

BIORESORBABLE COMPOSITIONS FOR IMPLANTABLE PROSTHESES

CROSS-REFERENCE TO RELATED APPLICATION

The present application is a divisional of co-owned U.S. Ser. No. 08/914,130 filed on Aug. 18, 1997 and now U.S. Pat. No. 5,854,382 which is hereby incorporated by reference.

FIELD OF INVENTION

This invention relates generally to coating compositions for medical devices. More particularly, the present invention relates to cross-linked compositions formed from a water insoluble copolymer having a bioresorbable region, a hydrophilic region and at least two cross-linkable functional groups per polymer chain. These compositions when placed in contact with an aqueous environment form hydrogels which are useful as sealants for porous materials and particularly for implantable prostheses. Furthermore, these hydrogels can be used as delivery vehicles for therapeutic agents. Medical devices coated and/or sealed with such hydrogels, processes for forming such devices and methods of making the hydrogels are also disclosed.

BACKGROUND OF THE INVENTION

It is generally known to provide a porous substrate, such as an implantable prosthesis, with a biocompatible, biodegradable sealant or coating composition which initially renders the porous substrate fluid-tight. Over time, such a sealant composition is resorbed and the healing process naturally takes over the sealing function of the sealant composition as tissue ingrowth encapsulates the prosthesis. The art is replete with examples of naturally derived, as well as chemically synthesized sealant compositions.

Natural materials, such as collagen and gelatin, have been widely used on textile grafts. U.S. Pat. Nos. 4,842,575 and 5,034,265 to Hoffman Jr., et al. disclose the use of collagen as a sealant composition for grafts. More recently, co-owned and co-pending U.S. Ser. No. 08/713,801 discloses the use of a hydrogel or sol-gel mixture of polysaccharides for rendering fluid-tight porous implantable devices. Such sealant compositions are beneficial in that they are able to seal an implantable device without the need for chemical modification of the surface thereof and provide improved bioresorbability as the healing process occurs. Furthermore, fibrin, an insoluble protein formed during the blood clotting process, has also been used as a sealant for porous implantable devices.

The use of such biologically derived sealant compositions, however, suffers from several drawbacks. One such drawback is the difficulty in producing consistent coatings due to variations inherent in natural materials. Another drawback is that the body may identify such compositions as foreign and mount an immune response thereto. Thus, biologically-based sealant compositions can cause inflammation, as well as infection at or around the site of implantation, which can lead to life-threatening complications.

Accordingly, attempts have been made to design sealant systems from chemically synthesized materials which are easier to manufacture and control the desired characteristics and qualities and which have less potential for causing adverse biological reactions. For example, U.S. Pat. No. 4,826,945 to Cohn et al. discloses synthetically produced

resorbable block copolymers of poly(α -hydroxy-carboxylic acid)/poly(oxyalkylene) which are used to make absorbable sutures, wound and burn dressings and partially or totally biodegradable vascular grafts. These copolymers, however, are not crosslinked. The poly(alkylene) segments of such bio-absorbable copolymers are disclosed to be water-soluble so that the body can excrete the degraded block copolymer compositions. See also, Younes, H. and Cohn, D., *J. Biomed. Mater. Res.* 21, 1301-1316 (1987) and Cohn, D. and Younes, H., *J. Biomed. Mater. Res.* 22, 993-1009 (1988). As set forth above, these compositions are uncrosslinked and, as a consequence, are relatively quickly bio-absorbed. Moreover, these uncrosslinked compositions generally require the presence of crystalline segments to retain their hydrogel-like consistency. As a result of such crystalline segments, these compositions have limited utility as sealants for vascular grafts.

Furthermore, U.S. Pat. No. 4,438,253 to Casey et al. discloses tri-block copolymers produced from the transesterification of poly(glycolic acid) and an hydroxyl-ended poly(alkylene glycol). Such compositions are disclosed for use as resorbable monofilament sutures. The flexibility of such compositions is controlled by the incorporation of an aromatic orthocarbonate, such as, tetra-p-tolyl orthocarbonate into the copolymer structure. The strength and flexibility which makes such a composition useful as a suture, however, does not necessarily make it appropriate for use as a sealant for a porous implantable prosthesis. Moreover, these tri-block copolymers are substantially uncross-linked. Thus, while compositions are somewhat hydrophilic, they do not form hydrogels.

Accordingly, attempts have been made to engineer biocompatible hydrogel compositions whose integrity can be controlled through crosslinking. For example, U.S. Pat. Nos. 5,410,016 and 5,529,914 to Hubbell et al. disclose water-soluble systems which when crosslinked utilize block copolymers having a water-soluble central block segment sandwiched between two hydrolytically labile extensions. Such copolymers are further end-capped with photopolymerizable acrylate functionalities. When crosslinked, these systems become hydrogels. The water soluble central block of such copolymers can include poly(ethylene glycol); whereas, the hydrolytically labile extensions can be a poly(α -hydroxy acid), such as, polyglycolic acid or polylactic acid. See, Sawhney, A. S., Pathak, C. P., Hubbell, J. A., *Macromolecules* 1993, 26, 581-587.

Furthermore, U.S. Pat. No. 5,202,413 to Spinu discloses biodegradable multi-block copolymers having sequentially ordered blocks of polylactide and/or polyglycolide produced by ring-opening polymerization of lactide and/or glycolide onto either an oligomeric diol or a diamine residue followed by chain extension with a di-functional compound, such as, a diisocyanate, diacylchloride or dichlorosilane. The general structure of such a composition is $R-(A-B-A-L)_x-A-B-A-R$, where A is a polyhydroxy acid, such as polylactide, polyglycolide or a copolymer thereof, B is an oligomeric diol or diamine residue, L is a diacyl residue derived from an aromatic diacyl halide or diisocyanate and R is H or an end-capping group, such as an acyl radical. A major difference between the compositions set forth in the Spinu '413 patent and those described by the Cohn references supra is that Spinu uses lactide blocks whereas Cohn uses lactic acid blocks. Furthermore, like the Cohn copolymers, the copolymers described in the Spinu '413 patent are not crosslinkable.

In general, all of the synthetic compositions set forth above describe copolymers having one or more segments