

METHODS OF MAKING MEDICAL IMPLANTS OF POLY (VINYL ALCOHOL) HYDROGEL

RELATED APPLICATIONS

[0001] This application is a continuation of U.S. patent application Ser. No. 10/199,554, filed Jul. 19, 2002, which is a divisional of U.S. patent application Ser. No. 09/846,788, filed May 1, 2001, which is a continuation of U.S. patent application Ser. No. 09/271,032, filed Mar. 17, 1999, which issued as U.S. Pat. No. 6,231,605 on May 15, 2001, and which is a CIP of U.S. patent application Ser. No. 08/932,029, filed Sep. 17, 1997, and issued Nov. 9, 1999 as U.S. Pat. No. 5,981,826, which claims priority to U.S. Provisional Application Ser. No. 60/045,875, filed May 5, 1997, the contents of which are hereby incorporated by reference as if recited in full herein.

FIELD OF THE INVENTION

[0002] The present invention relates generally to hydrogel materials. More specifically, the present invention relates to a poly (vinyl alcohol) ("PVA") hydrogel.

DESCRIPTION OF THE PRIOR ART

[0003] Most tissues of the living body include a large weight percentage of water. Therefore, in a selection of a prosthesis, a hydrous polymer (hydrogel) is considered to be superior in biocompatibility as compared to nonhydrous polymers. Although hydrogels do less damage to tissues than nonhydrous polymers, conventional hydrogels have historically included a serious defect in that they are inferior in mechanical strength. For that reason, the use of hydrogels has been extremely limited in the past.

[0004] Artisans have proposed a number of hardening means for improving mechanical strength. Some hardening means include treating the hydrogel with a cross-linking agent such as formaldehyde, ethylaldehyde, glutaraldehyde, terephthalaldehyde or hexamethylenediamine. Unfortunately, however, it is well known that those treatments decrease the biocompatibility of the hydrogel biomaterial. One example of a popular hydrogel which has been proposed for use as a biomaterial is PVA.

[0005] Numerous references generally describe the process of freezing and thawing PVA to create a hydrogel: Chu et al., *Poly(vinyl alcohol) Cryogel: An Ideal Phantom Material for MR Studies of Arterial Elasticity*, *Magnetic Resonance in Medicine*, v. 37, pp. 314-319 (1997); Stauffer et al., *Poly (vinyl alcohol) hydrogels prepared by freezing-thawing cyclic processing*, *Polymer*, v.33, pp. 3932-3936 (1992); Lozinsky et al., *Study of Cryostructurization of polymer systems*, *Colloid & Polymer Science*, v. 264, pp. 19-24 (1986); Watase and Nishinari, *Thermal and rheological properties of poly (vinyl alcohol) hydrogels prepared by repeated cycles of freezing and thawing*, *Makromol. Chem.*, v. 189, pp. 871-880 (1988). The disclosure from these references is hereby incorporated by reference.

[0006] Another such reference is U.S. Pat. No. 4,734,097, issued to Tanabe et al. on Mar. 29, 1988 ("Tanabe"). Tanabe proposes the construct of a molded hydrogel obtained by pouring an aqueous solution containing not less than 6% by weight of a polyvinyl alcohol which has a degree of hydrolysis not less than 97 mole percent and an average polymer-

ization degree of not less than 1,100 into a desired shape of a vessel or mold, freeze molding an aqueous solution in a temperature lower than minus 5° C., then partially dehydrating the resulting molded product without thawing it up to a percentage of dehydration not less than 5 weight percent, and if required, immersing the partially hydrated molded part into water to attain a water content thereof in the range of 45 to 95 weight percent.

[0007] The disadvantage to Tanabe et al. is that it necessarily requires a step of dehydration in preparing the PVA hydrogel. There are several disadvantages associated with the dehydration step. First, the dehydration step adds additional time and capital expense associated with machinery which must accomplish the dehydration step. Additionally, dehydration may denature bioagents included in the hydrogel.

[0008] Hyon et al., U.S. Pat. No. 4,663,358 is directed to producing PVA hydrogels having a high tensile strength and water content. However, this patent is not directed to hydrating the PVA with water alone, but rather uses a mixture of water and an organic solvent such as dimethyl sulfoxide (DMSO). DMSO is recognized as an initiator of carcinogenicity. Residual amounts of organic solvents in the resultant PVA hydrogel render such products undesirable for biomedical applications, particularly where the hydrogel is to be used for long term implants within the body.

[0009] With the foregoing disadvantages of the prior art in mind, it is an object of the present invention to provide a biocompatible PVA hydrogel which includes a mechanical strength range sufficient for a wide variety of applications as biomaterial.

[0010] It is another object of the present invention to provide a method for producing the PVA hydrogel which precisely controls the mechanical strength thereof, and which eliminates any dehydration step prior to implantation.

[0011] Other objects, features and advantages of the present invention will become apparent upon reading the following specification.

SUMMARY OF THE INVENTION

[0012] Generally speaking, the present invention relates to a novel poly(vinyl alcohol) ("PVA") hydrogel tissue replacement construct and a process for making the construct.

[0013] More specifically, the present invention relates to a non-dehydrated PVA hydrogel construct which is capable of being molded into a number of shapes, and which is capable of retaining a wide range of mechanical strengths for various applications.

[0014] The PVA hydrogel may comprise a PVA polymer starting material in the form of a dry powder wherein the degree polymerization of the PVA may range approximately 500 to 3,500. The tissue replacement in accordance with the present invention may include approximately 2 to approximately 40 parts by weight PVA and approximately 98 to 60 parts by weight water. Additionally, the hydrogel may include an isotonic saline solution substitute for water to prevent osmotic imbalances between the tissue replacement and surrounding tissues. The replacement may also include a number of bioactive agents including, but not limited to, heparin, growth factors, collagen crosslinking inhibitors