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(54) **N-ACYL AMINO ACID DERIVATIVES FOR TREATING SKIN CONDITIONS SUCH AS CELLULITE**

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JP	08-337515	12/1996
JP	2005-194252	7/2005
JP	2006183039	* 7/2006
JP	2007-153845	6/2007
JP	2007-314464 A	12/2007
RU	2245358 C2	1/2005
WO	90/14429 A1	11/1990
WO	2004/069240 A2	8/2004
WO	2006/029818 A2	3/2006
WO	WO2006029818	* 3/2006
WO	2006/082978 A1	8/2006

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(58) **Field of Classification Search**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,510,531 A 4/1996 Higuchi et al.
2003/0018081 A1 1/2003 Piomelli et al.
2005/0019372 A1 1/2005 Corkey et al.

FOREIGN PATENT DOCUMENTS

EP 0500332 A2 8/1992
EP 1938789 * 7/2008
JP H02-268145 A 11/1990

OTHER PUBLICATIONS

Kono, Mitsuyoshi et al. JP2006183039. Jul. 2006. Machine Translation.*
Caruso et al. (Journal of Plastic, Reconstructive & Aesthetic Surgery (2008) 61, 1321-1324).*
Thomas et al. EP1938789. Jul. 2008.*
Patani et al. (Chemical Reviews, 1996, vol. 96, No. 8).*
Enzo Emanuele, M.D. (Cellulite: Advances in treatment: Facts and controversies. Clinics in Dermatology (2013) 31, 725-730).*
See Lueberding et al. Cellulite: An Evidence-Based Review. Am J Clin Dermatol (2015) 16:243-256.*
Notification of Transmittal of the International Search Report and The Written Opinion of the International Searching Authority, or the Declaration, dated Aug. 24, 2011, 16 pages.
Article from Nutrition & Metabolism, Biomed Central; by Guo Wen et al., entitled "Modulation of Adipocyte Lipogenesis by Octanoate: Involvement of Reactive Oxygen Species"; vol. 3, No. 1, Jul. 27, 2006; 8 pages.
Article from Tetrahedron Letters, by Jin Zhuang et al., entitled "Copper Mediated Oxidation of Amides to Imides by Selectfluor"; vol. 52, No. 16, Apr. 20, 2011, pp. 1956-1959.
Fujimoto, Y., et al., 2006. Long Chain fatty acids induce lipid droplet formation in a cultured human hepatocyte in a manner dependent of acyl-CoA synthesis. Biol. Pharm. Bull. 29 (11) 2174-2180.
Guo, W., et al., 2006. Modulation of adipogenesis by octanoate: involvement of reactive oxygen species. Nutrition & Metabolism 3(30) 1-8.
Han, J., et al., 2002. Octanoate attenuates adipogenesis in 3T3-preadipocytes. J. Nutr. 132:904-910.
pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=4728815.
pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=37555064.
pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?sid=75064649.
New Zealand Examination Report dated Dec. 11, 2013, relating to New Zealand Application No. 605804.
Kawase, Tokuzo et al., "A Novel Synthesis of N-Alkoxy carbonyl Amino Acids and Surfactant Properties of Their Sodium Salts," Journal of Oleo Science, 59, (4) 191-201 (2010).

(Continued)

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(57) **ABSTRACT**

The invention relates to small molecules having biological and therapeutic activity. Particularly, the invention relates to small molecules having lipolytic and anti-adipogenic activity. Two examples of such molecules are 4-methyl-2-(octanoylamino) pentanoic acid and N-isopentyl octanamide. The invention further relates to methods of preventing or treating skin conditions such as cellulite using small molecules having lipolytic and anti-adipogenic activity.

20 Claims, 6 Drawing Sheets