US005641814A

United States Patent [19]

Martin

[11] **Patent Number: 5,641,814**

[45] **Date of Patent: Jun. 24, 1997**

[54] **ANTIKERATOLYTIC-WOUND HEALING COMPOSITIONS AND METHODS FOR PREPARING AND USING SAME**

[75] Inventor: **Alain Martin**, Ringoes, N.J.

[73] Assignee: **Warner-Lambert Company**, Morris Plains, N.J.

[21] Appl. No.: **445,808**

[22] Filed: **May 22, 1995**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 268,772, Jun. 30, 1994, abandoned, which is a continuation of Ser. No. 53,922, Apr. 26, 1993, abandoned, which is a continuation-in-part of Ser. No. 663,500, Mar. 1, 1991, abandoned.

[51] **Int. Cl.**[6] **A61K 31/045**; A61K 31/07; A61K 31/355

[52] **U.S. Cl.** **514/724**; 514/725; 514/458

[58] **Field of Search** 514/724, 725, 514/458

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,887,702	6/1975	Baldwin	424/61
3,920,835	11/1975	Van Scott et al.	424/311
3,984,566	10/1976	Van Scott et al.	424/283
3,988,470	10/1976	Van Scott et al.	424/283
4,105,783	8/1978	Yu et al.	424/283
4,158,057	6/1979	Stanko	424/252
4,170,821	10/1979	Booth	30/41
4,197,316	4/1980	Yu et al.	424/317
4,234,599	11/1980	Van Scott et al.	424/279
4,246,261	1/1981	Van Scott et al.	424/240
4,284,630	8/1981	Yu et al.	424/241
4,294,852	10/1981	Wildnauer et al.	424/317
4,307,717	12/1981	Hymes et al.	128/156
4,351,835	9/1982	Stanko	424/252
4,363,815	12/1982	Yu et al.	424/274
4,415,576	11/1983	Stanko	424/252
4,416,982	11/1983	Tsuda et al.	435/11
4,451,482	5/1984	Cagen	424/284
4,454,159	6/1984	Musher	424/258
4,496,536	1/1985	Moller	424/70
4,521,375	6/1985	Houlsby	422/29
4,533,637	8/1985	Yamane	435/240
4,548,937	10/1985	Stanko	514/251
4,615,697	10/1986	Robinson	604/890
4,645,764	2/1987	Stanko	514/251
4,663,166	5/1987	Veech	424/146
4,696,917	9/1987	Lindstrom et al.	514/54
4,725,586	2/1988	Lindstrom et al.	514/54
4,734,276	3/1988	Ziegler	424/10
4,812,479	3/1989	Stanko	514/557
4,847,069	7/1989	Bissett et al.	424/47
4,847,071	7/1989	Bissett et al.	424/59
4,847,072	7/1989	Bissett et al.	424/59
4,874,603	10/1989	Fratzer	424/10
5,084,482	1/1992	Hirsch et al.	514/562
5,296,307	3/1994	Martin et al.	435/252.1

FOREIGN PATENT DOCUMENTS

0348627A1	4/1989	European Pat. Off. .
0345082A	6/1989	European Pat. Off. .
0347056A1	12/1989	European Pat. Off. .
0410696A1	7/1990	European Pat. Off. .
3719097C1	6/1988	Germany .
51-032738	3/1976	Japan .
2009017	11/1978	United Kingdom .
2196348	9/1987	United Kingdom .

OTHER PUBLICATIONS

Giannelli, S. Jr., et al. (May 1976). Prevention of increased hemoglobin–oxygen affinity in open–heart operations with inosine–phosphate–pyruvate solution. *Annals of Thoracic Surgery,* vol. 21, No. 5, pp. 386–693.

Freese, E., et al. (1971). *Molecular mechanisms of mutations.* In *Chemical Mutations* (A. Hollander, ed.), Plenum Press, New York–London, pp. 46–48.

Marchek, A. C., et al. (Jun. 1977) Increased in vitro growth capacity of tracheal epithelium exposed in vivo to 7, 12 dimethylbenz(a)anthracene. *Cancer Research,* vol. 37, pp. 1811–1921.

Schwartz, C., et al. (May 7, 1979). Antagonism of cyanide intoxication with sodium pyruvate. *Toxicology and Applied Pharmacology,* vol. 50, pp. 437–441.

Ahmed, A. M., et al. (1979). Effects of ascorbic acid and various keto–acids on the glyoxalase enzyme system in mouse and rat liver. *IRCS Medical Science,* vol. 7, pp. 505.

Mochizuki, S., et al. (1980). Energy metabolism during reperfusion following ischemia. *J. Physiol., Paris,* vol. 76, pp. 805–812.

Cohen, M. H., (Spring, 1981). Cure of advanced L1210 leukemia after correction of abnormal red blood cell deformability. *Cancer Chemother. Pharmacol.,* vol.. 5, pp. 175–179.

Regitz, V., et al. (1981). Biochemical mechanism of infarct size reduction by pyruvate. *Cardiovascular Res.* vol. 15, pp. 652–658.

Wolters, M., et al. (1982). The effect of x irradiation on survival of mammalian cells substituted by poly unsaturated fatty–acids. *Radiat. Res.,* vol. 92 (3), pp. 474–482.

Puschmann, V. M. (1983). Animal experimental examinations of the gastric mucosa and demonstration of the analgetic and antipyretic effect after combined application of acetylsalicylic acid and sodium pyruvate. *Arzneim–Forsch/Drug Res.,* vol. 33 (I), nr. 3, pp. 410–415.

(List continued on next page.)

Primary Examiner—Theodore J. Criares
Attorney, Agent, or Firm—Jean B. Barish

[57] **ABSTRACT**

This invention pertains to therapeutic antikeratolytic-wound healing compositions. The compositions comprise a therapeutically effective amount of an antikeratolytic agent and a wound healing composition. In one embodiment the wound healing composition comprises (a) pyruvate; (b) an antioxidant; and (c) a mixture of saturated and unsaturated fatty acids. The therapeutic antikeratolytic-wound healing compositions may be utilized in a wide variety of topical and ingestible pharmaceutical products. This invention also relates to methods for preparing and using the therapeutic antikeratolytic-wound healing compositions and the pharmaceutical products in which the compositions may be used.

20 Claims, 11 Drawing Sheets