PROJECT

CHRONICAL OPEN WOUNDS TREATMENT

Authors and organisations

Organisations

Rode Kruis Ziekenhuis Beverwijk

Ardoz Research Gouda

Time schedule

Project started in 2001

Project is still in progress. This report is written in May 2004.

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General information

1.1 Abstract

The project was started by Ardoz Research Gouda and Rode Kruis Ziekenhuis Beverwijk for testing a liquid gel/composition developed by Ardoz for treatment of chronical open wounds that were treated in the past without result or progress.

This project concerns the use of a liquid gel/composition, capable of promoting the growth of tissue cells at the site of a wound, a process that promotes regeneration of tissue and wound healing. More particularly, the present gel relates to the use of a liquid gel/composition comprising a component (a) selected from the salts consisting of cations A_n^+ and anions derived from halogen oxides according to the general formula $[O_mX]^-$, a component (b) selected from the group of oxygen donors, and a component (d) selected from the group of liquid binders for the treatment of open wounds and burns.

All selected patients were treated in the past with other medication by other hospitals or specialists without success. The patients came from all over the Netherlands. Only patients with chronical open wounds were selected for this project. The preselection took place in the Rode Kruis Ziekenhuis by Prof. Dr. Kreis. Once in 2-8 weeks the patients returned to the hospital for consult until released by Prof. Dr. Kreis.

1.2 Introduction

The process of healing open wounds and burns is a very complex, not fully understood process. Nowadays the most common means of treating open wounds or burns mainly comprise temporary wound closure/covering for protection against e.g. moisture loss and infection using autografts, dermal replacement products or hydrogels such as alginates, administration of substances for cooling and pain relief, and promoting wound healing by administering drugs which are usually hemostatic for suppressing bleeding in the wound region, anti-inflammatory for suppressing inflammation, sterilizers for sterilisation so as to prevent miscellaneous bacteria from invading the wound, or drugs with a combination of the above pharmaceutical effects. However, at present "reconstruction of tissue" as the final stage of wound healing has to rely on the auto-therapy inherent in living bodies.

Open wounds or burns that have impaired blood flow are often characterised by a delay or complete failure of the healing process. This is ascribed to the fact that in hypoxic tissue resistance to infection is lower and the fact that the process of auto-therapy is compromised. Wound oxygenation therefore has long been known to be beneficial in the healing of (chronic) wounds and burns. The healing of wounds and the effect of oxygen thereon has been intensively studied, a useful summary is presented in J.D. Whitney, "Physiological Effects of Tissue Oxygenation on Wound Healing", HEART & LUNG, september 1989, Vol. 18 No. 5, pp. 466-474.
Supplying an environment, rich in molecular oxygen, to the open wounds or burns, is believed to be beneficial in wound healing by activating the cells present at the periphery of wound sites by promoting their metabolism and by stimulating phagocytosis and killing of bacteria by neutrophils or polymorphonuclear cells (PMNs), which involves the production of oxygen radicals and superoxides and is directly influenced by the oxygen concentration in the tissue.

Active oxygen is quite different in view of chemical species and biochemical activities from ordinary molecular oxygen. While ordinary oxygen contributes only to metabolism but does not function as bio-signals for the growth of the cells, the active oxygen does not contribute to the metabolism but function as bio-signals for the growth of the cells.
In auto-therapy, the reconstruction of the tissues at the wound site is conducted through the following processes: (1) macrophages gathering at the wound site yield growth factors and enzymes, (2) the growth factors and the enzymes are activated, (3) the activated growth factors and enzymes stimulate increase or movement of fibroblasts to grow the cells, and (4) the tissue is reconstructed (regenerated) by the grown new cells.
In the case of auto-therapy, macrophages gathering at the wound sites produce active oxygen and the active oxygen functions as bio-signals to activate the growth factors and the enzymes yielded also from the macrophage. That is, it is known that active oxygen contributes to activation of growth factors and enzymes in process of auto-therapy. Active oxygen supplied from the outside activates the growth factors and the enzyme together with active oxygen produced spontaneously from macrophage and promotes the growth of cells by the process similar with that of the auto-therapy. As a result, growth of the cells is further promoted and the tissues at the wound site are reconstructed (regenerated) in a shorter period of time.

A plurality of methods for supplying either normal molecular oxygen or active oxygen to open wounds or burns is generally known in the art.

There is thus still a need for a medicament for treatment of open wounds and burns, capable of promoting wound healing through the mechanism of auto-therapy, most preferably by supplying oxygen to the wound, either ordinary molecular oxygen or activated oxygen, which is convenient to use and easily and cost-effectively stored and produced.

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Description of the Study

2.1 Scientific/Medical Approach

Total number of patients involved in this project: ***60***

What kind of wound types were treated during the project: ***chronical open wounds, caused by diabetes, disfunction of vascular system or uncontrollable infection.***

What kind of treatment did the patients endure before the project: ***vaseline, corticosteroides, wound washes, unguents like Fucidine, Flamazine to resist staphylococcus infection, gentles, skin transplantation, surgical removal or amputation.***

Total number of patients with healed wounds: ***36***

Total number of patients still in treatment : ***23***

One patient died after heart attack: ***1***

Examples:

In **example A**, an open lateral wound on the left lower leg, which had arisen spontaneously in a diabetic patient, was treated by chemical sympathectomy and by topical application of a wound gel, that was prepared according to the present liquid gel/composition. It is generally known that the healing process of diabetic ulcers with the currently known treatments usually fail. After two weeks the wound was re-examined and an apparent improvement was seen; the wound surface had become cleaner. The treatment with the wound gel of the present liquid gel/composition was continued. In the following weeks the appearance of the wound became cleaner and after 14 weeks of treatment with the wound gel an apparent decrease in wound diameter became observable. The wound diameter had decreased 50 % when re-examined after 6 months of treatment. The treatment with the wound gel was continued. In table 2 a more extensive description of the healing process of the wound is presented by estimation of the wound surface and by description of the visual appearance of the wound at certain points during treatment.

In **example B**, an injury in the lower leg of a patient, which had become necrotic and contained haematoma, could not be treated with flammazine because of an allergy.

It was treated with a wound gel, according to the present liquid gel/composition, by filling the wound with the gel twice daily. After two weeks, re-examination revealed that the wound surface had decreased significantly and had a clean, normal appearance. It is generally known that the healing of necrotic injury with haematoma is almost untreatable with current common methods.

2.1.1. Project method

Patients selected for the project were seen by Prof. Dr. Kreis and Drs. W.F. van den Bosch. They agreed on the anamnesis of the patient and agreed on the treatment plan. Consulting took place on CWP (Chronische Wonden Poli) at the Rode Kruis Ziekenhuis Beverwijk. Patient information was gathered and registered by Prof.Dr. Kreis and Drs. Van den Bosch.

At the first consult the patient was told about the project they were selected for and treatment was started immediately. The patient received a certain amount of the liquid gel/composition and instructions how to treat the wound at home. Photographs were taken of the wound at the first consult in order to see the progress. The patients were asked to follow the instructions:

Instructions: Clean or wash the wound mechanically or rinse with water under the shower. Application of the liquid gel/composition of at least twice a day. After application close with ventilating wound-dressings.

After 2-8 weeks the patient returned for consulting. Photographs were taken in order to keep control on the progress. Patients received instructions to continue until treatment was not necessary anymore.

2.2 Results

We have surprisingly found that the active components from this gel can be used successfully for promoting the healing of open wounds and burns by, without being bound to theory, chemically slow releasing oxygen. A composition containing these components can be used for the manufacture of a medicament that, when applied topically, promotes the healing of open wounds and burns. In a preferred embodiment of the present gel this composition can be provided with an oxygen donor stabilising agent.

Please include supporting data such as photos, tables etc.

Chapter
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Discussion & Conclusion

3.1 Discussion

The composition is used for the manufacture of a medicament, which can be any type of medicament for topical application known in the art. Particularly preferred medicaments, according to the present liquid gel/composition, are a wound gel, a wound spray, or a wound dressing. The use of component (a) or component (b) in the manufacture of any medicament, which is intended to be used for treatment of open wounds or burns by combined application of component (a) and component (b) falls within the scope of the present liquid gel/composition. It may also be used to develop impregnated wound-dressings to cover burns/wounds.

The term "wound dressing", as used herein, particularly refers to any material applied to a wound for protection, absorbance, drainage, etc. Numerous types of dressings are commercially available, including films (e.g., polyurethane films), hydrocolloids (hydrophilic colloidal particles bound to polyurethane foam), hydrogels (cross-linked polymers containing about at least 60% water), foams (hydrophilic or hydrophobic), calcium alginates (nonwoven composites of fibers from calcium alginate), and cellophane (cellulose with a plasticizer). According to one embodiment of the present liquid gel/composition, the medicament is such a wound dressing, which is impregnated or coated with the liquid, wound healing composition of the present liquid gel/composition.

The compositions according to the present gel can optionally further contain additonal substances, which are customarily used in pharmaceutical products.
The composition, according to the present gel, is intended for use in the treatment of open wounds and burns. The term "open wound", as used herein, may refer to any type of tissue injury, but particularly to tissue injuries characterised by delay or complete failure of healing. Typical but non-limiting examples of such injuries are traumatic injury, including burns, injury resulting from surgery, diabetic wounds, pressure ulcers, arterial ulcers, decubitus ulcers, and venous stasis ulcers. The greatest benefits are achieved in injured tissues with compromised blood flow and oxygen supply.

Conclusion

Currently open chronical wounds are always very difficult to treat with common methods, as it can take (many)years to control and improve the wounds. The average treatment period is depending on external factors, like the condition of the patient, seriousness of the infection, size, depth and the medical cause of the wound. The involved patients in this project were problematic cases with failing treatment methods and without prospect of improvement. Sometimes amputation was indicated.

During this project it was found that about 80% of the chronical open wounds treated with the liquid gel/composition of Ardoz Research improved remarkably during the project. More than 50% of the patients (36 of 60) did not return for further treatment and could be sent home healed. The average treatment period is 3-12 months depending on wound depth and size. The treatment period did not depend on the medical cause of the wound. External factors like condition of the patient, seriousness of the infection influenced the treatment period.

The patients were content with the treatment: it was clean, it did not hurt, no operation needed, no dirty or stinky medication, no donor material needed, no addiction, no side-effects and positive involvement by the patients as the wounds improve.

During the project new type of wounds, such as burns and scars were selected for testing the liquid gel/composition. A revised report will be prepared in 2005.

Chapter
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List of References

Documents

Gouda	P207341 Ardoz Concept I	29/05/2003
Beverwijk	CWP bestand conc 14 11 03	05/02/2004

Chapter 5

Responsibility

Here come the signatures

Date: Prof. Dr. Kreis

Date: Drs. W.F. van den Bosch

Date: Drs. Ing. L. Changoer