Novel Native Collagen Dressing Featuring Bioactive 3D-Matrix Technology for Selective Binding of Wound Collagenases and Gelatinases

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Objective:
Chronic hard-to-heal wounds generate high costs and resource utilization in health systems and are the focus of intense efforts to improve healing outcomes. One approach is the application of biodegradable 3D-matrices to wounds to initiate and stimulate healing. A number of collagen-based materials have been historically proposed for this purpose, without necessarily optimizing their structure to maximize their effect. We introduce a novel collagen wound dressing that contains 90% native collagen and 10% alginate, Cutimed® Epiona, which structure is highly similar to human dermis (Fig. 1A & B). We compared it to established dressings like Promogran®, a mixture of bovine collagen and 30% regenerated oxidated cellulose and Endoform®, a 10% ECM of ovine forestomach dressing.

Methods/Material:
Matrices were analyzed by atomic force microscopy, scanning electron microscopy, and immunoelectron microscopy for tracking collagen types I, III and V. MTT viability assays were performed with NIH 3T3 fibroblasts. MMP binding was analyzed by tracking for MMP-2 and MMP-9 and the binding capacity of the wound dressings for the growth factor PDGF-BB was investigated.

Results:
Unlike Endoform® or Promogran®, the 3D structure of Cutimed® Epiona was found to be analogous to intact, native, dermal collagen (Fig. 2A-F, Fig. 3A & B). Fibroblasts seeded on Cutimed® Epiona showed exponential growth whereas in Promogran® or Endoform®, very low rates of proliferation were observed after seven days (Fig. 4). MMP sequestration was effective and significantly prolonged in Epiona (Fig. 5A & B). In addition, Epiona was able to significantly stabilize PDGF-BB in vitro (Fig. 6). Early clinical observations in Epiona revealed improvements in regranulation and revascularization, thereby, matching the matrix properties found in vitro.

Conclusion:
The authors hypothesise that the observed microstructure of Epiona allows for an effective binding of MMPs, a stabilization and protection of growth factors and also promotes the ingrowth of dermal fibroblasts leading to the recommencement of healing in previously recalcitrant wounds.

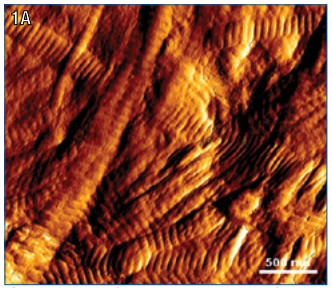


Figure 1A. Atomic force microscopic images of Cutimed® Epiona

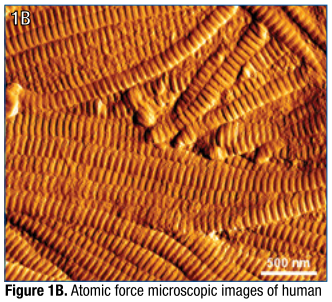


Figure 1B. Atomic force microscopic images of human dermis.

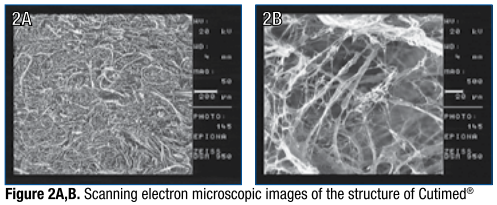


Figure 2A,B. Scanning electron microscopic images of the structure of Cutimed® Epiona.

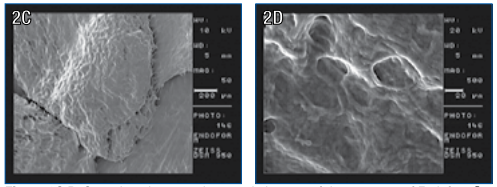


Figure 2C,D. Scanning electron microscopic images of the structure of Endoform®.

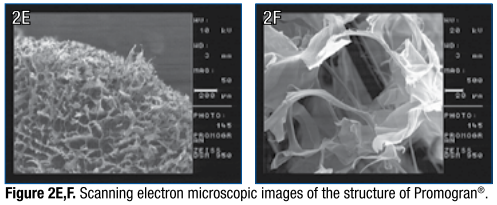
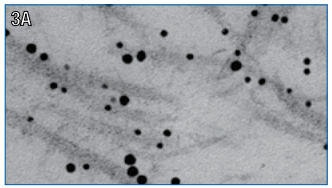


Figure 2E,F. Scanning electron microscopic images of the structure of Promogran®.



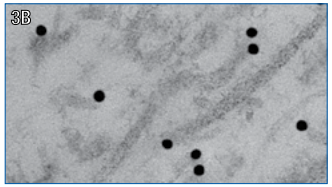


Figure 3. Immunoelectron microscopic images of Cutimed® Epiona showing (3A) type I and type III collagen and (3B) type V collagen.

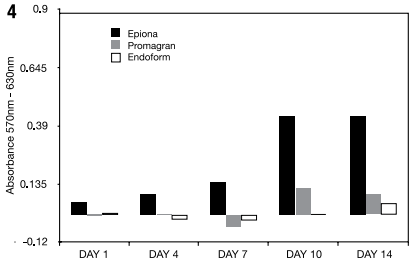


Figure 4. MTT assay results for Cutimed® Epiona, Promogran® and Endoform® measured at days 1, 4, 7, 10 and 14

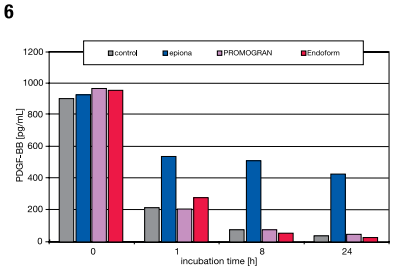


Figure 6. Effect of Cutimed® Epiona, Promogran®, and Endoform® on PDGF-BB in solution.

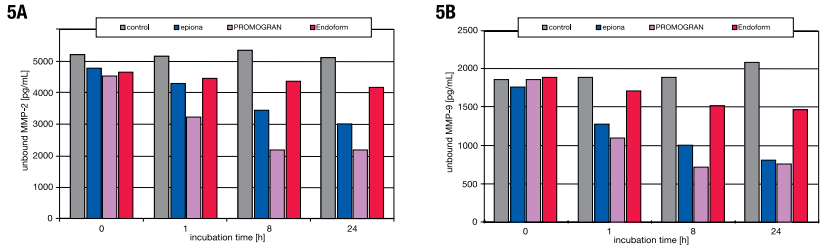


Figure 5. Effects of Cutimed® Epiona , Promogran® and Endoform® on unbound concentrations of (5A) matrix metalloproteinase (MMP)-2 and (5B) MMP-9.

Disclaimer:
Laboratory testing results are intended to illustrate a product's performance under controlled conditions. Acutal use results may vary.

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Endoform is the registered trademark of Mesynthes Limited