US005573934A

United States Patent [19]

Hubbell et al.

[11] **Patent Number: 5,573,934**

[45] **Date of Patent: Nov. 12, 1996**

[54] **GELS FOR ENCAPSULATION OF BIOLOGICAL MATERIALS**

[75] Inventors: **Jeffrey A. Hubbell**, Austin, Tex.; **Chandrashekhar P. Pathak**, Waltham; **Amarpreet S. Sawhney**, Newton, both of Mass.; **Neil P. Desai**, Los Angeles, Calif.; **Jennifer L. Hill-West**; **Syed F. A. Hossainy**, both of Austin, Tex.

[73] Assignee: **Board of Regents, The University of Texas System**, Austin, Tex.

[21] Appl. No.: **24,657**

[22] Filed: **Mar. 1, 1993**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 958,870, Oct. 7, 1992, Pat. No. 5,529,914, which is a continuation-in-part of Ser. No. 870,540, Apr. 20, 1992, abandoned.

[51] **Int. Cl.**[6] **C12N 11/02**; C12N 11/04; C12N 5/06; C12N 11/08; C08J 7/04; C08J 7/16; A61K 47/32

[52] **U.S. Cl.** **435/177**; 264/4; 264/4.1; 264/4.3; 424/93.7; 424/450; 424/451; 424/459; 424/460; 424/461; 424/462; 424/463; 424/477; 424/479; 424/487; 424/488; 424/489; 424/499; 427/2.14; 427/2.21; 427/213.3; 427/213.32; 427/213.34; 427/213.36; 428/402.22; 428/402.24; 435/182; 435/240.2; 435/240.22; 514/2

[58] **Field of Search** 427/213.35, 213.3, 427/213.32, 2.14, 2.21; 424/487, 488, 499, 489, 450, 451, 459–463, 477, 479, 93; 435/177, 180, 240.2, 240.22; 264/4, 4.1, 4.3; 514/2; 428/402.22, 402.24

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,295,762	10/1981	Slovinsky .	
4,298,002	11/1981	Ronel et al. .	
4,321,117	3/1982	Kaetsu et al. .	
4,329,332	3/1982	Couvreur et al. .	
4,359,483	11/1982	Kaetsu et al. .	
4,376,059	3/1983	Davis et al. .	
4,411,754	10/1983	Kaetsu et al. .	
4,434,150	2/1984	Azad et al. .	
4,450,150	5/1984	Sidman .	
4,511,478	4/1985	Nowinski et al. .	
4,526,938	7/1985	Churchill et al. .	
4,563,489	1/1986	Urist .	
4,590,068	5/1986	Berthet .	
4,605,622	8/1986	Hasegawa et al. .	
4,637,931	1/1987	Schmitz .	
4,647,536	3/1987	Mosbach et al. .	
4,652,443	3/1987	Yoshida et al. .	
4,745,160	5/1988	Churchill et al. .	
4,774,178	9/1988	Egerer et al. .	
4,804,691	2/1989	English et al. .	
4,822,535	4/1989	Ekman et al. .	
4,826,945	5/1989	Cohn et al. .	
4,888,413	12/1989	Domb .	
4,889,722	12/1989	Sheffield et al. .	
4,913,903	4/1990	Sudmann et al. .	
4,916,193	4/1990	Tang et al. .	
4,925,677	5/1990	Feijen .	
4,931,279	6/1990	Bawa et al. .	
4,938,763	7/1990	Dunn et al. .	
4,942,035	7/1990	Churchill et al. .	
4,950,596	8/1990	Cheng et al. .	
4,957,744	9/1990	della Valle et al. .	
5,037,656	8/1991	Pitt .	
5,149,543	9/1992	Cohen et al. .	
5,153,002	10/1992	McMullen .	
5,160,745	11/1992	Deluca et al.	424/499
5,183,690	2/1993	Carr et al. .	
5,185,408	2/1993	Tang et al. .	
5,219,564	6/1993	Zalipsky et al. .	
5,268,182	12/1993	Brinker et al. .	
5,271,961	12/1993	Mathiowitz et al. .	
5,278,201	1/1994	Dunn et al. .	
5,278,202	1/1994	Dunn et al. .	
5,286,495	2/1994	Batich et al. .	
5,288,500	2/1994	Ibsen .	
5,334,640	8/1994	Desai et al.	435/178

FOREIGN PATENT DOCUMENTS

0195304	9/1986	European Pat. Off. .
WO93/21266	4/1992	WIPO .
WO91/10425	7/1992	WIPO .
WO93/09176	5/1993	WIPO .
WO93/17669	9/1993	WIPO .

OTHER PUBLICATIONS

Buck, "Cell Surface Receptors for Extracellular Matrix Molecules," *Ann. Rev. Cell Bio.* 3:179–205 (1987).

Chesneau and Fouassier, "Polymerization induito sous Irradiation Lager Visible," J. Bio. Ang. Chemie. 135:41–64 (1985).

Chiang, W–Y, and Chan, S–C, "Preparation and Properties of UV–Autocurable BTDA–Based Polyester Multiacrylates, I. Effects of Acrylic Functionality and Polyol Molecular Weight," *J. App. Pol. Sci.,* 41:2971–2985 (1990).

Cohn and Younes, "Biodegradable PEO/PLA block copolymer," *J. Biomed. Materials Research,* 22:993–1009 (1988).

Coleman, et al., "Blood–materials interactions: the Minimum Interfacial free energy and the optimum polar/apolar ratio hypothesis", *J. Biomed. Materials Res.,* 16:381–398 (1982).

(List continued on next page.)

Primary Examiner—Herbert J. Lilling
Attorney, Agent, or Firm—Arnall Golden & Gregory

[57] **ABSTRACT**

Water soluble macromers are modified by addition of free radical polymerizable groups, such as those containing a carbon-carbon double or triple bond, which can be polymerized under mild conditions to encapsulate tissues, cells, or biologically active materials. The polymeric materials are particularly useful as tissue adhesives, coatings for tissue lumens including blood vessels, coatings for cells such as islets of Langerhans, coatings, plugs, supports or substrates for contact with biological materials such as the body, and as drug delivery devices for biologically active molecules.

16 Claims, 14 Drawing Sheets