

65 to 95 percent of its initial viscosity within 7 minutes of shearing at 0.1 sec⁻¹.

The melt temperature of the 2 percent collagen solution as determined by Differential Scanning Calorimetry is about 34° to 37° C.

EXAMPLE 16

Purified Type I collagen (750 ml), prepared according to Example 3, was treated at 4° C. with 10 N NaOH to raise the pH to 5.0. p-Fluorosulfonylbenzenesulfonyl chloride (0.0251 g) and 0.0124 g glutaric anhydride in 7.5 ml of acetone was added all at once to the vigorously agitating collagen solution. The pH was immediately increased to 11.7 and then decreased to 9.2 by addition of 10 N NaOH and 6 N HCl, respectively. The solution was agitated for 15 minutes to produce the coupled collagen product.

The coupled collagen solution was treated at 4° C. with the dropwise addition of glutaric anhydride (0.0642 g) in 7.5 ml of acetone, and the pH was maintained at 9.0±0.25 by addition of 1 N NaOH. After addition was complete the solution was agitated for 10 minutes. The pH was reduced to 4.0 using 6 N HCl, and the solution was agitated for another 10 minutes. The modified collagen precipitate was collected by centrifugation and washed four times with sterile water at a dilution of 10 parts water to 1 part wet precipitate.

A 2 percent by weight solution of the collagen in BSS™ was colorless and transparent as determined by both visual inspection and light/optical microscopy at 40 x.

The collagen solution 2 percent by weight in BSS™ was evaluated as an anterior chamber implant in New Zealand white rabbits using the McDonald-Shadduck system in accordance with the procedure described in Example 1. Such evaluation indicated overall equivalence or superiority of the chemically-modified collagen made according to this example with air, BSS™ and Healon™.

The collagen solution (about 2 percent by weight in BSS™) exhibits the Weissenberg Effect when tested in accordance with the procedure described in Example 1. The collagen solution is pseudoplastic, exhibiting decreasing viscosities at increasing shear rates when tested in accordance with the procedure of Example 1. The collagen solution is thixotropic, recovering about 65 to 95 percent of its initial viscosity within 7 minutes of shearing at 0.1 sec⁻¹.

The melt temperature of the 2 percent collagen solution as determined by Differential Scanning Calorimetry is about 34° to 37° C.

EXAMPLE 17

Purified Type I collagen, as prepared in Example 1, was reconstituted in 300 ml of a 0.1 M acetic acid solution to provide a 0.20 percent wt/wt solution. The collagen solution (300 ml) was chilled to 4° C. and the pH was adjusted to 8.0 with 10 ON NaOH. To the stirring collagen solution was gradually added 5-chlorosulfonyl-o-anisic acid chloride (0.030 g) dissolved in 3 ml acetone, while maintaining the pH at 8.0 by addition of 1 N NaOH. A reaction pH of 8.0 was used in order to reduce the concentration of available free amines thereby controlling the extent of coupling. After 6 minutes of reaction the pH was increased to 13 by addition of 5 N NaOH in order to hydrolyze any remaining coupler and stop the reaction. The pH was maintained

at 13 for 2 minutes and then reduced to 9.0 using 6 N HCl.

A solution containing glutaric anhydride (0.034 g) dissolved in 3 ml acetone was added to the collagen solution all at once. The pH was maintained at 9.0±0.25 by gradual addition of 1 N NaOH for a period of 30 minutes. The pH was then reduced to 4.0 using 6 N HCl to precipitate the chemically-modified collagen product. The precipitate was collected and washed according to the method described in Example 1. The collagen precipitate was dissolved in balance salt solution (BSS™) to provide a 2.0 percent wt/wt solution. The pH was then adjusted to 7.1 using 1 N NaOH.

The collagen solution (2 percent by weight in a phosphate-buffered solution¹⁵) is evaluated as an anterior chamber implant in New Zealand white rabbits using the McDonald-Shadduck system in accordance with the procedure described in Example 1. Such evaluation indicates overall equivalence of the chemically-modified collagen made according to this example with air, BSS™ and Healon™.

¹⁵ The phosphate-buffered solution contained 0.84 percent by weight NaCl, 0.054 percent by weight KCl, 0.017 percent by weight CaCl₂, 0.028 percent by weight Na₂HPO₄, and 0.004 percent by weight NaH₂PO₄.

The collagen solution (about 2 percent by weight in BSS™) exhibits the Weissenberg Effect when tested in accordance with the procedure described in Example 1. The collagen solution is pseudoplastic, exhibiting decreasing viscosities at increasing shear rates when tested in accordance with the procedure of Example 1. The collagen solution is thixotropic, recovering about 65 to 95 percent of its initial viscosity within 7 minutes of shearing at 0.1 sec⁻¹.

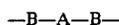
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What is claimed is:

1. A chemically-modified collagen compound which comprises at least two native collagen molecules which are coupled at at least one lysine epsilon amino group present on each said collagen molecule by a coupling group, said coupling group comprising at least two moieties selected from the group consisting of carbonyl and sulfonyl groups.

2. The chemically-modified collagen compound of claim 1 wherein said carbonyl and/or sulfonyl groups present in said coupling group are linked to each other through saturated or unsaturated alkylene, arylene or mixed alkylene-arylene coupling chains having less than about twenty carbon atoms, wherein said alkylene and/or arylene coupling chains may also contain heteroatoms selected from the group consisting of oxygen, sulfur and nitrogen, and may be substituted in available aromatic positions by carboxyl groups, straight or branched chain alkyl groups of about 1 to 4 carbon atoms, straight or branched chain alkoxy groups of about 1 to 4 carbon atoms, halogens and other non-reactive moieties, and in available aliphatic positions by carboxyl groups and alkyl or alkoxy groups of about 1 to 4 carbon atoms.

3. The chemically-modified collagen compound of claim 1 wherein said coupling group has the general formula:



wherein