Endorsed by academics and practitioners
No wound healing without oxygen

„In the absence of other wound healing inhibitory factors local hypoxia is the central problem of an impaired wound healing.“

Prof. Dr. med. Knut Kröger
Director of the Department of Vascular Medicine, HELIOS Klinikum Krefeld, Germany
Chronic wounds: Hypoxia prevents healing!

K. Kröger, J. Dissemend, M. Storck, A. Risse, P. Engels

ABSTRACT

In many chronic wounds, there is a prolonged undersupply of oxygen to the tissue (hypoxia). This rapidly leads to a slowing or stagnation of wound healing processes, since numerous molecular processes are dependent on a sufficient supply of oxygen or are induced by reactive oxygen species (ROS). The most common chronic wounds are venous crural ulcers, foot lesions in peripheral arterial occlusive disease (PAOD) and/or diabetes mellitus and decubitus. What they all have in common is a vascular component that either promotes their development or prevents their healing through local hypoxia. If no other wound-healing inhibitory factors such as infections, hypothermia, macerations or pressure are present, local hypoxia is the pathophysiological correlate of impaired wound healing. Besides causal treatment of the primary disease to improve the supply of oxygen to the affected tissue, phase-adapted wound treatment is the basis for a positive healing prognosis. Beyond this, innovative therapeutic options are now available for wound treatment by means of an additional local improvement of the oxygen supply in the wound.

KEYWORDS

Chronic wound, hypoxia, oxygen, wound healing, reactive oxygen species, crural ulcers, PAOD, diabetes mellitus

Prof. Dr. med. Knut Kröger
Director of the Department of Vascular Medicine,
HELIOS Klinikum Krefeld GmbH
Lutherplatz 40 - 47805 Krefeld,
E-Mail: knut.kroeger@helios-kliniken.de

Prof. Dr. Joachim Dissemend
Department of Dermatology, Venerology and Allergology, with Outpatient Clinic
Essen University Hospital

Prof. Dr. Martin Storck
Clinic for Vascular and Chest Surgery, Karlsruhe

Prof. Dr. Alexander Risse
Klinikzentrum Nord Diabetes Centre, Dortmund

Dr. Peter Engels
EngelsConsult, 51429 Bergisch Gladbach

From: Kröger et al, Wundmanagement 05/2012: Chronic wounds: Hypoxia prevents healing!
Wound healing: An innovative solution

“As a natural transporter substance, haemoglobin allows oxygen diffusion to the wound base.”

Dr. Alexander Risse
Doctor in Charge, Center for Diabetes, University Hospital Dortmund, Germany
With Granulox

Haemoglobin is able to bind oxygen and then release it again. When sprayed onto the wound, the water-soluble, red haemoglobin spray Granulox is uniformly distributed in the exudate, binds oxygen from the surrounding air and transports it to the wound base, from where it diffuses into the cells. This process repeats itself continuously and without using up haemoglobin. In this way, large quantities of oxygen can be brought to the wound base.

Without Granulox

Increased oxygen requirement, but poor oxygen supply. The need for oxygen is particularly high in all phases of wound healing because of increased metabolic activity. The primary disease (CVI, pAOD, diabetes) leads to inadequate oxygen supply via the vascular system (hypoxia). Even oxygen from the outside cannot reach the wound base, because the wound exudate forms a diffusion barrier.

The oxygen supply of the cells is increased, the hypoxia reduced. The wound situation improves and wound healing is accelerated.
Clinical proven efficacy

“It’s simple, it’s effective and there are no side effects!”

Prof. Dr. Petr Arenberger
Head of Department of Dermatology, Charles University, Prague, Czech Republic
Topical hemoglobin promotes wound healing of patients with venous leg ulcers

Abstract

Background. Improvement of oxygenation is getting increasing attention as an important aspect in the modern wound care. The aim of such complementary wound care approaches is to improve and accelerate wound healing.

Patients and methods. A solution comprising purified hemoglobin was added to the standard wound care procedure of patients with venous leg ulcers and compared to a second group without addition of the hemoglobin. In each group, 36 patients were included. The duration of treatment was 13 weeks. Primary end point was reduction of wound size or wound closing.

Results. In the group treated with the additional hemoglobin solution, an average of 53% of wound size reduction was obtained. No statistically significant reduction was observed in the second group.

Conclusion. The addition of hemoglobin solution in the wound care procedure for venous leg ulcers showed a significant improvement of wound healing in comparison to a control group.

Keywords
Oxygen · Wound healing · Wound therapy · Wound area · Wound treatment

Mean relative wound reduction

With Granulox: 53% average reduction in wound size after 13 weeks
Superior cost efficiency

“From a financial point of view, the Granulox combination treatment is superior to all other alternative treatments.”

Prof. Dr. Dr. Wilfried von Eiff
Healthcare Economist and Head of Centre for Hospital Management,
Westphalian Wilhelms University of Münster, Germany
4. **Conclusion**

Granulox combination therapy has proved to be economically markedly superior to all other therapeutic approaches, both in the HTA approach, taking into consideration quality and risk components, and in the standard calculation, as well as in the individual case studies.

The treatment time up to wound closure of 60 days is five times lower (conventional dry therapy) or 53.3% shorter (hydroactive therapy) than in alternative therapy regimens. The costs of overall therapy are 10 times (conventional dry therapy) or 28.3% (hydroactive therapy) lower.

On the basis of the surrogate parameters early wound closure, social mobility and low number of visits to the doctor, the patient outcome can be rated as significantly better than in all other alternative therapeutic approaches.

The present expert report impressively demonstrates the efficiency-boosting contribution made by innovations in the health care system. The mechanism of action of Granulox removes an obstacle to wound healing that delays the healing process, which could not be overcome by existing products. A complementary application of Granulox is therefore to be recommended on a broad front in order to achieve a sustained increase in the efficiency of existing therapy regimens and reduce the cost burden on the health care system.

---

**Average total costs of wound therapy from start to successful wound closure**

- **Granulox therapy**: 630,77 €
- **Hydroactive therapy**: 809,47 €
- **Conventional dry therapy**: 4,960,48 €

The Granulox combination therapy saves 22% in costs compared to a modern hydroactive therapy and 87% compared to a conventional dry treatment.
Convinced experts

“Its rapid – and international – establishment on the market can only be regarded as desirable.”

Prof. Dr. Joachim Dissemond
Doctor in Charge, Clinic and Policlinic for Dermatology, Venerology and Allergology,
University Hospital Essen, Germany
Dear Mr. Sander,

it is a great pleasure for me to provide you with my assessment of Granulox.

Where no other factors are at play to inhibit wound healing, then local hypoxia represents one central aspect and is the pathophysiological correlate of disturbed wound healing. Although these mechanisms have been known for decades, Granulox is the first topical product offering an effective and at the same time cost-efficient approach to solving this problem. Its innovative mechanism of action using highly purified haemoglobin to transport oxygen through the exudate into the base of the wound appears just as simple as it is ingenious.

I can confirm from my own experience and from discussion with numerous colleagues that wound healing is often clearly accelerated by Granulox or, in some particularly refractory disease courses, only made possible by it. To have also substantiated its efficacy with a clinical trial is an absolute and commendable exception for a medicinal product.

When combined with an adequate causal form of therapy, Granulox therefore offers not only many wound patients the perspective of a more rapid recovery with a significantly improved quality of life, but potentially also economic relief for doctors and the health system as a result of the often significantly shorter treatment times. Its rapid - and international - establishment on the market, as well as the generation of further clinical experience, can therefore only be regarded as desirable.

Yours sincerely,

Prof. Joachim Dissemond, MD
Convincing practical experiences

“The wound had persisted for several years. After a few weeks of Granulox treatment, the wound had closed.”

Nesat Mustafi
Head of Outpatient Wound Care, Hospital Frankfurt North-West, Germany
Only 6 from thousands of successfully healed wounds

Start of treatment | After 22 weeks
--- | ---
Patient: 85 years, female, arterial crural ulcer Existing for 7 years before Granulox

Start of treatment | After 15 weeks
--- | ---
Patient: 43 years, male, venous crural ulcer Existing for 8 years before Granulox

Start of treatment | After 8 weeks
--- | ---
Patient: 65 years, female, amputation wound Existing for 8 weeks before Granulox

Start of treatment | After 11 weeks
--- | ---
Patient: 75 years, female, ulcus cruris arteriosum Existing for 3 years before Granulox

Start of treatment | After 4 weeks
--- | ---
Patient: 44 years, male, surgical wound Existing for 9 weeks before Granulox

Start of treatment | After 24 weeks
--- | ---
Patient: 73 years, female, ulcus cruris venosum Existing for 6 years before Granulox
Granulox at a glance

„At last, not just another PU foam, but a genuine innovation!“

Anita Mysor
Wound Manager, Wundmanagement Mysor, Straelen, Germany

Ingredients
10% carbonylated haemoglobin; 0.7% phenoxyethanol; 0.9% sodium chloride; 0.05% N-acetylcysteine; to 100 ml with water.

Interactions
Do not use with locally-acting drugs such as antibiotics. Action impaired by: disinfectants and proteolytic (enzymatic) debridements.

Contraindications
For safety reasons, Granulox should not be used on infected wounds or during pregnancy. Sufficient data is not yet available to evaluate these cases.

Storage
Long periods of non-use: refrigerator, 2°C - 8°C. On days of use: room temperature, max. 25°C. On daily use it may also be stored for up to 6 weeks.
Granulox is a haemoglobin spray to support the healing of chronic wounds.

Works for many kind of wounds
Granulox accelerates wound healing for a multitude of indications, e.g. diabetic foot ulcers, secondary healing of surgical wounds, venous crural ulcers, arterial crural ulcers, mixed crural ulcers, decubitus ulcers.

Reimbursable
Granulox can be invoiced pursuant to section 3 subsection 1 of the German Social Security Code (SGB V).

30 applications per spray container
One spray of 1-2 seconds is normally sufficient to cover a wound area of 2 x 3 cm.

No side effects
Granulox contains pure haemoglobin – a completely natural oxygen transporter, existing in the body’s red blood cells as well. Thus, side effects are not known – even if applied to frequently.

Easy application
Application of the red Granulox spray can be adapted to the usual rhythm of dressing changing (i.e. every 1-3 days, depending on the wound phase).

1. Thoroughly flush the wound with a physiological solution within the scope of routine wound cleaning.
2. Spray with Granulox from a distance of 5 to 10 cm.
3. Cover the wound with a breathable/non-occlusive wound dressing.