BIOPAD & BIOSPRAY

The safe and fast way to heal Wounds

EURORESEARCH
natural growing, natural healing

About us

Euroresearch is an Italian company that was founded in 1983. It operates in various pharmaceutical fields, with particular focus on research and development, marketing, licensing and trading. With over 30 years of experience, Euroresearch has developed high quality products and positioned itself as a leading company in the collagen market.
Because of its well-estab¬lished manufacturing processes, Euroresearch products typically have a high degree of purity and safety, thus ensuring optimum quality. The company's mission began with research and development of highly effective, innovative solutions for the treatment of chronic injuries. Based on this experience, Euroresearch developed the idea of investing in new technological solutions in the following areas: aesthetic medicine, traumatology and dentistry.

A market leader in high quality, innovative products

Euroresearch's mission started with research and development of innovative solutions for wound management. With its innovative and highly effective wound healing products, Euroresearch adds value to the everyday job healthcare professionals in wound management: the peculiarity of Euroresearch's approach could be summarized in "not to cover but to care". The company's commitment in developing new and cost-effective wound healing products continues day by day, to provide patients the best and fastest solutions to their needs. Innovation is at the core of Euroresearch's daily work, with the aim of striking a balance between the needs of patients and those of medical treatments. The experience achieved in wound management enables Euroresearch to offer new and valid products in a number of different areas.
The dynamism and professionalism characterizing Euroresearch's staff ensures a high-quality service to medical practitioners and - eventually - to patients. Euroresearch's goal in health care is to expand its range of products and services to better meet the needs of both physicians and patients, either in hospitals or at home, while assuring the necessary resources to provide educational programs and assistance to doctors and nurses.


BIO
SPRAY 75

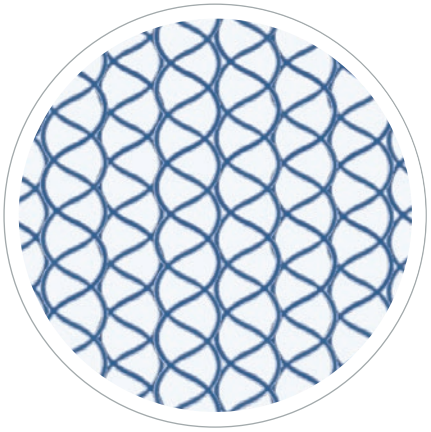
What is healing?

Healing is a complex, dynamic biological process aimed at repairing damaged organs or tissues. This physiological process is conventionally divided into four stages, each of them closely interconnected and dependent upon the others.
Hemostasis, inflammation, proliferation and remodeling make up a (seemingly simple) pathway that leads to healing through physical, chemical and biological mechanisms. In most cases the perfection of the human body guarantees a successful outcome; however, failures must not be overlooked. These are often linked to either overall conditions or local imbalances: as far as the latter are concerned, collagen surely fits in and plays a paramount role. Collagen is the protein most commonly found in the extracellular matrix: this component represents 25% to 80% of the proteins that make up the skin, and it is indeed considered the most crucial structure to achieve good tissue reconstruction results.

What is collagen, and what role does it play in the healing process?

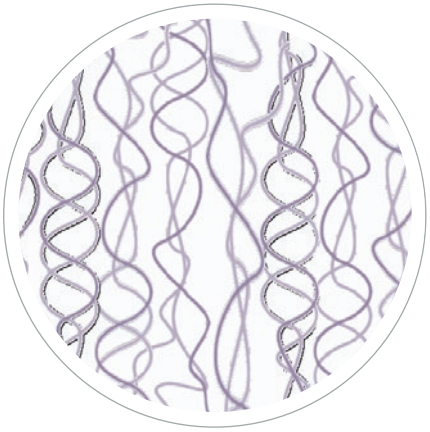
From a structural point of view, collagen is made of a triple helix of diversely composed filaments, differentiated by polypeptide amino-acids.
Collagen molecules are predominantly synthesized by fibroblasts, but also by chondroblasts, osteoblasts and epithelial cells. These molecules are then stored in the extracellular matrix (ECM), where the triple helix structure, composed of three alpha-chains, connects with other more complex fibrils of a reticular and elastic nature, thus reinforcing its characteristics.
This assembly can be considered a real tissue matrix, capable of taking on different degrees of elasticity and flexibility (*figure 1*).

Native Collagen



Collagen dressing
with native structure

Hydrolized Collagen



Collagen dressing
with denatured structure

Ushiki T. Collagen fibers, Reticular fibers and Elastic fibers, a comprehensive understanding from a morphological viewpoint.

Collagen is a fibrous protein found in the ECM of human tissues such as skin, tendons, ligaments, cartilage, bones, and teeth; it makes up approximately 25% of all proteins in the human body. Collagen plays an important role in the biological process of cicatrization, in that it is the driver of tissue repair processes.

Its mechanical action provides structural support and contributes to:

- offering a load-bearing structure (scaffold) to recover substance loss
- controlling differentiation, migration and synthesis of several cell proteins
- fostering physiological production of fibroblasts, granulation tissue and native collagen
- facilitating contact between platelets and coagulation factors (hemostasis)
- favoring the formation of new capillaries (angiogenesis).

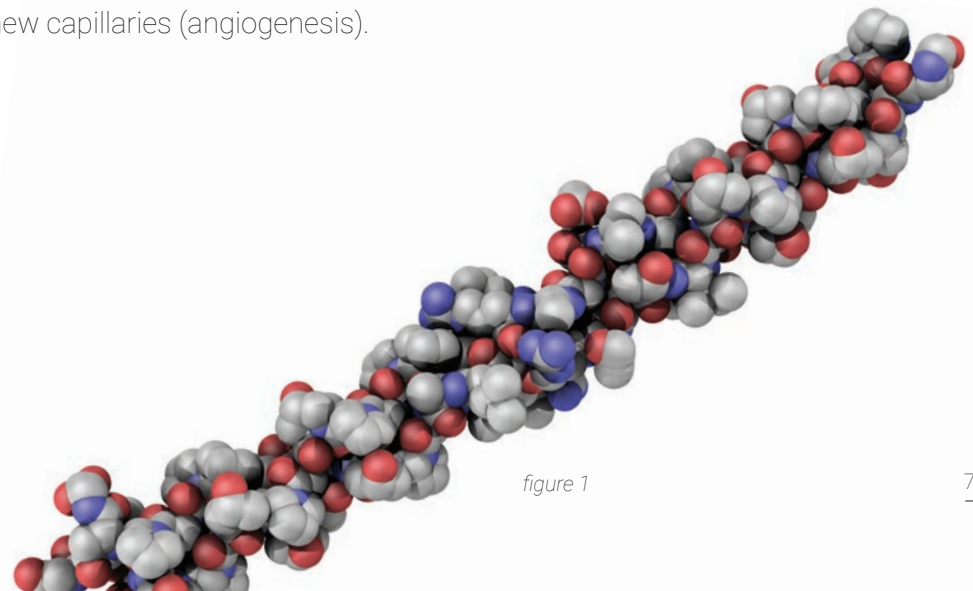


figure 1

What happens in chronic wound healing?

1

Deposition of new collagen is delayed[1]

2

Recruitment of fibroblasts (that synthesize collagen) is delayed[1]

3

High levels of MMPs and elastase are responsible for the proteolytic degradation of collagen[1]

4

Age-related delayed wound healing is caused by impaired collagen synthesis and increased degradation[2]

5

In diabetic patients, hyperglycemia reduces collagen production and induces the formation of abnormal rigid collagen[2]

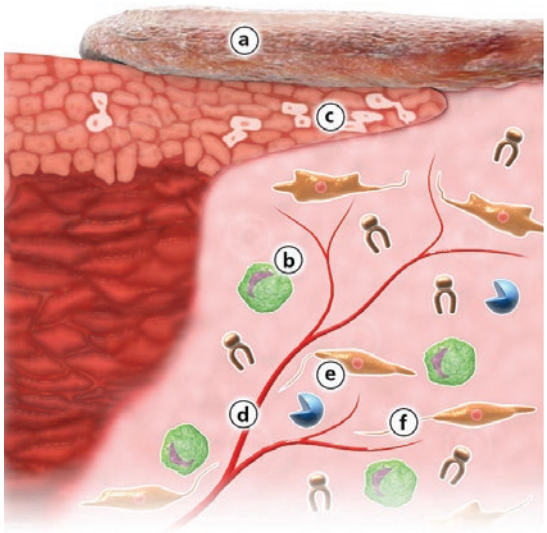
Chronic wounds are characterized by a destroyed or damaged ECM incapable of contributing to wound healing.

The most common types of chronic wounds are:

- pressure sores
- venous leg ulcers
- diabetic foot ulcers
- ulcers of different etiology.

In chronic wounds, growth factor activity is reduced and matrix metalloproteinases (MMPs) are superabundant. The combination of these two features leads to ECM degradation.

Normal healing process in acute wounds



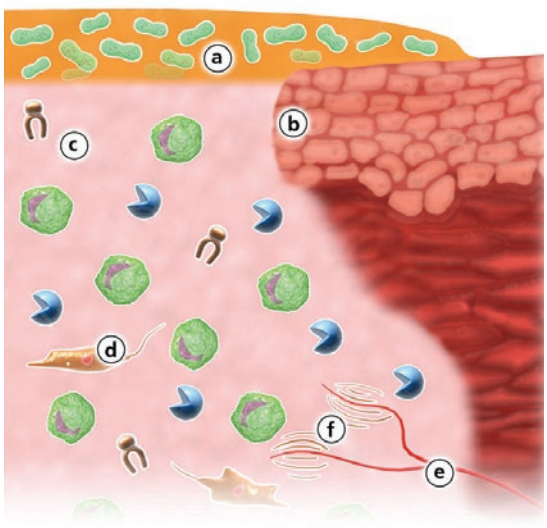
Initial phase

ⓐ Scab formation
ⓑ Immune cell infiltration

Healing phase

ⓒ Re-epithelialisation
ⓓ Angiogenesis
ⓔ Fibroplast migration
ⓕ Collagen deposition

Impaired healing process in chronic wounds



Chronic wound abnormalities

ⓐ Colonization and infection
ⓑ Hyperproliferative epidermis
ⓒ Inflammation, exudate
ⓓ Fibroplast senescence
ⓔ Impaired angiogenesis
ⓕ Fibrin cuffs (barrier to oxygen)

What are BIOPAD's advantages?

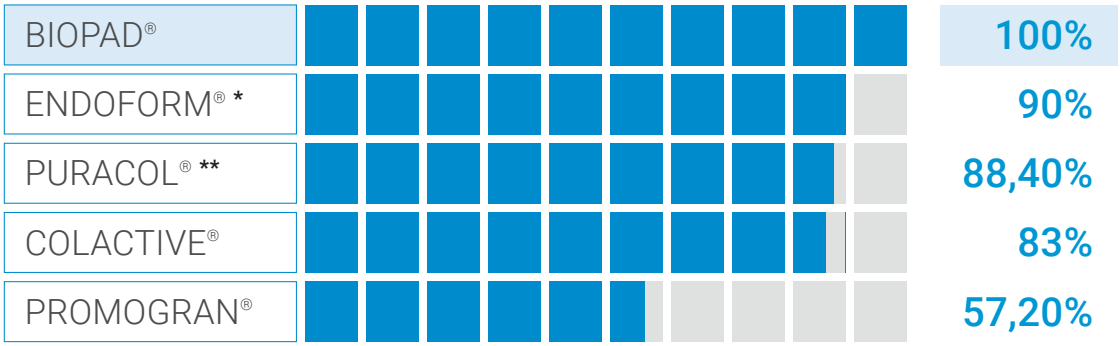
- it speeds up the wound healing processes
- it prevents traumas to the granulation tissue
- it has a hemostatic effect
- It is free from BSE-related risks
- It is not affected by chemical cross-linking processes
- It is well tolerated and easy to use
- It is available in different formulations

Our solution

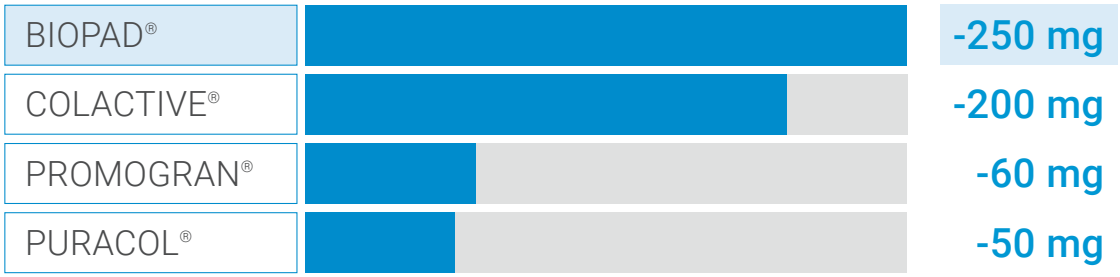
BIOPAD® is an ivory-white soft sponge made exclusively of type I collagen of equine origin that keeps its native structure

BIOPAD® has the highest collagen content currently on the market (250 mg of collagen)[3]

Collagen content (%)[3]



Collagen content (mg)[3]



***** Manufacturer's statement
****** Puracol collagen content determined under this method was 88.4%, which differs from the manufacturer's statement of 100% collagen content
Collagen content (%)3
Collagen content (mg)3

(3) JC. Karr et al (2011): Adv Skin Wound Care 24:208-216

BIOPAD® indications

- pressure sores
- donor sites and other bleeding surfaces
- dehisced surgical incisions
- draining wounds
- lacerations
- venous stasis ulcers
- diabetic ulcers
- partial and full thickness wounds
- post-laser surgery
- podiatry
- surgical and traumatic wounds

Preparations

1. Prepare the wound bed as per the facility's wound care protocol and debride the wound when necessary.

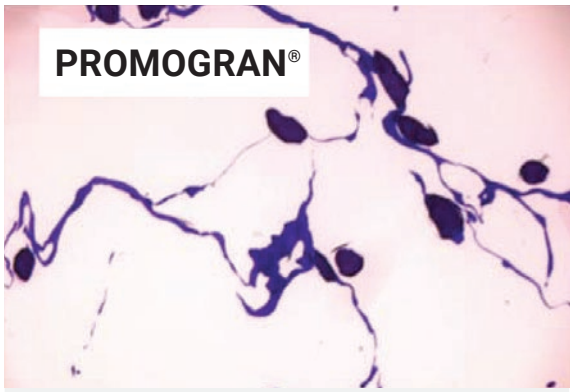
2. Cut BIOPAD®, if necessary, to fit the size of the wound
Wound with limited exudate: hydrate BIOPAD® with sterile saline solution
Wound with heavy exudate: do not hydrate BIOPAD®. Rinse out the wound bed with saline solution prior to application.

Application

3. Apply it directly onto the wound bed, covering the entire wound; do not overlap the edges of the wound. The gel that is formed with the wound exudate is biodegradable and does not need to be removed.

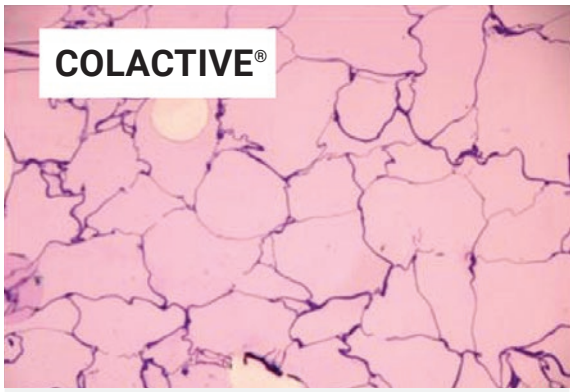
4. Apply a secondary dressing as per the physician's protocol to cover BIOPAD®.
Depending on the amount of exudate, BIOPAD® can be reapplied every day or as per the physician's protocol. If the wound has a small amount of exudate, BIOPAD® can be reapplied every 48 hours or as per the physician's protocol.

Competitive analysis.
Why is BIOPAD® better than others?



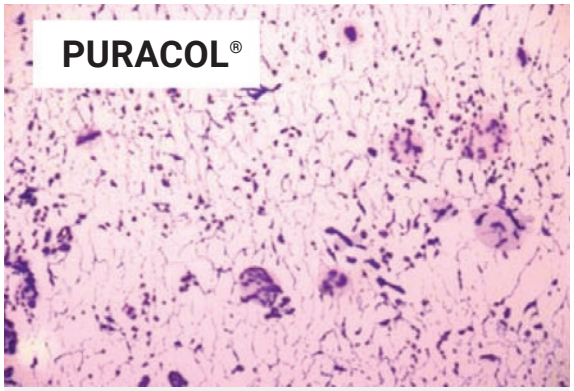
The high value for the mesh area indicates that there are too few collagen strands (8 µM - 12 µM)

Fibroblasts do not interact very easily with PROMOGRAN®



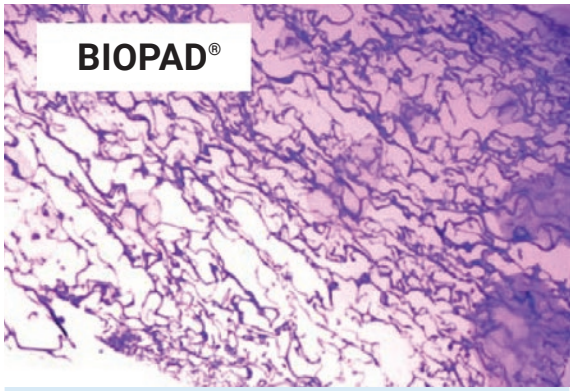
COLACTIVE® has a reasonable value for the mesh area, but this value is associated with thin collagen strands (< 2 µM)

Fibroblasts do not interact very easily with COLACTIVE®



Collagen strands are densely distributed, but this value is associated with thinner collagen strands (0.2 µM)

Fibroblasts do not interact very easily with PURACOL®



BIOPAD® has a reasonable value for the mesh area and this value is associated with thicker collagen strands (4 µM)

Fibroblasts have an "active behavior"

Ultrastructural investigation on fibroblast interaction with collagen scaffold

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Abstract: Collagen-based scaffolds are used as temporary or permanent coverings to help wound healing. Under natural conditions, wound healing is affected by such factors as cell types, growth factors and several components of the extracellular matrix. Due to the complexity of the cell-to-matrix interaction, many cell based mechanisms regulating wound healing *in vivo* are not yet properly understood. However, the whole process can be partially simulated *in vitro* to determine how cells interact with the collagen scaffold in relation to such features as physico-chemical properties, matrix architecture and fiber stability. Under these conditions, cell migration into the collagen matrix can be easily assessed and causally correlated with these features. In this study, we aimed at providing a structural analysis of how NIH3T3 fibroblasts migrate and proliferate *in vitro* when seeded on a native type-I collagen scaffold. To this end, samples were collected at regular time intervals and analyzed by light microscopy (LM), scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Through this experimental approach we demonstrate that collagen is gradually frayed into progressively thinner fibrils as fibroblasts migrate into the matrix, embrace the collagen fibers with long filopodia and form large intracellular vacuoles. A key role in this process is also played by microvesicles shed from the fibroblast plasma membrane and spread over long distances inside the collagen matrix. These observations indicate that a native type-I equine collagen provides favorable conditions for simulating collagen processing *in vitro* and eventually for unraveling the mechanisms controlling cell uptake and intracellular degradation. © 2015 Wiley Periodicals, Inc. J Biomed Mater Res Part A: 00A:000–000, 2015.

Key Words: fibroblasts, collagen matrix, electron microscopy, *in vitro* culture, microvesicles

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INTRODUCTION

Wound healing is a physiological process naturally addressed to repairing skin injury. It consists of a complex cascade of molecular events, from removal of damaged tissues to restoration of normal morphogenesis.[1,2] To this end, the extracellular matrix provides a structural scaffold for cells to migrate through the wound area and differentiate into specific functional types.[3] As a major constituent of the extracellular matrix, the collagen plays a key role in the regenerative process of the wound by acting as an anchoring support for the migrating cells.[4,5] Because of its relative abundance in bodily proteins, low immunogenicity and high stability, the collagen is *par excellence* the best biomaterial employed as a prosthetic medical device to treat dermal injury.[6,7] However, to satisfy these requirements, the collagen scaffold should be endowed with such physico-chemical properties as mechanical integrity, structural uniformity and have a matrix porosity suitable for sustaining cell migration.[8] In addition, the matrix itself should be such to be retained on the wound bed for time intervals sufficient to complete tissue remodelling.[9]

Prosthetic collagen matrices differ in absorption and stability depending on the type and concentration of chemical substances added to modulate these capacities.[10–12] Therefore, a wide variety of collagen-based dressings differing in structural and biochemical properties have been developed with the intent to simulate the overall function of the extracellular matrix and improve the regenerative process of the injured area in normal or chronic situations.[13,14] Amongst the physiological variables that characterize the collagen matrix, the overall three-dimensional architecture and porosity are the most relevant since they condition such cell behaviours as proliferation, migration and, ultimately, signalling and differential gene expression.[15–17] Matrices with high porosity values provide healthier healing environments, especially in case of chronic wounds, due to their capacity to absorb more efficiently blood and lymphatic fluids from the wound area.[9,18]

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