

## **Effects of Prisma® Skin dermal regeneration device containing glycosaminoglycans on re-epithelialization and granulation processes.**

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Prisma® Skin is a new pharmaceutical device developed by Mediolanum Farmaceutici S.p.a. It includes alginates, hyaluronic acid and mainly mesoglycan. The latter is a natural glycosaminoglycan preparation containing chondroitin sulfate, dermatan sulfate, heparan sulfate and heparin and it is utilized in the treatment of vascular disease. Glycosaminoglycans may contribute to the re-epithelialization in the skin wound healing, as components of the extracellular matrix. Here we describe, for the first time, the effects of Prisma® Skin in in vitro cultures of adult epidermal keratinocytes and dermal fibroblasts. Once confirmed the lack of cytotoxicity by mesoglycan and Prisma® Skin, we have shown the increase of S and G2 phases of fibroblasts cell cycle distribution. We further report the strong induction of cell migration rate and invasion capability on both cell lines, two key processes of wound repair. In support of these results, we found significant cytoskeletal reorganization, following the treatments with mesoglycan and Prisma® Skin, as confirmed by the formation of F-actin stress fibers. Additionally, together with a significant reduction of E-cadherin, keratinocytes showed an increase of CD44 expression and the translocation of ezrin to the plasma membrane, suggesting the involvement of CD44/ERM (ezrin-radixin-moesin) pathway in the induction of the analyzed processes. Furthermore, as showed by immunofluorescence assay, fibroblasts treated with mesoglycan and Prisma® Skin exhibited the increase of Fibroblast Activated Protein  $\alpha$  and a remarkable change in shape and orientation, two common features of reactive stromal fibroblasts. In all experiments Prisma® Skin was slightly more potent than mesoglycan. In conclusion, based on these findings we suggest that Prisma® Skin may be able to accelerate the healing process in venous skin ulcers, principally enhancing re-epithelialization and granulation processes.