
THE MAGNETISM OF
PURACOL® PLUS
collagen microscaffold™ wound dressings
MEDLINE

Medline is pleased to introduce **Puracol Plus**, *an advanced native collagen wound dressing based on state of the art biomaterial science and technology.* **Puracol Plus** *is predominantly Type I, bovine collagen.*

A chronic wound has specific imbalances that **Puracol Plus** *helps restore to equilibrium through its potential to biochemically alter the wound environment.*

Puracol Plus offers a unique three-dimensional structure known as the MicroScaffold. It acts similar to a magnet by binding destructive enzymes, thus keeping them away from newly deposited granulation tissue and allowing the body's own collagen to heal the wound.

Schematic illustration of collagen's triple helix structure.

Here's the challenge

A chronic wound is trapped in the inflammatory phase, with destructive enzymes such as elastase and MMPs present at abnormally high levels.[6]

Normal wound healing involves three specific, but overlapping phases:

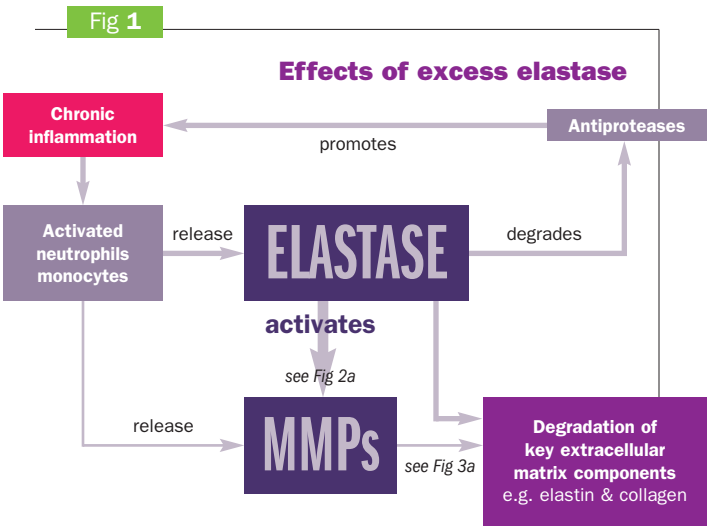
- **Inflammatory –** The immune system cleanses the wound and eliminates pathogens.
- **Proliferation –** Collagen, elastin, and other components of the extracellular matrix (ECM) are secreted. Cells migrate and wound contraction and epithelialization occurs.
- **Maturation –** Collagen and ECM continues to reorganize, and remodeling of scar tissue occurs over many months after epithelialization is completed.

Destructive enzymes in a chronic wound include:

- **Elastase** *(fig. 1)*: This enzyme is secreted by neutrophils and has at least three harmful effects in the chronic wound: [1,2]
  1. Elastase destroys elastin. Elastin is a key component of the ECM and, as its name implies, contributes to the elasticity of skin.
  2. Elastase plays a key role in activating another class of destructive enzymes, MMPs, in the wound bed *(fig. 2a)*.[3]
  3. Elastase also destroys other useful proteins such as tissue inhibitors of matrix metalloproteinases (TIMPs). TIMPs are described as "anti-MMPs" and must outnumber the MMPs for the wound to heal. In a chronic wound, the MMP to TIMP ratio is in favor of these collagen-destroying enzymes, MMPs.[4]

  Elastase is involved in several other generally destructive roles in prolonging the chronic status of a wound.[5]
- **Matrix metalloproteases (MMPs)** are proteases, the most problematic of which are specific to collagen, or fragments of collagen. These MMPs seek out collagen or collagen-like molecules and chemically break them down *(fig. 3a)*.[6] MMPs are activated by elastase *(figs. 1 and 2a)*.

Fig **1**



1. Edwards J et al, *In vitro* inhibition of human neutrophil elastase by oleic acid albumin formulations from derivatized cotton wound dressings. Int J Pharmaceutics 284: 1–12, 2004.

2. Cullen B et al. Mechanism of action of PROMOGRAN, a protease modulating matrix, for the treatment of diabetic foot ulcers. Wound Rep Regen 10:16-25., 2002.

3. Zhu Y et al. Synergistic neutrophil elastase-cytokine interaction degrades collagen in three-dimensional culture. Am J Physiol Lung Cell Mol Physiol. 281: L868-878, 2001.

4. Ladwig G et al, Ratios of activated matrix metalloproteinase-9 to tissue inhibitor of matrix metalloproteinase-1 in wound fluids are inversely co-related with healing of pressure ulcers. Wound Rep Regen, Jan-Feb 26-37, 2002.

5. Yager D et al, Ability of chronic wound fluids to degrade peptide growth factors is associated with increased levels of elastase activity and diminished levels of proteinase inhibitors. Wound Rep Regen 5:23-32, 1997.

6. Schultz G et al, Molecular analysis of the environment of healing and chronic wounds: Cytokines, proteases, and growth factors. Wounds 10 (6 Suppl F): 1F-9F, 1998.

Puracol Plus meets the challenge with two modes of action

1. **Puracol Plus binds and traps elastase** *(figs. 6 and 2b)* **and MMPs** *(figs. 8 and 3b)*. Such binding (similar to the binding of iron particles to magnets) keeps these destructive enzymes occupied in the activity of breaking down the dressing material *(figs. 2b and 3b)*, instead of being involved in the degradation of any new *(de novo)* collagen made by the wound fibroblasts. The dressing, in essence, is a sacrificial substrate for the destructive wound enzymes present in the chronic wound.
2. **Puracol Plus creates a fibroblast-friendly wound environment.** Fibroblasts produce collagen and other ECM components that fill the wound bed, contributing to healing.

Puracol Plus collagen wound dressing.

Fig **2a**

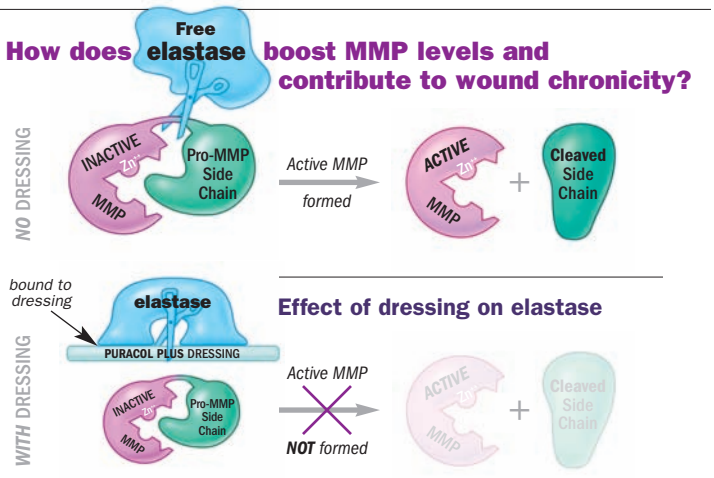


Fig **2b**

Fig **3a**

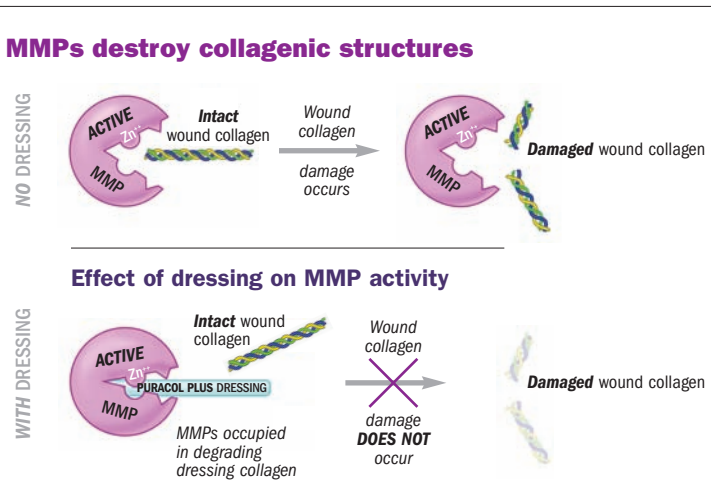


Fig **3b**

Schematic illustrations only.

Denatured versus Native Collagen, Enzyme Binding, and the MicroScaffold

Puracol Plus wound dressing *as seen through an optical microscope.*

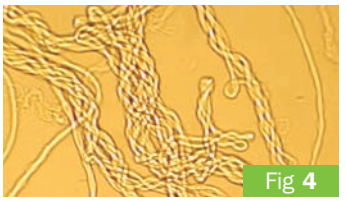


Fig **4**

The intact super-structure (above) provides strong evidence that the nativity of the collagen triple helix is preserved.

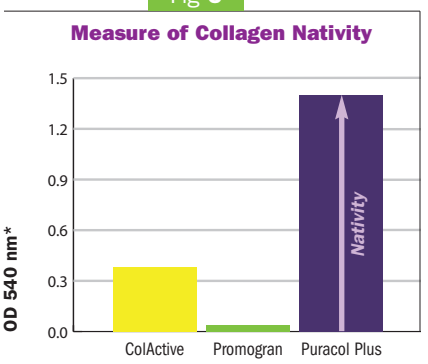
Denatured collagen, commonly used in some wound care products available today, is processed chemically to the extent that it has lost the sophisticated triple helix structure of the collagen building block. The preservation of the triple helix is essential in maintaining the proper complex architecture of skin collagen. Scientific evidence suggests that this native structure of collagen is attractive to fibroblasts.[7]

Analytical tests and microscopy show that **Puracol Plus** has a high degree of retained triple helical structure (nativity) compared to other collagen-based products *(figs. 4 and 5)*.

Fibroblasts also thrive in structures that they can occupy in a three-dimensional sense.[7] The main function of these critical cells is to secrete collagen, other important materials of the ECM, as well as growth factors. Using **Puracol Plus**, a collagen product with a clearly visible three-dimensional architecture (MicroScaffold), potentially allows the fibroblasts to act in an optimal fashion in the challenging environment of a chronic wound *(fig. 7)*.

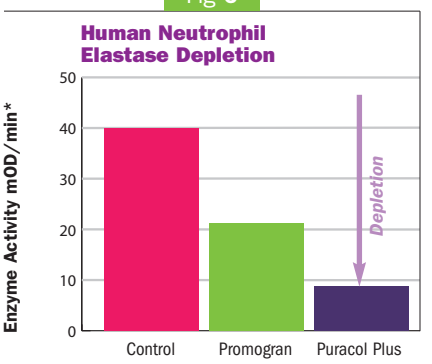
Why native collagen-based dressings such as **Puracol Plus** interact intensively with the destructive elastase enzyme *(fig. 6)* is still under investigation. Binding of a dressing material to elastase obviously reduces the concentration of the elastase in the wound bed, which means that less of the fibroblast expressed elastin is destroyed. But, perhaps more importantly, elastase is known to play a role in creating the final destructive form of MMPs *(fig. 2a)*. Reducing elastase concentration in the wound reduces production of MMPs in the wound bed *(fig. 2b)*. Elastase is also known to destroy the beneficial TIMP proteins that keep the MMPs in check. A reduced elastase

Fig **5**



**Proportional to the extent of nativity, higher nativity is desirable.*

Fig **6**



**Proportional to elastase activity, lower activity is desirable.*

7. Doillon C. J. et al, Fibroblast-Collagen sponge interactions and the spatial deposition of newly synthesized collagen fibers *in vitro* and *in vivo*. Scanning electron microscopy 1984, Volume 111, Pages 1313-1320.

level potentially allows the TIMP concentration to reach a level that keeps MMP activity low in the wound bed.

What happens to the dressing once applied to the chronic wound? As it is 100 percent pure collagen, it will be broken down at a chemical level by the MMPs to which it was bound. The by-products of this binding and processing are collagen fragments, which are consumed by the fibroblasts. The fibroblasts will synthesize fresh collagen and elastin and secrete it out into an environment relatively free of elastase and MMPs. Without the removal of these enzymes, the newly synthesized collagen and elastin would have been destroyed, delaying wound healing.

By using Puracol Plus there is a good chance that the chronic wound will heal.

Puracol Plus microscaffold *as seen with an electron microscope.*

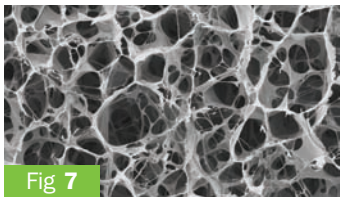


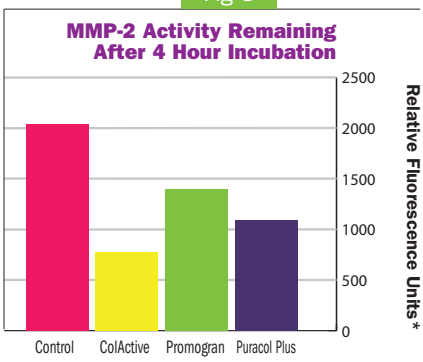
Fig **7**

The open porous structure increases the internal surface area for maximal interaction with wound fluids and wound fibroblasts.

Ordering Information

Item #	Description	Packaging
MSC8622	Puracol Plus, 2" x 2.25"	10/bx, 5 bx/cs
MSC8644	Puracol Plus, 4.25" x 4.5"	10/bx, 5 bx/cs
MSC8522	Puracol, 2" x 2"	10/bx, 5 bx/cs
MSC8544	Puracol, 4" x 4.25"	10/bx, 5 bx/cs

Fig **8**



**Proportional to MMP activity, lower MMP activity is desirable.*

Puracol is also available in 1 mm thickness.

For more information on Puracol Plus, call your sales representative or 1-800-MEDLINE.

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Not all products are currently available for sale in Canada.

Please contact your Account Representative for additional information.

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