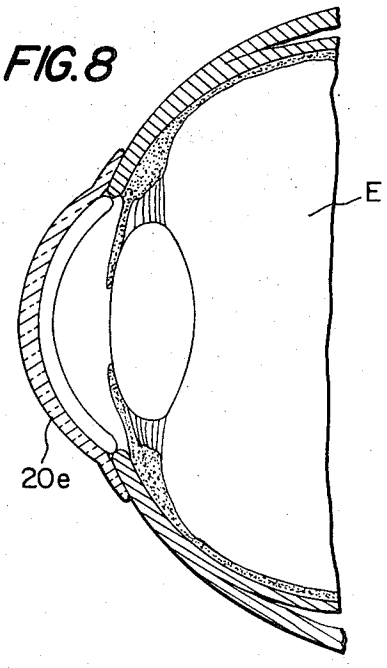



FIG. 8



# OCULAR IMPLANT

## BACKGROUND OF THE INVENTION

In O'Driscoll et al, U.S. Pat. No. 3,700,761, compositions consisting of HEMA (hydroxyethyl methacrylate) or HPMA (hydroxypropyl methacrylate) with PVP in proportions of 20–45 percent, with up to 1% MA and with about 0.2% EDMA were disclosed. Low and critical ranges of proportions of first stage initiators are thermally decomposed at 40°–60° to provide solid buttons which after second stage curing at 110°C radiation curing and hydration provide remarkably high water content of about 50–65 percent in lenses which are cut when dry on both convex and concave surfaces on the conventional hard-lens lathe after the step of radiation curing.

## SUMMARY OF THE INVENTION

The present invention is an improvement of the initial step of the method of preparing the hygroscopic lens in the dry state and depends upon the casting of the lens after a critical induction period in a break-away curved-bottom plastic mold in static condition from the liquid mixture of ingredients in critical porportions and under controlled temperature and inhibitor concentration conditions which prevent heat transfer through the mold so that an improved anisotropic lens is produced which has predictable and reproducible characteristics. This anisotropic lens of the present invention is characterized by different swelling and expansion between dry and wet states in the lateral direction and in the vertical direction but these changes are now reproducible and predictable to match diameters and steepeness of the cross-section and thereby assure a substantially rigid and accurate fit to the eye without drift in diameter or slope or stiffness and to provide longtime and precision correction of the optical condition.

As a result of the swelling, and uniquely due to the very high water uptake (50–65 percent), the lens made by the method of the present invention is found to shape itself by evaporation forces, in an unusual manner to steepen the vault or slope of the lens closely resting on the cornea and sclera of the eye, shaping being similar to that of hard-lens memory characteristics. In contrast to all other types of soft lenses commercially available, reproducibility and predictability are achieved by the critically controlled amounts of PVP, HEMA, EDMA, MA, Water and inhibitor which is used to stabilize the HEMA and which will produce a lens having 50–65 percent in the saline-stored condition.

In the eye, the lens drops in water content from 55 –65 percent down to 45–55 percent. Surprisingly, the higher amount of water retained in the lenses in saline drops to the lower value in from thirty seconds to two minutes after insertion into the eye. This water content drop-off from about 50–65 percent occurs in most patients to a value of about 45–50 percent. The variations mentioned are found in testing hundreds of patients whose eye conditions varied from "wet eye" to "dry eye" as it is known in the art.

It was discovered that this evaporation which occurs provides a slight difference in the shape of the lens which results in a natural astigmatic condition which contributes in a new way to accurate fitting based on the secure adhesion to the limbal area, or areas of the



lens rim which contract and tighten on the corneal center so that this contraction effects a closer fit, in cantilever fashion, and prevents dislodging movements of the lens away from the scleral area. The larger contact rim of the semi-rigid, rubbery lens water-laden with precise dimensional predictability, is uniquely aided for fitting of the entire scleral area and based upon the geometry of the limbal area of the lens, serves to confine the individual's own tears beneath the lens. This aids in the interchange of tear fluid, oxygen and carbon dioxide, all essential to corneal respiration. The steepness of the vault permits accurate centering on the cornea while the circulation of tear fluid permits a respiration result comparable to that due to the permeability of the cornea itself, and this permeability is based upon the high $O_2$ & $CO_2$ permeability of the lens material.

In accordance with the invention, the casting against the curved shape of a disposable mold permits a range of dry lenses for fitting eyes of all dimensions and the range is based upon a simplified manufacturing procedure, using a break-away mold bottom eliminating the grinding of the cast surface while providing a simple number of base curves (5) and a simple number of diameters (5) to true and time-stable dimensions in $x,y$ and $z$ planes.

## BRIEF DESCRIPTION OF THE DRAWINGS

The invention is further illustrated in the drawings in which:

FIG. 1 is a sectional view which shows a break-away mold with curved bottom into which the composition is cast and polymerized against a curved inner-surface which surface requires no further grinding or polishing.

FIG. 2 is a sectional view which shows the breaking of the button from the mold by ram pressure and movement.

FIG. 3 is an exploded view showing separation of the break-away bottom from the button.

FIG. 4*a* shows the first stage of cutting on the lathe as shown in diagramatic form in FIG. 5.

FIG. 4*b* shows the second stage.

FIG. 4*c* shows the third stage of cutting.

FIG. 4*d* shows the finished lense

FIG. 5 shows the mounting of the lense for cutting in stages 4*a*, 4*b* and 4*c*, with a conventional hard lense lathe of the type shown in FIG. 6 and 9 of Mullen, U.S. Pat. No. 2,330,837.

FIG. 6 shows the finished lense with the rim cut after the cutting stage in FIG. 4d, this rim cut being illustrated in FIG. 5. FIG. 6 shows the dimensions of rim cut lenses of the type shown in FIG. 5.

FIG. 7 shows the mounting of the lense of FIG. 5 on the eye with space between the rim and sclera before evaporation contracts the lense.

FIG. 8 shows lense of FIG. 7 after contractile evaporation.

## DESCRIPTION OF THE PREFERRED EMBODIMENTS

The accuracy of manufacture of the present invention is based upon the discovery that critical proportions are required of PVP, MA, EDMA, HEMA, Water with the initiator amounts used for first and second stage initiation in the Driscoll U.S. Pat. No. 3,700,761, and that initial amounts of hydroquinone stabilizer are required to assure storage stability and to give predict-

ability and reproducibility between dry and wet states, these initial amounts permit economy, safety, and reliability in supply and in fitting. The example and drawings illustrate an improved method, based upon the discovery of first stage initiation which must be carried out in a preliminary induction stage at room temperature and which requires that the liquid mixture in static condition in the mold of FIG. 1, subjected to a room temperature stage for the conversion of mobile liquid to stringy liquid at a temperature between 15° – 30° C for 2½ – 6 hours, the longer time being required at the lower temperatures. This induction period in the static mold of FIG. **1**, must be carried out before the first stage initiation under thermal decomposition (40° – 60° C) which decomposes the rest of the initiator and changes the thickened liquid into a transparent solid button. Only when this first stage polymerization is broken down into two stages; first, a quiescent room temperature induction stage at 15° – 30°C and then a thermal stage at 40° for four hours or longer can the chain length of the copolymer grafted onto the PVP be brought up in uniformity, density, etc., up to the necessary length chains which will provide the necessary balance and semi-rigid, highly extensible and brittle properties of the rigid dry polymer. This dry polymer is subjected to further high temperature polymerization, as taught in the O'Driscoll Patent after the first stage without removing from the mold and this second stage is essential to impart hardness and brittleness which creates a button that can be ground to a tolerance of 0.01 millimeters and will maintain its shape after hydration regardless of the shape of eye to which it is applied. In short, the improvement of the present invention controls opposite properties in the contact lens of rubberiness, rigidity, hardness for grinding, dimensional stability and reproducibility in a new and unusual manner by controlling the time for chain growth during a preliminary induction period prior to rapid first stage initiation which occurs in at least four hours at 40°C in the oven and in the mold.

All of the ingredients — HEMA, EDMA, PVP, HPMA, MA, $H_2O$ and inhibitor (HQ or MEHQ) control the chain growth with given initiators. However, a critical element for the achievement of storage stability of the lens in the wet state is the requirement that no more than one hundred parts per million (preferably 60 – 80 parts per million) of hydroquinone-type polymerizing inhibitor, used exclusively with HEMA, such as hydroquinone (HQ) or mono-methyl ether of hydroquinone (MEHQ). It was unexpected to discover that more than 100 parts per million of HQ inhibitor in HEMA would cause drifting, spreading and an increase in size of the diameter with decreased steepness of lenses which were placed in storage in isotonic saline for long periods of time (two weeks to six months). In short, only those compositions in which the inhibitor content is controlled within critical limits of less than one hundred parts per million based upon the HEMA monomer can provide lenses which can be stored in the wet state for weeks or for several months or up to a year without increasing the critical dimensions of diameter and slope.

## IMPROVED MANUFACTURING PROCEDURE ILLUSTRATED IN THE DRAWINGS

Reference is made to the manufacturing procedure which was illustrated and described in O'Driscoll et al, U.S. Pat. No. 3,700,761, wherein hard-lens cutting and polishing technology was used (see FIGS. **4***a*, **4***b*, **4***c*, & **4***d*) after the button was pushed under pressure and moved out of the Teflon cylindrical mold with the ram **13** in contact with the planar top of the button.

The present disposible mold **11** with break-away curved bottom **11**b is shown in FIG. **1** as being filled with the polymerizable composition **20** which hardens in static condition through the room-temperature induction stage (2 ½ – 6 hours) of the present invention (see examples below), the first stage initiation under thermal break down of first initiator to assume the solid state in rubbery condition (40° – 60° C), the second stage under thermal break-down of second initiator (110°C – 1½–4 hours).

Not until the final cut is made in the form shown in FIG. **4** and rimming is accomplished to provide double-gauged (inner and outer sphericities inspected) lens **20** as shown in FIG. **4***d* is the lens ready for the radiation post curing step. In the present invention the compositions made by the new method of bottom ejection of the buttom permit eliminating all cutting operations from the back (curved concave surface) of the lens **20***e* and more important, provide a superior lens which resists breakage since cutting inherently introduces microscopic scratches which act as stress points, initiating cracking and tearing. Eliminating all stress points on the inner-surfaces provides a stronger, longerwearing, more tear-resistant lens in hydrated condition.

The bottom ejection illustrated in FIGS. **2** and **3**, shows break-away frangible section **11***f* in annular shape which serves as the means for permitting movement of dome portion **11**d with the concave surface of the button. The ram **13** is positioned so that its diameter fits precisely under frangible positions **11**f for free expulsion of the button (see FIGS. **2** and **3**).

## LENS IMPROVEMENTS BASED UPON ADAPTING HARD-LENS GRINDING TECHNOLOGY USED FOR GRINDING THE NEW COMPOSITION

As shown in FIGS. **5** and **6**, the hard-lens cutting and grinding technology of Mullen U.S. Pat. No. 2,330,837 permits the hard guasi-rubbery buttons to be accurately cut and ground and polished in the dry state by the same experienced personnel who fit hard contact lens. However, only on optically corrective surface is present for cutting in accordance with the invention and this method of cutting only the outer surface provides a superior lens which requires only an inner rim cut, shown at **20***r* in FIG. **5** and is in an area of the lens which is non-correcting.

Obviously the invention comtemplates the use of a modified form of break-away curved bottom in the mold which will have the rim cut dimension put in the mold part and for more automated manufactoring this method of casting and mold contour information is part of the present invention.

The importance of the rim, which can be prescription ground to meet the various requirements of scleral slope encountered by precise examination or which can be molded as explained, can be seen by the comparison of views in FIGS. **7** and **8**. The lens **20***e* has just been put back on the mounting chuck **15** which is carried on the lathe spindle **16** of the conventional machine in the Mullen Patent. This view illustrates a finishing polish step of the convex surface after this rim has been made. The terminology herein defining "rim cut" relates to

both the "rim cut" casting or that which has been trimmed by cutting.

In FIG. 7 the lens **20***e* is shown in the stage just after removal from isotonic saline and being placed on the eye. Under the rim **20***r* of the lens, the tear fluid flows freely and contractile forces based upon evaporation of water begin their effect. The exposed outer surface of the lens **20**e loses water from a range of 50 – 65% $H_2O$ down to 45 – 50% $H_2O$ and the rim **20** thereby moves downwardly and inwardly gripping the sclera and thereby entrapping a liquid film of tear fluid, thereunder the contracted form is shown in FIG. **8.**

## EXAMPLES SHOWING SCOPE OF PROPORTIONS IN TABLES 1 & 2

The following examples illustrate the scope of initial porportions of the new compositions used for static casting in the curved-bottom molds of the O'Driscoll Patent as well as in the disposable break-away bottom molds of the present invention.

This mixing technique is identical with that in the O'-Driscoll Patent, care being taken not to entrap air and to degas the mixture under vacuum and bleeding nitrogen gas back into the system.

The two tables below summarize the compositions which provide reproducibility and predictability. Table 1, illustrates the fomulations which have been completely analyzed, the EDMA, HEMA, MA all being done by gas-liquid chromatography, (GLC) with HQ and MEHQ being done by titration and being double checked by GLC. The water content was determined by Karl Fisher's method. All values in the tables below are on a weight basis. The PVP in these tables is Plasdone C, (K=30) and in its place PVP (K=15) or (K=90) can be used but best results are achieved with Plasdone C, for the reason that greater uniformity in dryness of the material, supplied by the manufacturer, is found as a result of testing.

The water content of Table 1 is based upon testing average of about 500 samples of Plasdone C, averaging 3 – 3.5 percent water, since the Plasdone C content varies from about 15 to about 28 percent (spread of 2 percent) of the present composition for contact lenses, the average contribution of water in the mixture is less than 1 percent and that Table is entitled substantially dry (less than 1 percent)

Table 2 illustrates the addition of 5 percent of water to HEMA. All water, in both tables 1 and 2, determinations are made by testing "dry" and before and after additions of water and all ingredients added to the mixture are tested in the same way. Suprisingly and unexpectedly the EDMA content is raised by 1 percent as a result of the addition of 5 percent of water and thus increase is reflected in Table 2 and emphasized by the notation (asterisk) after EDMA.

TABLE 1

SUBSTANTIALLY DRY (LESS THAN 1% $H_2O$)

| Ingredient | Series A | Series B | Series C |
|---|---|---|---|
| HEMA | 79.3 | 77.8 | 71.8 |
| PVP (K=30) | 15.0 | 20.0 | 28.0 |
| EDMA | 3.2 | 0.7 | 0.1 |
| MA | 2.5 | 1.5 | 0.1 |
| $H_2O$ | less than 1 | less than 1 | less than 1 |
| HQ or MEHQ | 50 – 100 ppm | 50 – 100 ppm | 50 – 100 ppm |

TABLE 2

5% $H_2O$ ADDED TO HEMA

| Ingredient | Series E | Series F | Series G |
|---|---|---|---|
| HEMA | 74.3 | 72.9 | **67.2** |
| PVP (K=30) | 14.25 | 19.0 | 26.6 |
| EDMA * | 4.04 | 1.67 | 1.1 |
| MA | 2.40 | 1.43 | 0.1 |
| $H_2O$ | 5 | 5 | 5 |
| HQ or MEHQ | 50 – 100 ppm | 50 – 100 ppm | 50 – 100 ppm |

In all of the preparations of Series A, B, C, E, F and G the first stage initiators were the three mentioned in O'Driscoll U.S. Pat. No. 3,700,761 and the second stage initiator was benzoyl peroxide. This invention is limited to these initiators, e.g. the first stage are: disecondary butyl peroxy dicarbonate, cyclohexanone peroxide and acetyl peroxide. First and second stage initiators are used at a concentration of 0.05 to 0.15 percent by weight of the batch.

## UTILITY OF DIFFERENT COMPOSITION FOR SPECIAL LENS MANUFACTURE

In Table 1, series B and in Table 2, series F represent the best groups for simple corrective hydrated lens which meet 90 percent of the connections in nearsightedness, far sightedness and minor astigmatigmatism (less than 2.0 diopters). As shown in FIGS. **6 – 8** for a minus lens, the lens extends beyond the cornea, the distance beyond the limbus being from about 0.5 – 2.0 mm. and the overall diameter varying from about 13.5 – 15.5 mm. and the inner rim being beveled in a flat curve in a width of 0.30 – 0.70 mm., preferably 0.35 – 0.40 mm. the same rim is used with the plus lens.

Center thicknesses in the minus lens in the dry state vary from 0.30 mm. to about 0.16 mm., depending upon the power. Thinner lenses are more highly corrected and these are made from Series C and G in Tables 1 and 2. Center thicknesses in the plus lenses vary from 0.30 mm. up to 0.45 mm., depending upon the power and the thicker lenses are the highly corrected ones which can be made from Series A, B, E or F compositions in Tables 1 and 2.

Astigmatic lenses with minus correction can be cast ground by the hard lens technology of Feinbloom, U.S. Pat. No. 3,227,507, but the selection of the composition is important since the cylindrical correction may be cast into the inner or bottom surface and a special mold may be made and used with Series G and C in accordance with the elliptical shapes taught in Feinbloom. The result of cutting the outer surface as the lathe as to provide a very thin and fragile center of the prescription ground lens which must have flexibility and rubber-like properties when dry. The strongest thin lenses which can be made are based uppm the more rubbery compositions having a higher PVP content, thus the Series C and Series G compositions would be selected, depending upon whether the patient had a "dry eye" to fit or the normal "wet eye". Manifestly, Series G provides better fitting for the dry eye and Series C provides better fitting for the wet eye.

In production, grinding rates are higher and manufacturing time schedules are more easily met by Series A and E since these Series provide harden buttons (highter EDMA content) and for plus lenses much higher production schedules can be met.

For dispensing of medication, Series E - G are obviously more effective, the higher water content accom-

modating greater total dosages for sparingly soluble eye medicaments.

The water soluble medicaments from O'Driscoll et al, U.S. Pat. No. 3,700,761 can be incorporated in the HEMA by dissolving in $H_2O$ and by adding 5 percent of $H_2O$ to the HEMA; especially useful lenses are made in this manner to provide hydrated lens which contain 60 – 65% $H_2O$, as against 55 – 60% $H_2O$ when the 5% $H_2O$ addition is omitted. With 5 percent added $H_2O$ the lens after hydration is more spongy, and can release medication more efficiently. Uniquely precision reproducibility and predictability, dry to wet, and resistance to storage creep in long time saline storage (two weeks to one year) is achieved only with the narrow range of formulations of the present invention.

The preferred ophthalmologically acceptable medicaments are know and include corticosteroids, sulfonamide, disinfectants, antiseptics, penicillin, pilocarpine, belladonna, dibenzyline, hydergine, methacholine, carbachol, bethanechol and the like.

It should be emphasized that the foregoing examples are the result of thousands of formulations, tested completely in the laboratory, and then on patients under the supervision of qualified ophthalmologists, these results had to be interpreted in the light of a host of parameters and only experience showed the relationship which are summarized above, in conjection with HEMA as the major ingredient. There is not predictability from HEMA to HPMA (hydroxypropyl analogue) and there is no basis for reproducing water uptakes at 50 – 65 percent in hydrated lenses with any other monomer than HEMA. These parameters, in addition to the composition, include the batch size contents of all ingredients as listed; time of mixing, induction period, viscosity changes, heat transfer, presence of convection currents etc.

Although certain preferred emboidments of eye bandage containing medicaments have been described herein above in terms of hard polymer formed by adding up to 5 percent water and subjecting the composition to the stages of induction for 2 ½ – 6 hours, first stage initiation at 40°C and second stage initiation at 110°C for 1 ½ – 4 hours, it is emphasized that changes in manufacture can be made, for example, cutting down the time at 110°C to ½ hour to prevent excessive drug decomposition and to thereby provide drug dispensing solid precisely cut products for any type of known medication which are specifically adapted for topical administration. For example, using the same lathe as in the Mullen Patent a sheath or a tube may be turned for encircling a blood vessel to which a slow-release water soluble drug is administered to reduce blood pressure. A sheath may be encircled about a nerve bundle or about a bone and medication administered to aid in repair and bone growth (calciferol for example). Since hydration occurs in saline, the implant which is at the same osmotic pressure as body tissues and as blood contains, in the same electrolyte environment, a very precisely dosed amount of drug which can be used to produce a degree of precision in dosage not heretofore obtainable. If the drug is used for the eye where a high degree of precision of drug dosage is needed, it may be preferable to set up a fountain solution in saline which drops the saline solution containing the drug onto the lens to deliver the dosage to the eye at a constant rate for a controlled time. Obviously, fountain supplies of this type may be used with other implants.

It is therefore seen that new compositions of the invention create new articles of commerce which are hygroscopic buttons in hard form and are cast from new and disposable molds with break-away bottoms. The buttons can be turned on a lathe to make new shaped products such as implants and contact lenses which are adapted to be hydrated in saline for water uptake of 50 – 65 percent. These disposable molds form hard products whose inner surfaces are free from fissures and cracks and which resist tearing by crack propogation from these fissures.

In the foregoing specification and in the following claims, the abbreviations are as follows:

HEMA — Hydroxyethyl Methacrylate
PVP — Poly-N-Vinyl Pyrrolidone
EDMA — Elthylene Glycol Dimethacrylate
MA — Methacrylic Acid
$H_2O$ — Water
ppm — parts per million
HQ — Hydroquinone
MEHQ — Methyl Ether of Hydroquinone

What is claimed is:

**1.** A shaped ocular implant comprising a composition in dry form for medicament delivery which is subjected to cutting and thereafter hydrating in saline to form an implant having from 50 – 65% $H_2O$, said implant in dry form consisting essentially of polymerized random graft copolymer containing 67.2 to 79.3% HEMA, 14.25 to 28% PVP, 0.1 to f.04% EDMA, 0.1 to 2.5% MA, from about 1.0 up to 5.0% $H_2O$ and from 50 – 100 ppm of hydroquinone stabilizer, the composition having been polymerized with a low temperature initiator and a high temperature initiator each in concentration of 0.05 to 0.15 percent after an induction period at 15° – 30°C for a period of 2.5 to six hours.

**2.** An implant as claimed in claim **1** in the form of an optical bandage containing an ophthalmologically acceptable medicament incorporated in the dry form of the implant.

**3.** An implant as claimed in claim **1** in the form of an optical bandage hydrated to 50 – 65% $H_2O$ in combination with a fountain solution of ophthalmologically acceptable medicament dissolved in saline solution.

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