



US009241979B2

(12) **United States Patent**
Winslow et al.

(10) **Patent No.:** **US 9,241,979 B2**
(45) **Date of Patent:** ***Jan. 26, 2016**

(54) **COMPOSITIONS FOR OXYGEN TRANSPORT COMPRISING A HIGH OXYGEN AFFINITY MODIFIED HEMOGLOBIN**

(71) Applicants: **Nancy Jo Winslow**, La Jolla, CA (US)
Sangart, Inc., San Diego, CA (US)

(72) Inventors: **Robert M. Winslow**, La Jolla, CA (US);
Kim D. Vandegriff, San Diego, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **13/923,617**

(22) Filed: **Jun. 21, 2013**

(65) **Prior Publication Data**

US 2013/0288949 A1 Oct. 31, 2013

Related U.S. Application Data

(63) Continuation of application No. 13/714,853, filed on Dec. 14, 2012, now abandoned, which is a continuation of application No. 13/180,291, filed on Jul. 11, 2011, now Pat. No. 8,377,868, which is a continuation of application No. 12/625,900, filed on Nov. 25, 2009, now Pat. No. 7,989,414, which is a continuation of application No. 11/717,364, filed on Mar. 13, 2007, now Pat. No. 7,625,862, which is a continuation of application No. 11/088,934, filed on Mar. 23, 2005, now abandoned, which is a continuation of application No. 10/925,067, filed on Aug. 24, 2004, now Pat. No. 6,974,795, which is a continuation of application No. 10/340,141, filed on Jan. 10, 2003, now Pat. No. 6,844,317, which is a continuation-in-part of application No. 10/114,400, filed on Apr. 1, 2002, now abandoned.

(60) Provisional application No. 60/347,741, filed on Jan. 11, 2002.

(51) **Int. Cl.**
A61K 38/00 (2006.01)
A61K 38/42 (2006.01)

(52) **U.S. Cl.**
CPC **A61K 38/42** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,518,982 A 7/1970 Timmins et al.
3,925,344 A 12/1975 Mazur
3,956,259 A 5/1976 Garcia et al.
4,001,200 A 1/1977 Bensen et al.
4,001,401 A 1/1977 Bensen et al.
4,053,590 A 10/1977 Bensen et al.
4,061,736 A 12/1977 Morris et al.

4,064,118 A 12/1977 Wong
4,113,853 A 9/1978 Funakoshi et al.
4,133,874 A 1/1979 Miller et al.
4,179,337 A 12/1979 Davis et al.
4,209,300 A 6/1980 Thibault
4,301,144 A 11/1981 Iwashita et al.
4,336,248 A 6/1982 Bonhard et al.
4,377,512 A 3/1983 Ajisaka et al.
4,401,652 A 8/1983 Simmonds et al.
4,412,989 A 11/1983 Iwashita et al.
4,439,357 A 3/1984 Bonard et al.
4,473,494 A 9/1984 Tye
4,473,496 A 9/1984 Scannon
4,526,715 A 7/1985 Kothe et al.
4,529,719 A 7/1985 Tye
4,532,130 A 7/1985 Djordjevich et al.
4,584,130 A 4/1986 Bucci et al.
4,598,064 A 7/1986 Walder
4,600,531 A 7/1986 Walder
4,650,786 A 3/1987 Wong
4,670,417 A 6/1987 Iwasaki et al.
4,710,488 A 12/1987 Wong
4,738,952 A 4/1988 Ecanow et al.
4,777,244 A 10/1988 Bonhard et al.
4,826,811 A 5/1989 Sehgal et al.
4,831,012 A 5/1989 Estep
4,857,636 A 8/1989 Hsia
4,861,867 A 8/1989 Estep
4,900,780 A 2/1990 Cerny
4,911,929 A 3/1990 Farmer et al.
4,920,194 A 4/1990 Feller et al.
4,987,154 A 1/1991 Long, Jr.

(Continued)

FOREIGN PATENT DOCUMENTS

DE 24 30 898 A1 8/1976
EP 0 340 908 A2 11/1989

(Continued)

OTHER PUBLICATIONS

Tsai, A. G., et al., "Local Tissue Oxygenation by Statistically Distributed Sources," *Microvascular Research*, Sep. 1992, pp. 200-213, vol. 44, No. 2.

Tsai, A. G., et al., "Microcirculatory Consequences of Blood Substitution with AlphaAlpha-Hemoglobin," *Blood Substitutes, Physiological Basis of Efficacy*, 1995, pp. 155-174.

Vandegriff, K. D., et al., "Hemoglobin-Oxygen Equilibrium Binding: Rapid-Scanning Spectrophotometry and Singular Value Decomposition," *Methods in Enzymology*, 1994, pp. 460-485, vol. 232.

Vandegriff, K. D., et al., "Stability and Toxicity of Hemoglobin Solutions," Chapter 8, *Blood Substitutes: Physiological Basis of Efficacy*, 1995, pp. 105-131.

Vandegriff, K. D., et al., "Colloid Osmotic Properties of Modified Hemoglobins: Chemically Cross-Linked Versus Polyethylene Glycol Surface-Conjugated," *Biophysical Chemistry*, Nov. 1997, pp. 23-30, vol. 69, No. 1.

(Continued)

Primary Examiner — Maury Audet

(74) *Attorney, Agent, or Firm* — Senniger Powers LLP

(57) **ABSTRACT**

The present invention relates to blood products, and more particularly to compositions comprising a modified oxygenated hemoglobin having a high affinity for oxygen and methods for making such compositions. Such compositions according to the present invention have better stability to auto oxidation and superior oxygen carrying characteristics.

30 Claims, 10 Drawing Sheets