Collagen Powder in Wound Healing

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ABSTRACT

Chronic wounds, such as pressure ulcers, diabetic foot ulcers, and venous leg ulcers, are associated with high costs, poor quality of life, and significant morbidity and mortality. A chronic wound develops when progression through the normal phases of wound healing goes awry, creating a hostile environment with elevated levels of pro-inflammatory cytokines, increased matrix metalloproteinases (MMPs), destruction of extracellular matrix (ECM) components, and diminished activity of growth factors and other soluble mediators. The advent of advanced wound care therapies allows for a targeted approach to the treatment of nonhealing wounds by addressing specific molecular defects in healing. Collagen is an essential building block of the skin that when utilized as an adjunctive wound therapy stimulates and recruits immune cells and fibroblasts and martyrs itself for degradation by MMPs, thereby preserving native ECM structure and promoting healing. Particulate or powdered collagen is processed to minimize covalent cross-linking and is purported to exert its biologic activity immediately upon application. This article critically reviews the current evidence for collagen powder as an adjunctive therapy for chronic wounds and presents indications, limitations, and principles of use. In general, there is a need for high quality studies and randomized control trials to support its use in clinical practice.

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INTRODUCTION

Approximately 6.5 million people in the United States live with chronic cutaneous ulcers, with over 25 billion health care dollars spent annually on treatment.[1] Such wounds fail to progress through the normal stages of wound healing, with factors including an overactive and prolonged inflammatory response, altered protease levels, and deficient extracellular matrix (ECM) contributing to wound chronicity.[2,3] As a result, state-of-the-art advanced wound care therapies including collagen dressings, growth factors, and skin substitutes are under development to target the molecular abnormalities present in chronic wounds.[4,5] Collagen is the most abundant protein found in the human body and is a major component of the ECM, constituting 1/3 of total body protein and 3/4 of the dry weight of human skin.[6] Collagen molecules are synthesized by fibroblasts and are composed of three polypeptide chains that together form a triple-helical structure.[7] Proteolytic processing and covalent cross-linking of the chains allows the formation of larger fibrils and fibers that comprise the ECM and provide remarkable tensile strength and structural support to skin and other connective tissues.[5,8] Besides its function as a scaffold in skin, collagen plays a pivotal role as a signaling molecule in the regulation of all phases of wound healing. Polypeptide fragments released by proteolytic degradation of native collagen exhibit chemotactic properties and facilitate cellular differentiation, migration, and recruitment of cells including macrophages and fibroblasts.[5] Collagen-based wound care products are capable of fostering healing by targeting specific defects in the chronic wound environment.[5]Fractionated or powdered collagen preparations exhibit minimal cross-linking and are hypothesized to have the advantage of functioning as signaling molecules directly upon application, without requiring further enzymatic breakdown.[9] Herein, we will review the evidence for collagen powder as an adjunctive treatment in wound healing and will discuss potential advantages, disadvantages, and principles of usage.

Beyond Structural Support: The Role Collagen in Wound Healing

Wound healing is a complex process that occurs in four overlapping phases: hemostasis, inflammation, proliferation, and remodeling.[10] Collagen plays an important role in each of these phases. Hemostasis ensues immediately following tissue injury as collagen is exposed from damaged vascular endothelial

cells, leading to platelet adherence, activation, aggregation, and subsequent clot formation.[2] Platelets release chemotactic and growth factors such as transforming growth factor-β (TGF-β), which attracts fibroblasts and inflammatory cells including neutrophils and macrophages.[2,11] In the inflammatory phase, neutrophils secrete proteolytic enzymes that degrade collagen and release fragments of ECM material that act as chemotactic factors for the recruitment of neutrophils, macrophages, and other inflammatory mediators.[11]Macrophages release tumor necrosis factor-α (TNF-α), which causes self-induction of interleukin-1β (IL-1β) production.[12]TNF-α and IL-1β are mitogens for fibroblasts and collagen deposition and cause up-regulation of matrix metalloproteinases (MMPs) that degrade ECM proteins and allows for cellular migration.[13]