

Larval Enzyme Therapy: The New Answer for Chronic Wounds?

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Keywords

Chronic wound, Maggots, Antibacterial, Biobag

How to cite this article:

Sharma, P. K. and Sakshi. 2026. Larval Enzyme Therapy: The New Answer for Chronic Wounds? *Vigyan Varta* 7 (10): 77-80.

ABSTRACT

Chronic wounds are difficult to heal, and typically need periodic debridement and infection management. A strange but hopeful alternative is the use of therapeutic fly larvae, sometimes known as maggots, to debride and assist the healing of such wounds. Larval treatment, in particular using *Lucilia sericata*, utilizes the natural capacity of the larvae to feed on dead tissue, eliminate harmful microbes and biofilms, and produce enzymes and antimicrobial compounds that may aid tissue healing. Although loose larvae may be challenging to utilize due to escape and patient acceptance, modern enclosed systems such as BioBag® provide a more practical and regulated alternative. Recent case experience has shown this strategy to be helpful in the elimination of necrotic tissue and moving toward wound healing. The development of larval delivery technologies and an increased knowledge of their biological properties have made larval therapy a promising approach for the treatment of difficult-to-heal chronic wounds.

INTRODUCTION:

Skin wound healing is critical in restoring homeostasis after damage, with 1-2% of the world's population

suffering from chronic wounds. Available treatment options include various dressings and active wound care, which is experiencing



significant growth (20.6% CAGR from 2016-2022) due to its cost-effectiveness and specificity. The use of fly larvae for biological debridement has been studied in the management of chronic wounds in animals and humans, where larval activity helps to remove necrotic tissue and may contribute to improved wound healing (Choudhary *et al.*, 2016; Bazaliński *et al.*, 2023). Active debridement with proteases derived from animal secretions, particularly maggots (*Lucilia sericata*), has shown promise in improving wound healing and managing chronic wounds, which is also known as Maggot Debridement Therapy (MDT) or biosurgery (Morris *et al.*, 2023). Biological debridement effectively eliminates devitalized tissue, lowers biofilms, and improves pain management, but it has been neglected in outpatient settings due to social stigma and classified as a last-resort treatment since its first use in 1929. Larval treatment is contraindicated for some illnesses, restricting its widespread acceptability despite its demonstrated advantages.

Traditional Larval Therapy

The conventional method of applying larval treatment, known as loose or free-range larvae application, is a challenging procedure. It entails immediately applying 5-8 larvae per square centimetre to the wound, followed by creating an exterior cage-like dressing to encapsulate the larvae. This approach is time-consuming, has limited dose control, and is prone to larval escape. Notably, larvae escape from the dressing in 43% of instances, posing major hurdles for outpatient therapy due to possible infection-control hazards at home and presumably reducing patient consent to treatment (Bazaliński *et al.*, 2023).

Mode of Action

Larvae release a variety of enzymes, including chymotrypsin and trypsin-like proteases, which aid in wound healing by breaking down

fibrin clots and necrotic tissues. Maggot proteases (MaPs) increase fibroblast activity, TGF- β signalling, and endothelium and keratinocyte migration, resulting in better wound closure. MaPs also restrict neutrophil migration and diminish pro-inflammatory mediators, and they have antibacterial effects against pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* (Bazaliński *et al.*, 2023). Recent results have highlighted the antibacterial action of a peptide termed Lucifensin produced from larval secretions, which is effective against a variety of bacterial species (Morris *et al.*, 2023). Additionally, recombinant enzymes like as Chymotrypsin I are being employed to reduce the hazards associated with direct larval treatment.

Antibacterial Action

In outpatient wound care, it is critical to reduce infection and sepsis risk while avoiding antibiotic abuse. Larvae exhibit antimicrobial activity against a wide range of microbes, including planktonic bacteria, mature biofilms, and fungi, with a focus on MRSA, *S. aureus*, and *P. aeruginosa* (Morris *et al.*, 2023). Research indicates that larvae physically remove both gram-positive and gram-negative bacteria, which they then destroy in their gut. Furthermore, larvae create an alkaline environment (pH of 8-8.5), which is unsuitable for bacterial growth. Their presence on wounds promotes the production of exudate, which aids in the removal of bacteria from the wound site.

Suitable/Unsuitable Wound Types

Larval treatment is an efficient approach for debriding necrotic, nonhealing wounds, with quick results in instances characterized by soft, wet tissue (Choudhary *et al.*, 2016; Bazaliński *et al.*, 2023). Important contraindications include the danger of bleeding, allergies to polyester or fly larvae, and wound settings that

cannot maintain the larvae's life, such as non-offloaded regions. Common side effects include periwound inflammation and increased discomfort. Treatment should be discontinued if the wound has made progress and is no longer considered nonhealing, suggesting that debridement is no longer required.

Advances

BioBag® (BioMonde® Gainesville, FL) is a patented, natural larval treatment device used to debride nonhealing skin and soft tissue wounds. It includes a heat-sealed porous polyester bag containing larvae in five sizes, each with a predefined dose dependent on the wound area. The bag enables for a four-day therapy without directly handling the larvae, which successfully debride the lesion due to the bag's porous construction. This administration approach decreases the possibility of larvae escape and the time required for application, allowing for faster therapy than surgical debridement. Furthermore, caregivers can do clothing changes at home with ease (Bazaliński *et al.*, 2023).

Medicare Patient Case Studies (Dynarska *et al.*, 2025)

This article presents two case studies that demonstrate the use of BioBag in wound treatment in outpatient settings. In the first case, a 96-year-old female developed a nonhealing necrotic lesion on her left anterior lower thigh as a result of radiation therapy for squamous cell carcinoma. After 11 months of fruitless therapies, including hyperbaric oxygen therapy, Dakin's solution, and Manuka honey, she self-referred to a new facility where sodium oxychlorosene was delivered, followed by BioBag treatment. Tissue improvement was visible after three BioBag treatments, with new granulation tissue developing following the first application. By the end of therapy, the malodor had subsided substantially, and the

wound had healed to 80%, allowing for further procedures such as collagen powder application and a split-thickness skin transplant.

The second case includes a 75-year-old man with a history of immunocompromise caused by antirejection medicines who developed necrotising fasciitis after an abrasion became infected with *Aeromonas hydrophila*. His condition deteriorated quickly, demanding surgical intervention. Initially, the incision showed severe necrosis with exposed muscle, tendon, and bone, necessitating a thorough examination to establish the likelihood of healing. Two BioBag treatments were performed over a 10-day period, resulting in significant debridement and allowing the patient to transition to negative pressure wound care and hyperbaric oxygen therapy shortly after. The wound healed effectively without requiring amputation, eventually reaching complete closure with grafting and compression treatment. Notably, the BioBag therapy was less painful than typical surgical procedures.

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