

[54] VISCOELASTIC COLLAGEN SOLUTION FOR OPHTHALMIC USE AND METHOD OF PREPARATION

85/04413 10/1985 PCT Int'l Appl. .

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OTHER PUBLICATIONS

Kawakami "Operation for Aftercataract with the Injection of Collagen Gel into the Anterior Chamber", *Excerpta Medica International Congress Series*, Netherlands 2/450 (1975), 1432-1434.

[73] Assignee: Minnesota Mining and Manufacturing Company, St. Paul, Minn.

Rubin et al, "Collagen as a Vehicle for Drug Delivery" Preliminary Report, *Journal of Clin. Pharm.*, Aug.-Sep. 1973, pp. 309-312.

[\*] Notice: The portion of the term of this patent subsequent to Dec. 15, 2004 has been disclaimed.

Rubin et al, "Collagen: Medical and Surgical Applications", *J. of Macro, Science Chemistry*, A 3(1) (Jan. 1969), pp. 113-118.

[21] Appl. No.: 104,777

Chuapil et al, "Medical and Surgical Applications of Collagen", *International Rev. of Conn. Tis. Res.* 6(1973), pp. 1-16.

[22] Filed: Oct. 5, 1987

Stenzel et al, "Collagen Gels: Design for a Vitreous Replacement", *Science*, 164 (Jun. 13, 1969), pp. 1282-1283.

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 890,847, Aug. 6, 1986, Pat. No. 4,713,446, which is a continuation-in-part of Ser. No. 773,310, Sep. 6, 1985, abandoned.

Dunn et al, "Collagen-Derived Membrane: Corneal Implantation", *Science*, 157 (1967) pp. 1329-1330.

[51] Int. Cl.<sup>4</sup> ..... A61K 31/78; A61B 17/00

Balazs et al, "Replacement of the Vitreous with Hyaluronic Acid, Collagen and Other Polymers," *Advances in Vitreous Surgery*, ed., by Irvine et al, Springfield, IN, pp. 601-623.

[52] U.S. Cl. .... 530/356; 128/DIG. 8; 514/2; 514/801; 514/912; 523/113; 604/51

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[58] Field of Search ..... 530/356, 353, 402; 128/DIG. 8; 604/51; 514/21, 801, 912; 523/113; 3/1

References Cited

[57] ABSTRACT

U.S. PATENT DOCUMENTS

Chemically-modified collagen is prepared by reacting native collagen with a di or tri-carboxylic acid halide, di or tri-sulfonyl halide, di or tri-anhydride, or di or tri-reactive active ester coupling agent. The reaction is done in a controlled manner so that the degree of cross-linking is limited. Any remaining lysine epsilon amino groups present in the coupled collagen product may be converted to carboxyamido or sulfonamido groups by acid halide, anhydride, sulfonyl halide or active ester amine-modifying agents. The resultant product when dissolved in a physiological buffer provides a viscoelastic solution having therapeutic application in a variety of surgical procedures, particularly in ophthalmic surgery. This viscoelastic solution "melts," i.e., exhibits a dramatic loss of viscosity, when subjected to temperatures of between 32° and 48° C.

[56]			
	2,127,841	8/1939	Gellendien ..... 530/353
	3,949,073	4/1976	Daniels et al. .... 424/177
	4,141,973	2/1979	Balazs ..... 424/110
	4,164,559	8/1979	Miyata et al. .... 424/14
	4,260,228	4/1981	Miyata ..... 351/160
	4,264,155	4/1981	Miyata ..... 351/160
	4,264,493	4/1981	Battista ..... 530/356
	4,328,803	5/1982	Pape ..... 128/276
	4,382,081	5/1983	Sundeen et al. .... 424/177
	4,404,033	9/1983	Steffan ..... 106/161
	4,409,332	10/1983	Jeffries et al. .... 435/188
	4,424,208	1/1984	Wallace et al. .... 424/177
	4,532,267	7/1985	Allan ..... 523/106
	4,540,568	9/1985	Trager et al. .... 424/81
	4,559,304	12/1985	Kasai et al. .... 435/240

FOREIGN PATENT DOCUMENTS

0183136	6/1986	European Pat. Off. .
57-48028	3/1982	Japan .

12 Claims, No Drawings