Proteases are enzymes that act on proteins by breaking them down into peptides and amino acids. They are necessary for healing by degrading damaged extracellular matrix proteins in wounds and ulcers and facilitating tissue regeneration, cell migration, and granulation tissue formation. Unfortunately, control of these proteases does not occur in some wounds resulting in elevated protease levels which damage tissue and delay healing of chronic wounds, especially venous ulcers and diabetic ulcers. This occurs when the proteases degrade growth factors and their receptors, angiogenic factors, and extracellular matrix. The major proteases in wound healing are matrix metalloproteases (MMPs) and serine proteases. MMPs are expressed by numerous cells involved in the healing process and require zinc to be active. In an attempt to control these unregulated proteases and their damage, new dressings have been developed that reduce wound bed protease levels aiding in healing these ulcers.

There are different approaches to reducing wound protease levels. One is to use oxidized regenerated cellulose and collagen to reduce wound bed protease levels by inactivating proteases, and decreasing production of additional proteases by removing reactive oxygen species molecules. A second is to utilize collagen combined with ethylenediaminetetraacetic acid (EDTA) to absorb and isolate the protease in the wound bed by acting as a sacrificial substrate, while the EDTA binds with zinc, the essential co-factor necessary for the protease to function thereby reducing the active form of the protease. In an attempt to reduce MMP levels and restore the wound to a healing course, we compared two products known for their ability to reduce the wound bed MMP levels and determine if the EDTA/collagen product is equally or more effective than the ORC/collagen product in reducing these levels.

Four (4) patients were randomly assigned to receive the EDTA/collagen product and three (3) patients were assigned to treatment with the ORC/collagen product. Patients in each group received weekly dressing changes for three (3) weeks. All patients received short-stretch compression bandages. Protease levels were measured before treatment began and with each dressing change. Protease levels were determined using ELISA assays for active MMP-1, -2, and -9.

Results & Discussion

- For MMP-1 the EDTA/Collagen dressing showed a 46% decrease from week 0 to week 2, while the ORC/Collagen dressing exhibited an 84% increase from week 0 to week 2.
- For MMP-2 over the 2 weeks of treatment the EDTA/Collagen showed a steady decrease, 86% from week 0 to week 2. The ORC/Collagen dressing demonstrated a substantial increase over the 2 weeks (2760%).
- Again with MMP-9 the ORC/Collagen dressing showed a steady increase in MMPs in the wound, 200% from week 0 to 2. The EDTA/Collagen dressing showed at 40% decrease from week 0 to 2.

Conclusions

Over the course of this three (3) week study, the EDTA-containing product was shown to be more effective in reducing wound bed protease levels than the ORC-containing product, which consistently demonstrated an overall increase in the three matrix metalloproteases studied.