Letters from the Lactide Frontiers 2019

H. Haller, F. Sander, B. Hartmann
BG Trauma Hospital Berlin, Burn Center with Plastic Surgery, HLMedConsult

Polylactic Membranes (PLMs) based on Polymers from mixtures of lactic acids have been used in burns treatments for nearly twenty years. They are established as a well-recognized treatment method that allows for short healing time, low complications, excellent cosmetic results in superficial, deep partial thickness and even small full thickness burns [1–9] under reduced pain. This poster will try to explain the basic and the “**Lactate Effect**” in burns treatment and correlate this with implications for the clinical use.

We know that polylactides degenerate to chemical fragments releasing lactate and lactic acid [10]. Lactate and lactic acid **serve as an energy source** for the cells [10,11]. Both substances can permeate the cell membranes either due to their molecule size or to active transport by the monocarboxylate transporter (MCT) protein shuttle system. Inside of the cell, **lactate** can serve as an energy source via the Cori cycle or lactate can oxidize to **pyruvate** (via lactate dehydrogenase), which can then oxidize to acetyl-CoA and fuels the TCA cycle in mitochondria producing the metabolic products carbon dioxide, water, and NADH which provides the energy-rich NAD.

Lactate and pyruvate **act as potent antioxidants** [10,12–14] within the cells. Medical literature describes the role of oxidative stress in an increasing manner. Lactate **acts on cytokines** and increases TGF- β activation, Hypoxia Inducible Factor, VEGF, and others as many studies showed [15–18].

Polylactic membranes act as **activators in wound healing** and support curing by **supplementation of energy**. Telomeres conservation will contribute to a reduction of cell-aging and eternization, maintaining the rate of duplications and the quality of the skin. **TGF- β** affects **keratinocytes**, completing the activation status for healing. In dermal tissue, it **increases fibroblast growth, collagen, and extracellular matrix synthesis** as well as **neovascularization**. It acts as a **radical scavenger** as well. Clinical findings bolster these laboratory results.

Using these effects enables you to use polylactides as a toolbox for a broad range of indications.

Surface and structure effects

- **Wake, Patrick, and Mikos 1994:** Positive correlation between pore size and formation of fibrous tissue was found.
- Yannas and Burke 1980 mention the significance of pore size for cell ingrowth.
- Pinney 2000 described the effect of fibroblasts seeded on a 3D scaffold on vasculogenesis.
- Ring et al. demonstrated in 2011 that **structure** as bimodal foam influences the amount of vasculogenesis positively: VEGF mRNA was expressed in a 22fold amount in the three-dimensional structure greater than a monolayer

Barrier effects

Membranes reduce fluid and energy loss

Membranes protect against Superinfection

PLM protects against Infection even in DPT burns with non-wound associated infections- No difference in healing time

Grp	Mean	Std.	SEM	Media n	n
Inf.	7,82	4,03	0,65	7	39
No Inf.	8,17	5,24	0,66	7	64

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Chemical effects

Polylactides degrade to Lactate and lactic acid

Metabolic effects

Lactate fuels cell energy

Wound healing effects

“Externally applied lactate simulates hypoxic conditions under normal oxygen pressure”

Philp A, Macdonald AL, Watt PW. J Exp Biol 2005;208:4561–75

Lactate acts as a signal molecule promoting wound healing

Lactate acts on dermal tissue

Lactate activates

- **TGF- β** and **VEGF** even without the HIF pathway.

An addition of extracellular lactate leads to

- significant short-term elevation of **interleukin-1b**, a long-term elevation of **VEGF** and **transforming growth factor- β 1**, and a 50% elevation in **collagen deposition**

Fibroblast proliferation (Penn 2012)

ECM formation like hyaluronan (Stern 2002)

Collagen synthesis and deposition (Penn 2012)

Angiogenesis (Ring 2011, Porporato 2012)

Lactate acts on epidermal tissue via TGF

IL-1
TNF – activation state
Dedifferentiation
ECM creation
Cell motion, forming of filopodia
Proliferation
Redifferentiation
reverting keratinocytes to basal phenotype

Rousselle P, 2018

Systemic effects

Acts as Free Radical Scavenger

Use in moist Desquamation due to Radiation: Rothenberger 2016

Reduces oxidative stress

PLM versus HFAG: Total oxidant and Total Antioxidant Capacity

Reduces systemic inflammatory response

Fluid creep
Stabilization of glycocalyx
Scar development

Gürnlüoğlu K¹, Demircan M¹, Taşçı A¹, et al 2019