United States Patent [19]

Bucci et al.

[11] **Patent Number: 4,584,130**

[45] **Date of Patent: Apr. 22, 1986**

[54] **INTRAMOLECULARLY CROSS-LINKED HEMOGLOBIN AND METHOD OF PREPARATION**

[75] Inventors: **Enrico Bucci; Clara Fronticelli-Bucci,** both of Baltimore; **Ramachandra Hosmane,** Columbia, all of Md.

[73] Assignee: **University of Maryland,** Baltimore, Md.

[21] Appl. No.: **717,783**

[22] Filed: **Mar. 29, 1985**

[51] **Int. Cl.**[4] **C07C 103/52;** A61K 35/18; A61K 37/02; C07K 13/00

[52] **U.S. Cl.** ..... **260/112 B;** 260/112.5 R; 260/115; 424/101; 514/6

[58] **Field of Search** ..... 260/112 B, 112.5 R, 260/115; 424/101; 514/6

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,925,344	12/1975	Mazur	260/112.5 R
4,001,200	1/1977	Bonsen et al.	260/112 B X
4,001,401	1/1977	Bonsen et al.	424/101 X
4,053,590	10/1977	Bonsen et al.	260/112 B X
4,061,736	12/1977	Morris et al.	260/112 B X
4,064,118	12/1977	Wong	260/112.5 R
4,136,093	1/1979	Bonhard et al.	260/112.5 R
4,320,111	3/1982	Hirsch et al.	260/112 B X
4,401,652	8/1983	Simmonds et al.	260/112 B X
4,473,496	9/1984	Scannon	260/112 B
4,529,719	7/1985	Tye	260/112 B X

OTHER PUBLICATIONS

Biochemistry, 11, No. 19, 3576–3582 (1972), Benesch et al.

Biochemical & Biophysical Res. Communic. 63, No. 4 (1975), 1123–1130, Benesch et al.

Fed. Proc. 34, No. 6, (1975), 1458–1460, Mok et al.

J. Biol. Chem., 254, No. 3 (1979), 702–707, McDonald et al.

J. Biol. Chem., 258, No. 19, (1983), 11890–11895, Didonato et al.

Primary Examiner—Howard E. Schain

Attorney, Agent, or Firm—Sughrue, Mion, Zinn, Macpeak & Seas

[57] **ABSTRACT**

Stroma-free hemoglobin cross-linked with reagents that mimic 2,3 diphosphoglycerate and transform stroma-free hemoglobin into a physiologically competent oxygen carrier which is retained in vivo for adequate periods of time and thus can be used in fluids for transporting oxygen; reagents for cross-linking stroma-free hemoglobin and method for cross-linking stroma-free hemoglobin.

42 Claims, No Drawings