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United States Patent [19]

Rhee et al.

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[54] **COLLAGEN-SYNTHETIC POLYMER
MATRICES PREPARED USING A MULTIPLE
STEP REACTION**

4,725,671	2/1988	Chu et al.	530/356
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FOREIGN PATENT DOCUMENTS

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[21] Appl. No.: **236,769**

[57] **ABSTRACT**

[22] Filed: **May 2, 1994**

Related U.S. Application Data

[60] Continuation-in-part of Ser. No. 198,128, Feb. 17, 1994, which is a division of Ser. No. 922,541, Jul. 30, 1992, Pat. No. 5,328,955, which is a continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

The present invention discloses collagen-synthetic polymer matrices which are prepared using a multiple step reaction. The first step of the reaction generally involves reacting collagen with a functionally activated synthetic hydrophilic polymer to form a collagen-synthetic polymer matrix. The synthetic hydrophilic polymer may be mono- or multifunctionally activated, but is preferably difunctionally activated, resulting in the formation of a crosslinked collagen matrix. The second step comprises modifying the collagen-synthetic polymer matrix according to one or more of the following methods: further crosslinking the matrix using a multifunctionally activated synthetic polymer, conjugating the matrix using a monofunctionally activated synthetic polymer, coupling biologically active molecules or glycosaminoglycans to the matrix, crosslinking the matrix using conventional chemical crosslinking agents, or modifying the collagen in the matrix by means of various chemical reactions. An optional third step may include further modification of the collagen-synthetic polymer matrix by covalently binding, for example, biologically active molecules or glycosaminoglycans to the matrix by means of available active groups on the synthetic hydrophilic polymers. Collagen-synthetic polymer matrices prepared according to the methods of the present invention have very low immunogenicity and can therefore be used to prepare biocompatible implants for use in a variety of medical applications.

[51] **Int. Cl.⁶** **C08G 63/48; C08G 63/91**

[52] **U.S. Cl.** **525/54.1; 525/54.2; 525/54.21; 525/54.22; 525/54.23; 525/54.24; 523/113; 530/356**

[58] **Field of Search** **525/54.1, 54.2, 525/54.21, 54.22, 54.23, 54.24; 523/113; 530/356, 840**

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26 Claims, 7 Drawing Sheets