COLLAGEN SOFT CONTACT LENS

This is a continuation of application Ser. No. 753,556 filed Dec. 22, 1976, now abandoned.

This invention relates to a soft contact lens consisting of colagen and/or chemical modifications of such collagen. The invention also relates to the production of such lenses preferably by irradiation of the collagen substance in a lens mold with gamma rays.

Contact lenses have been known as a commercial product for over 25 years. Contact lenses to date have been made from chemically synthesized materials which do not occur in nature. For example, most early contact lenses were made from polymethylmethacrylate or chemical modifications thereof, from hydroxyethylmethacrylate, from cellulose acetate butyrate, from silicones, etc. To the knowledge of the applicants no lens, prior to this invention, was made from naturally occurring animal materials and especially from materials having physiological and immunological properties possessed by constituents of the eye itself, e.g., the cornea. The state of the art on contact lenses is reviewed in a current article "A Contact Lens Update"--Contact Lens Forum, p. 16–23 (May 1976).

The chemistry, molecular structure and biochemical properties of collagen have been well established. An up-to-date review article by the current inventors (Annual Review of Biophysics and Bioengineering, Vol. 3, p. 231–253, 1974) contains an excellent compilation of references on the subject.

Collagen is a major protein of connective tissue such as skin, cornea, etc., and can be solubilized, separated and purified by the treatment with proteolytic enzymes (other than collagenase), e.g., proctase, pepsin, trypsin and pronase. Enzyme solubilized collagen is telopeptides-poor, relatively inexpensive, and useful as a biomedical material. The collagen is redispersed as a clear aqueous gel up to 30% (the balance being essentially water) and placed in a lens mold (glass, brass, stainless steel, and/or plastic) and gamma-irradiated to polymerize the collagen. A collagen soft contact lens prepared by this method is optically clear, flexible, stable and comfortable to wear.

Collagen has been used by the present inventors in various drug and medical applications, e.g., as a vehicle for drug delivery in opthalmic application; as dialysis membranes; as vitreous implants, and in other medical and surgical applications. Their studies have been published widely in medical journals. The inventors know of no utilizations of collagen described hereunder as a soft contact lens material prior to their own discovery.

The present invention is illustrated in detail in the following description: Calfskin collagen was used as a starting material, but other sources such as steer hide, cowhide and pigskin may also be utilized. Dehaired and cleaned skin is solubilized with a protelytic enzyme (pepsin for example) and solubilized collagen is precipitated at pH 7 after inactivation of enzyme activity by caustic treatment at pH 10. Precipitated solublized collagen is defatted by repeated extractions with ethanol-ethyl ether mixture (1:1). This defatting process is essential to obtain transparent collagen gel for lens production.

Solubilized collagen contains many NH_2 and COOH groups in its structure, and chemical modifications of the molecule can be readily made, e.g., all or some of the amino groups may be acylated by reaction with a mixture of acetic anhydride and acetic acid, or other anhydride such as succinic anhydride. All or some of the carboxyl groups contained in the molecule may be esterified by the standard reaction with acidified alcohol, preferable a water soluble aliphatic alcohol, such as methanol, ethanol, etc. In the above reactions the isoelectric point of collagen can be controlled, either negative or positive, or completely neutralized. Excellent soft contact lenses have been made from succinylated and methylated collagen.

Gels having collagen concentrations ranging from 1% to 30% can be utilized for lens production, but the preferable concentration is 1% to 20% with the balance being water. As the collagen content of the gel increases substantially above about 20%, the material becomes gummy and difficult to handle and work. A collagen soft contact lens of higher water content is more pliable, superior in oxygen diffusion and more comfortable to wear. However, the mechanical strength of the lens is improved with decreasing water content.

Cross-linking of the solubilized transparent collagen is necessary in order to stabilize the molecule. Cross-linking is accomplished by irradiation with gamma or ultraviolet rays or by heating, drying or simple aging. Cross-linking can also be accomplished by treating with certain chemicals such as aldehyde, e.g., formaldahyde, glutaraldahyde or with acids such as chromic acid. The mechanism of cross-linking of collagen is well-known and has been fairly well documented. In the preparation of soft contact lenses in accordance with this invention, the preferred cross-linking method is irradiation in the presence of nitrogen. Nitrogen atmosphere is preferred to air because the presence of nitrogen increases the cross-linking of collagen while maintaining the rate of breakdown of collagen at a low level. Irradiation is preferred to chemical treatment since the irradiation process introduces no potentially toxic foreign material into the collagen gel structure.

The effectiveness of gamma-irradiation is a function of the collagen concentration of the gel and of the atmosphere of the irradiation. For example, the gamma-irradiation in presence of air induces some damage of the collagen molecule concurrent with introduction of cross-linkages. The irradiation in the presence of nitrogen mimimizes the destruction of collagen and enhances gel stabilization by cross-linking. The optimal irradiation dose depends on the collagen concentration. Irradiation of 500~900 K rads at a dose rate of 82 K rads per hour is necessary to introduce enough cross-linkages into 5% collagen gel; however, a dose of 1200~1600 K rads is required for 10% collagen gel in presence of nitrogen.

Chemically modified collagens can be also used as a lens material as well as native collagen (without chemical modification). Since native collagen is soluble in acidic pH, clear gel is obtained only below about pH 4.0. Lens material made from this gel must be neutralized. On the other hand, chemically modified collagen such as succinylated collagen, or methylated collagen is soluble in physiologic condition (pH 6–8); and neutralization of the lens material is not necessary. The effect of gamma-irradiation is similar on native and chemically modified collagens.

Glass, stainless steel, brass and plastics (teflon, polyethylene, polycarbonate) may be used as a lens mold material. Glass and metals are generally preferably to plastics because of the stability against gammairradiation.