

Claim Substantiation for L-Lactic Acid (Ingredient in Theraderm Fruit Acid Exfoliant)

Academic Journals/Articles, Plastic Surgeons and Dermatologist Reports:

1. L-lactic acid in Theraderm Fruit Acid, used twice daily, has shown reproducible, consistent reaction effects and results as compared from physician to physician. The formulation has consistently been an effective concentration and at a low pH. It has been used by several *hundreds of thousands* of patients around the world for over 20 years. This low pH would seem to cause it to be harsh and irritating, but in reality the pH of a regular Coca-Cola is about the same. PH refers to the ability of an acid to dissociate into free, active, dissociated lactate (-) and hydrogen (+) ions for maximum loosening of skin surface cells allowing natural shedding without irritation.

Melvin Elson, MD, a Nashville dermatologist, stated 20 years ago that "**Glycolic acid performs inconsistently based on many formulation factors including acid percentage, neutralization technique, and length and frequency of application.**" (*Effective peeling agents in the Plastic Surgeon's Practice, June 1994, Plastic Surgery Products-Article*)

2. Lactate is a crucial metabolite in the two principal energy (ATP)-producing processes that power life: glycolysis and oxidative phosphorylation (OxPhos). Glycolysis in the mitochondria of cells converts glucose into two molecules of pyruvate with the concomitant generation of 2 ATP molecules of stored energy. Pyruvate is the molecule that links these two reactions. Because the rate of glycolysis can increase two to three orders of magnitude faster than OxPhos, glycolysis can briefly provide far more ATP. Excess pyruvate will rapidly accumulate and is diverted to lactate in order for glycolysis to proceed.

During recovery, lactate is converted into pyruvate. In both directions this is catalyzed by the ubiquitous enzyme lactate dehydrogenase (LDH). Thus, when rapidly large amounts of energy are required, such as under circumstances of cellular stress, lactate serves as a critical buffer that allows glycolysis to accelerate. (*Ann Intensive Care. 2013; 3:12. Published online May 10, 2013. Doi:10.1186/2110-5820-3-12, Clinical use of lactate monitoring in critically ill patients, Jan Bakker, Maarten WN, Nijsten Tim, C Jansen.*)

3. The topical application of alpha hydroxy acids modulates the secretion of cytokines by Keratinocyte Cells. Regulation of KC-derived growth factors and cytokines by AHAs might represent a mechanism contributing to their therapeutic effects in disorders such as photoaging. (*Topically applied lactic acid increases spontaneous secretion of vascular endothelial growth factor by human reconstructed epidermis (M. Rend11, C. Mayerl, W. Weninger, E. Tschachler, British Journal of Dermatology Volume 145, Issue 1, pages 3-9, July 2001)*)
4. L-Lactic acid is a "left-handed" molecule. All human amino acids (thus all proteins in the body) are left-handed. Glycolic acid does not exist in a left or right handed isomer. Therefore it cannot react in normal body metabolism reactions and must be excreted as a crystal by the kidney. (*On Lactic Acid, Mike Bollman, Plastic Surgery Products, April 1994.*)
5. L-Lactic acid is manufactured commercially by the natural process of fermentation of molasses. Glycolic acid is actually manufactured by bubbling carbon monoxide through *formaldehyde*. (*Cosmetic Dermatology, volume 6, No. 7, July 1993*)
6. Lactic acid salts, most notably sodium lactate, have been hypothesized to be part of the skin's own natural moisturizing system. (*Middleton, JD, Sodium lactate as a Moisturizer, Cosmetic Toiletries 1978; 93:85-86*)

7. **Low concentration of L-lactic acid (10%) increased exfoliation. and this increased cell shedding triggers a faster replacement rate. This results in cosmetically improved and younger looking skin.** (Smith, WP, *Epidermal and Dermal Effects of Topical Lactic Acid* (J Am Acad Dermatol 1996; 35:388-91)
8. **High L -Lactate concentrations constitute highly specific metabolic signals that activate macrophages to release factors that stimulate cellular proliferation, stimulate collagen synthesis, and angiogenesis as a normal part of the inflammatory process.** *Effect of Lactate, Pyruvate, and pH on Secretion of Angiogenesis and Mitogenesis Factors by Macrophages.* (Jensen, Hunt TK, *Laboratory Investigation*, Vol. 54, . 574-578, 1986)
9. **15 mM lactate stimulates collagen synthesis by cultured fibroblasts.** (Green. Goldberg, *Collagen and Cell Protein synthesis by Established Mammalian Fibroblast Line- Nature* 1964; 204:347-9)
10. **High lactate levels are significantly necessary for collagen matrix synthesis.** (*Principles of Wound Healing*, Hunt TK, *Journal of Trauma*, December 1990)
11. **Lactate also increases activity of prolyl hydroxylase, a crucial enzyme in mature collagen synthesis.** (*Wound Microenvironment, Wound Healing and Biochemical and Clinical Aspects*, Hunt TK, 1992: 274-81)
12. **Aerobically derived Lactate stimulates tissue repair via redox mechanisms.** (Hunt TK Aslam RS, *Lab Invest.* 1996; 74:644-49)
13. **Lactate is a central player in cellular, regional and whole body metabolism.** (Gladden LB, *J Physiol*; 2004:5-30)
14. **Lactate instigates signals for repair and tissue growth including Vascular Endothelial Growth Factor (VEGF), transforming growth factor (TGF-B), and interleukin.** (Hunt TK, et al, *Oxygen Transport to Tissue*; 2008:73-80)
15. **Prevention of UVB-Induced Production of the Inflammatory Mediator in Human Keratinocytes by Lactic Acid Derivatives.** (Ayako Aoiki-Yoshida, et al, *Biosci. Biotechnol. Biochem*, 77 (8), 1766-1768, 2013)
16. **Ultraviolet light induced injury: Immunological and inflammatory effects.** (Clydesdale GW, Dandie GW, Muller HK, *Immunol. Cell Biol.* 2001 Dec; 79(6) 547-568)
17. **The Sunburn Cell: regulation of death and survival of the keratinocyte.** (Van Laethem A, Claerhout S, Garmyn M, Agostinis P, *Int J Biochem Cell Biol.* 2005 Aug;37(8): 1547-53)
18. **L- and D-lactate enhance DNA repair and modulate the resistance of cervical carcinoma cells...** [Waldemar Wagner](#), [Wojciech M. Ciszewski](#),[#] and [Katarzyna D. Kania](#), *Cell Commun Signal.* 2015; 13: 36. Published online 2015 Jul 25.
19. **Lactate Up-Regulates the Expression of Lactate Oxidation Complex-Related Genes**, Daniele Gabriel-Costa, Telma Fatima da Cunha, Luiz Roberto Grassmann Bechara, et. al., Published: May 21, 2015, DOI: 10.1371/journal.pone.0127843
20. **Lactate sensitive transcription factor network in L6 cells: activation of MCT1 and mitochondrial Biogenesis**, Takeshi Hashimoto,* Rajaa Hussien,* Saji Oommen,† Kishorchandra Gohil,† and George A. Brooks*, 1 *Department of Integrative Biology, University of California, Berkeley, California, USA; † Center for Comparative Respiratory Biology and Medicine, University of California, Davis, California, USA, *FASEB J.* 21, 2602–2612 (2007)
21. **EPR detection of free radicals in UV-irradiated skin: mouse versus human.** [Jurkiewicz BA](#), [Buettner GR.](#), Free Radical Research Institute, University of Iowa, [Photochem Photobiol.](#) 1996 Dec; 64 (6):918-22.

22. **Oxidative Stress in the Pathogenesis of Skin Disease**, David R. Bickers¹ and Mohammad Athar¹, *Journal of Investigative Dermatology* (2006) 126, 2565–2575. doi:10.1038/sj.jid.5700340
23. **Ultraviolet light induced injury: Immunological and inflammatory Effects**, GAVIN J CLYDESDALE, GEOFFREY W DANDIE[†], KONRAD MULLER, *Immunology and Cell Biology* (2001) **79**, 547–568
24. **Mechanism of L-lactate Catalytic reaction dehydrogenase: an *ab initio* study**, PKU-HKU Joint Laboratory on Rare Earth Materials and Bioinorganic Chemistry, Peking University, Beijing 100871, China, August 1, 2000
25. **Lactate Dehydrogenase Reaction Mechanism**,
http://www.chem.uwec.edu/webpapers_f99/pages/webpapers_f99/busbyrc/pages/mechanism/mech.html
26. **Lactic Acid Controls the Energy Transfers for the Inflammatory Response**
Beckman J, personal clinical findings and observations
27. **Points of control in inflammation**, Nathan C, *Department of Microbiology and Immunology and Graduate Programs in Immunology and Molecular Biology, Weill Medical College of Cornell University*
28. **Radiation skin reactions**, *Mary Wells, Sheila MacBride*
29. **Protecting the radiation-damaged skin from friction: a mini review**, Patrics M Herst, MPhil, *J Med Radiat Sci.* 2014 Jun; 61(2): 119–125.