Modulation of Pain in Burn Injuries Through Lactate-Mediated Mechanisms: A Mechanistic Review of Polylactic Acid Membranes Clinical and Biological Impact

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Background

Objective:

- To explore the clinical and mechanistic evidence supporting **pain reduction in burn patients** treated with **polylactic acid (PLA) membranes**, emphasizing lactate-mediated modulation pathways.

Burn pain as a clinical problem:

- **Pain in burns, particularly partial thickness burns, is often exquisite**, representing one of the most challenging and distressing symptoms in burn care.
- Poorly controlled pain can lead to complications such as delayed healing, impaired mobility, psychological distress, and long-term morbidity.
- Traditional pain management relies heavily **on opioids** and non-steroidal anti-inflammatory drugs (NSAIDs), which may impair wound healing and are often contraindicated in patients with comorbidities.
- These limitations highlight the **need for alternative pain-modulating strategies** in burn management.

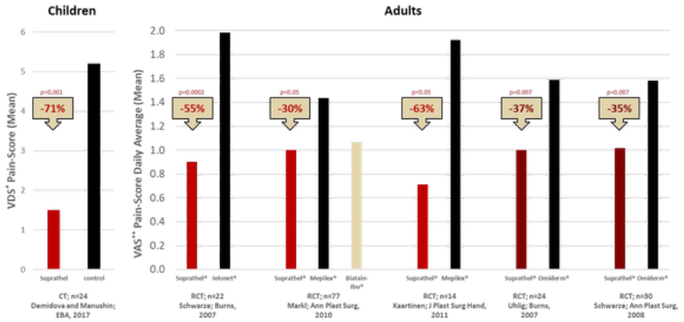
Polylactic acid membranes as an innovative solution:

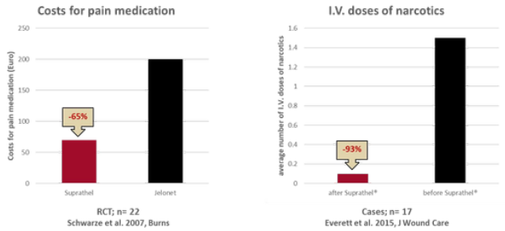
- **Suprathel®** is a fully synthetic, polylactic acid–based epidermal membrane developed for the treatment of partial thickness burns and similar wounds.
- It has demonstrated **outstanding benefits**, including:
  - Excellent adherence to the wound bed without need for frequent dressing changes.
  - Promotion of re-epithelialization and improved cosmetic outcomes.
  - Favorable safety profile compared to biologic or pharmacologic alternatives.
- Across randomized clinical trials and real-world empirical evidence, **the use of Suprathel is consistently associated with profound and sustained pain relief**.

Methods

- This work was designed as a **mechanistic narrative review** of the clinical and biological evidence supporting the pain-modulating effects of polylactic acid (PLA) membranes in burn care.
- Evidence was drawn from three main **sources**:
  - **Randomized clinical trials (RCTs)** reporting pain outcomes in burn and donor site patients treated with PLA membranes.
  - ***In vivo* experimental models** exploring the effects of PLA degradation products, particularly lactate, on inflammation and nociception.
  - **Molecular and cellular studies** examining the pathways of inflammatory modulation, neuroreceptor signaling, and microenvironmental changes relevant to pain.
- Studies were identified through targeted searches of PubMed and Embase, as well as manual review of relevant references.
- The findings were organized along **two dimensions**:
  - **Clinical outcomes:** timing, magnitude, and sustainability of pain reduction and reduced analgesic consumption.
  - **Mechanistic insights:** lactate-driven effects on pH, TRPV1 modulation, cytokine expression, and tissue stability under hypoxia.
- This integrative approach allowed the alignment of clinical analgesic effects with their biological underpinnings, providing a coherent framework to propose PLA membranes as both a skin substitute and a pain-modulating intervention in burn care.

Results





Clinical Evidence of Pain Reduction:

- Across 6 RCTs, **PLA membranes consistently demonstrated rapid and sustained pain reduction** in children and adults with partial thickness burns and skin graft donor sites.
- By reducing pain intensity, PLA membranes contributes to:
  - **Improved patient comfort and mobility**,
  - **Reduced need for systemic analgesics**,
  - **Facilitation of wound care procedures and dressing changes**.

A 9-year old children suffered a partial-thickness scald burn to the face. The burn was debrided and PLA membranes applied without any secondary dressings to the injured areas. Pain significantly improved after 24 hours, allowing the clinical team to manage her only using acetaminophen. The children's mood and engagement with the clinical team significantly improved in the subsequent days and was discharged with the burn fully epithelialized after 10 days.

Note: the use of these images was assented by the patient and consented by her guardian.

Mechanistic Evidence – Lactate-Mediated Pain Modulation

- PLA membrane degradation **releases lactate**, a biologically active metabolite with direct effects on pain and inflammation through:
  - **Acidification of the wound bed:** Mild pH reduction desensitizes nociceptors and decreases neural excitability, contributing to early pain relief.
  - **TRPV1 receptor modulation:** Lactate downregulates vanilloid pain receptor activity, reducing neurogenic transmission and local inflammation.
  - **Cytokine modulation:** Suppression of key pro-inflammatory mediators (IL-1β, TNF-α) lessens inflammation-driven nociception.
  - **Support under hypoxia:** Lactate provides an energy substrate for keratinocytes and fibroblasts, stabilizing the wound microenvironment and reducing hypoxia-related pain signals.
  - **Immune balance and neuroimmune crosstalk:** Lactate helps normalize immune responses, indirectly reducing peripheral sensitization.
- PLA membranes are **fully synthetic**, thereby providing a standardized product that ensures consistent bioactive release **without biologic variability**.
- Provides a **dual mechanism of action**:
  - Functions as a **membrane** for wound coverage and epithelization.
  - Acts as a **bioinductor** modulating pain and inflammation through lactate pathways.

Discussion

- **Pain in partial thickness burns remains one of the most significant challenges in acute burn care**, with limited safe and effective alternatives beyond opioids and NSAIDs.
- PLA membranes provides not only reliable wound coverage but also **clinically validated pain relief**, demonstrated across multiple randomized controlled trials with reductions up to 71% compared to standard dressings.
- Their **dual mechanism of action**, as both a protective matrix and a pain-modulating bioinductor, is **unique** among epidermal substitutes.

Taken together, the mechanistic evidence and robust clinical outcomes strongly support the routine use of Suprathel® in burn units as a first-line strategy not only for wound healing but also for effective and safe pain modulation.

Selected References

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