Granulox®

Spray for treatment of chronic wounds

Haemoglobin spray for wound healing
Haemoglobin spray for wound healing

The Company

The Market

The Efficacy

The Product
The company

scientists

90%

90%

25%

75%

Sangui BioTech International, Inc.

Sangui BioTech GmbH, Witten
– patent holder –

SanderStrothmann GmbH

SastoMED GmbH
– worldwide licensee –
Overview

Germany

4,000,000* Wounds
5,000 Amputations

*Mean value from literature, information differ between 2.5 and 6 Mio.
Overview | Germany

This costs the economy 6.000.000.000 € annually.
diabetes - number 1 public health problem

5% prevalence rate of diabetes mellitus worldwide (WHO, 2012)

development of diabetic foot ulceration in 20% of the 346 million people with diabetes worldwide (WHO, 2012)

438 million people will suffer from diabetes by 2030, of which up to 25% may develop foot ulceration (WHO)

hence 109.5 million chronic wounds just due to diabetes in 2030
Chronic wounds | Germany

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic foot syndrome (DFS)</td>
<td>650,000</td>
</tr>
<tr>
<td>Artery occlusive disease (AOD)</td>
<td>455,000</td>
</tr>
<tr>
<td>Ulcus cruris (UC)</td>
<td>357,000</td>
</tr>
<tr>
<td>Secondary healing</td>
<td>747,500</td>
</tr>
<tr>
<td>Other wounds</td>
<td>455,000</td>
</tr>
<tr>
<td>Decubitus</td>
<td>585,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3,250,000</strong></td>
</tr>
</tbody>
</table>
Chronic wounds
Diabetic foot syndrome (DFS)

- syndrome related to diabetes mellitus
- destruction of bones and tissue of the foot connected with polyneuropathy
Chronic wounds | Arterial occlusive disease (AOD)

Disturbance of peripheral arterial circulation of extremities

- arteriosclerosis
- narrowing (stenosis) or closure (occlusion) of supplying artery
Chronic wounds
Ulcus cruris (UC)

Ulcer on the lower leg

Types:
ulcus cruris venosum,
mixtum, arteriosum and more

Frequent cause:
chronic venous insufficiency
(venous weakness)
Chronic wounds | Decubitus

Decubitus ulcer, bedsores

- locally limited damage to the skin and/or the underlying tissue

Cause:
bedsore/ lying in one spot for a long period of time
Hospital and ambulatory care

- only 5% of all treatments take place within hospitals
- 95% are dependent on ambulatory, home care
Main functions of wound care products:
1. moisture management
2. protection

Illustration from the book: Vasel-Biergans, Anette „Wundauflagen für die Kitteltasche“
Why is this situation still the same – after so many years?

... because all allegedly innovations are missing at least one important target!

To change this situation fundamentally, the treatment approaches have to be:

- effective
- available for ambulatory care
- affordable

for patients, treating physicians and health insurances.
Key success factors

**Effectiveness**
- Quicker and better healing than existing concepts, also for stagnant wounds.

**Availability**
- To make products available for ambulant care it has to be ensured that the acquisition costs of required materials and utensils, treatment time per procedure, transportability of the necessary materials and the training expense of the implementing personnel for mobile nursing services are supportable.

**Affordability**
- Treatment costs within a frame, which can be financed permanently by benefactors within the healthcare system.
Joint aetiology

- different primary diseases lead to a circulatory disorder
- this results in a local oxygen deficit (hypoxia)
- almost all chronic wounds are hypoxic

Especially wounds need a lot of oxygen!
- massive tissue formation, division of cells, immunoactivity require significantly more oxygen metabolism activity within a wound than within intact tissue
- the required additional energy is provided by consumption of oxygen.
- the oxygen demand increases!

If the wound is missing oxygen, healing or regeneration processes are not taking place or only delayed!
Dependence of different metabolic processes from the oxygen saturation
Consequence:
Stagnation of the wound healing in the case of hypoxia

- TcPO2 << 30mmHg
- Injury / wound
- Inflammation
- Proliferation / granulation
- Healing stagnation
- Collagen III synthesis
- Fibronectin synthesis
- Collagen I
- Neutrophil
- Myofibroblasts
- Macrophages
- Fibroblast
- Increase the elasticity
The conclusions are that neither the optimum rate of epidermal cell migration nor the maximum new cell production of which the epidermis is capable is expressed during normal wound healing. The path of the migrating epidermal cells and damage to the superficial blood vessels causes an acute shortage of oxygen at the wound surface. The results of the various experiments reported here strongly suggest that the epidermis can utilise more oxygen if it is made available by switching from anaerobic to aerobic metabolism of carbohydrates which results in more rapid epidermal regeneration. Nature can be improved upon by using dressings that prevent scab formation and are oxygen permeable.

>> Wound healing requires hypoxia control. <<

George D. Winter
Hypoxia | Background

Problem: Partial pressure of oxygen is insufficient

- cells need at least 20 mm Hg to survive (minimum)
- complex metabolism activities, especially wound closure / granulation require a minimum of 40 mmHg

Most chronic wounds are in this area.

- normal condition
- critical zone, wound healing impossible
- the tissue dies in most cases

Partial pressure of oxygen in mmHg
Hypoxia | Treatment options

- Improvement of oxygen supply due to improvement of blood circulation within the frame of an adequate causal therapy

→ Oxygen is provided from the inside.

- Additional support by oxygen supply from the outside

→ Oxygen from the air has to be made available for cellular activity at the base of the wound.
Oxygen barrier

■ The exudate presents a diffusion barrier for oxygen.

■ Already a liquid film of 20 micrometer blocks 95% of the diffusion.

→ Even though sufficient oxygen is available within the air, it can’t get to the base of the wound due to the diffusion barrier. Therefore the oxygen requirement of the cells can’t be fulfilled.
Oxygen barrier

The exudate prevents the supply of oxygen from the surrounding air to the base of the wound.
Principle of haemoglobin

- use of a natural oxygen transporter
- transporter takes oxygen from the surface down to the base of the wound
- unloading at the base of the wound
- transporter takes again oxygen from the surface
- rotating procedure

→ Principle of simplified diffusion!
Principle of Haemoglobin

Haemoglobin as transport molecule takes oxygen to the base of the wound.
1 g hemoglobin transports 1 liter oxygen within one day
Granulox® | Legal status

- the principle of facilitated diffusion is solely physical
- neither a pharmacologic nor an immunologic or a metabolic effect takes place
- there is no interaction with a cellular component
- therefore the product is Medical Device Class III
Easy use

1. cleaning/flushing of wound

2. application of Granulox®

3. covering of wound area
Granulox® | Suitable wound dressings

<table>
<thead>
<tr>
<th>hydropolymer dressings / foam dressings</th>
<th>spacer grids</th>
<th>superabsorbents/ hydrofibres</th>
</tr>
</thead>
<tbody>
<tr>
<td>adhesive / nonadhesive</td>
<td>Adaptic®, Sytagenix UrgoTül, Urgo</td>
<td>Aqualcel, ConvaTec Cutisorb®Ultra, BSN Suprasorb®X, Lohmann&amp;Rauscher</td>
</tr>
<tr>
<td>with and without silicone coating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tegaderm™Foam, 3M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mepilex®, Mölnlycke</td>
<td></td>
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<tr>
<td>Tielle®, Sytagenix</td>
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<tr>
<td>Allevyn®, Smith&amp;Nephew</td>
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<tr>
<td>Cutimed®, BSN</td>
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<tr>
<td>UrgoCell, Urgo</td>
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<tr>
<td>Hydro Tac, Hartmann</td>
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<tr>
<td>Suprasorb®P, Lohmann&amp;Rauscher</td>
<td></td>
<td></td>
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<tr>
<td>Biatain, Coloplast</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Granulox® | limited suitable dressings

<table>
<thead>
<tr>
<th>hydrogels</th>
<th>film dressings</th>
<th>alginateas</th>
</tr>
</thead>
<tbody>
<tr>
<td>NuGel, Systagenix</td>
<td>Tegaderm™ Film, 3M</td>
<td>Sorbalgon, Hartmann</td>
</tr>
<tr>
<td>UrgoHydrogel, Urgo</td>
<td>Bioclusive®, Systagenix</td>
<td>Trionic, Systagenix</td>
</tr>
<tr>
<td>Intrasite Gel, Smith&amp;Nephew</td>
<td></td>
<td>Melgisorb®, Mölnlycke</td>
</tr>
<tr>
<td>Hydrosorb Gel, Smith&amp;Nephew</td>
<td></td>
<td>Cutimed® Alignat, BSN</td>
</tr>
<tr>
<td>Hartmann Purilon, Coloplast</td>
<td></td>
<td>Kaltostat®, ConvaTec</td>
</tr>
</tbody>
</table>
Granulox® | Unsuitable wound dressings

- Hydrocolloid dressings
- Occlusive film dressings
- VAC-systems
Available? – YES!
Studies confirm the efficacy of this treatment approach!
Inclusion criteria

- **patients > 18 years**
- **ulcus cruris venosum**
  - > 8 weeks
- **wound area**
  - > 2.5 cm² < 50 cm²
- **ABI**
  - > 0.8
  (ankle brachial index)

Additional diagnostic measures for characterization of patients: ultrasound duplex scan and foot pulse measure

- **hospitalisation**
  - for 2 weeks
- **treatment**
  - according to current hospital therapeutic schedule

  **incl. compression***
  - before inclusion until start of treatment – during the day: compression therapy
  - perpetuation of the compression therapy during the whole treatment period - integral part and monitored
  - compression bandages with fairly high compression pressure through a constant perimeter at the ankle

- **no treatment success**
  - = inclusion

  **T₀ of treatment**

- **treatment success**
  - = no inclusion, continuing the therapy
Results
Absolute & percentage change of the wound area

Continuous reduction of the wound size during the treatment period in the hemoglobin group.
Results

Significant reduction of wound size by using hemoglobin spray; in comparison to the control group average 53% (p<0.0001)
Examples of application

Male patients; 43 years; for 8 years | relapsed undulant ulcer
Period of treatment: 1. half year 2012
Treatment location: Pflegedienst Duisburg, Germany

Before the treatment with Granulox the patient opposed a recommendation for amputation.

Today the wound is healed totally.
Examples of application

Male patient; 58 years | Ulcus cruris on the lower left leg; CVI; Diabetes mellitus
Period of treatment: 1. half year 2012
Treatment location: Krankenhaus Nordwest, Frankfurt a.M., Germany

start

2 weeks

4 weeks

7 weeks
Effective? – YES!
Affordable?

- can sufficient for approx. 30 uses
- costs per use between 2 and 4 € in Germany
Influence of Granulox® on speed of healing.
Comparison of healing speed

Absolute decrease of wound size in mm² per day

- Hydroactive: 3*
- Granulox®: 9.3

*Mean value from literature
Comparison of healing speed

Study Result

- The healing speed of Granulox is with a wound decrease of 9.3 mm² per day three times as quick as with hydroactive treatment.

Economic View

- For reasons of care a 33.33% safety margin is taken into account and the healing speed is considered only twice as high.
Economy

- *110 days* for Hydroaktive
- *61,80 €* in costs/week for Hydroaktive
- *971,14 €* in total costs for Hydroaktive
- *55 days* for Hydroaktive + Granulox®
- *74,30 €* in costs/week for Hydroaktive + Granulox®
- *583,79 €* in total costs for Hydroaktive + Granulox®

50% quicker healing time
40% decrease total costs

*Source: Augustin et al. 1999*
The clinical center Munich Pasing is an efficient clinical center with space for 430 patients – with focus on specialised medical services. Comprehensive modern diagnostic and therapeutic facilities as the best option for an individual care in the specialised departments.

- approximately 550 patients with chronic wounds per annum
- 115,180 € costs per annum for wound care
  (not included: vacuum therapy and maggot therapy)
Case Study 1

patient: male, 74 years
primary disease: pAOD, stage IV according to Fontaine
wound: ulcer cruris arteriosum lower leg (left)

Wound treatment before Granulox®:
- amorphous gel
- collagen
- protection of wound edges
- superabsorbent
- UAW

Dressing change cycle:
- 2-3 per week
Case study 1: Costs per dressing

<table>
<thead>
<tr>
<th></th>
<th>without Granulox®</th>
<th>costs</th>
<th>with Granulox®</th>
<th>costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>material</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>amorphous gel</td>
<td></td>
<td>1,36 €</td>
<td>Granulox®</td>
<td>5,32 €</td>
</tr>
<tr>
<td>collagen</td>
<td></td>
<td>7,98 €</td>
<td>absorbent dressing</td>
<td>3,18 €</td>
</tr>
<tr>
<td>superabsorbent</td>
<td></td>
<td>5,37 €</td>
<td></td>
<td></td>
</tr>
<tr>
<td>protection of wound edges</td>
<td></td>
<td>1,08 €</td>
<td></td>
<td></td>
</tr>
<tr>
<td>sum</td>
<td></td>
<td>15,79 €</td>
<td>sum</td>
<td>8,50 €</td>
</tr>
</tbody>
</table>
Case study 1:
Total treatment costs

![Graph showing costs over weeks with and without Granulox®.](image-url)
Case Study 2

patient: male, 75 years
primary disease: chronic venous insufficiency III according to Widmer
wound: ulcus cruris venosum, lower leg (left)

Wound treatment before Granulox®:
- amorphous gel
- Drainage-able PU foam dressing
- protection of wound edges
- Debrisoft

Dressing change cycle:
- 2-3 per week
Case study 2:
Costs per dressing

<table>
<thead>
<tr>
<th>Material</th>
<th>Without Granulox®</th>
<th>With Granulox®</th>
</tr>
</thead>
<tbody>
<tr>
<td>silver-calcium alginate</td>
<td>5.12 €</td>
<td>7.98 €</td>
</tr>
<tr>
<td>PU-foam dressing</td>
<td>10.33 €</td>
<td>10.33 €</td>
</tr>
<tr>
<td>protection of wound edges</td>
<td>1.08 €</td>
<td></td>
</tr>
<tr>
<td><strong>Sum</strong></td>
<td><strong>16.53 €</strong></td>
<td><strong>18.31 €</strong></td>
</tr>
</tbody>
</table>
Case study 2: Total medical costs

Without Granulox®:
- Average cost per week: €49.74
- Total cost: €2,586.48

With Granulox®:
- Average cost per week: €44.60
- Total cost: €178.40
Affordable? – YES!
Effective → Superior
Affordable → Cost-cutting
Available → Ubiquitarian
Spray for treatment of chronic wounds

Granulox® succeeds to improve the oxygen supply of chronic wounds and to support the granulation of new tissue. Granulox – an effective addition to causal therapy.