WOUND HEALING & CELL BIOLOGY

Detailed phases of the healing process with the use of Derma GeL®, providing moist environment in conjunction with a porous isolating protective film – acting like a framework to enable:

- **a maximum rate of granulation;**
- **an increased wound contraction;**
- **a faster and healthy re-epithelialization.**

Including:

- **regulation of fibroblast proliferation and collagen synthesis by cytokines associated with standardized triterpenoids extracted from Calendula officinalis flowers and their topical anti-inflammatory activity;**
- **influence of Asiatic acid, Madecassic Acid and Asiaticoside extracted from Centella asiatica on collagen synthesis of type I and III .**

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There are four main phases in wound healing:

- **Haemostasis;**
- **Inflammation;**
- **Proliferation;**
- **Maturation.**

All wounds – including those made deliberately with a great deal of sterility during surgery – traverse these phases during the healing process.

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Haemostasis

Tissue damage leads to the release of a large number of chemical mediators and intercell messenger substances, called cytokines (interleukin-1beta, TGF beta). These messenger substances may be either growth or inhibitory factors and can initiate a complex interrelated series of events, which leads to haemostasis and healing or to disordered haemostasis and uncontrolled healing .

When the blood vessels are damaged , platelets which are present in the exposed blood that leaks into the wound are activated by contact with exposed collagen fibres in the vessels wall. They become sticky and adhere to each other and the vessel wall. The platelets form aggregates by the action of a prostaglandin called thromboxane A2. This aggregation of platelets can form a temporary plug in the vessel and reduces bleeding. Platelets release serotonin and other vasoconstrictors which reduces blood loss by vasoconstriction.

The clotting cascade is activated by the platelets, the vessel wall and coagulation factors (thromboplastin). The end products of each reaction in the cascade activates the next level. These reactions cause prothrombin to be converted to thrombin which in turn converts fibrinogen to fibrin. Induced by the presence of propylene glycol, hydrogenated castor oil, sodium bicarbonate, glycerin and standardized polyssacharides, the fibrin forms a stronger mesh like structure which acts like a framework to trap cellular elements of the blood and stabilize the platelet bung.

Following initial vasoconstriction the inflammatory process begins with the release of prostaglandin and activated complement proteins causing controlled vasodilatation and inflammation.

Findings:

The use of inappropriate products on wounds can interfere or modify haemostasis and can lead to negative repercussions on the following phases of the healing process.

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Inflammation

With the increase in blood from vasodilatation there is an increase in capillary permeability allowing blood plasma to leak into the surrounding tissue which produces **inflammatory exudates**.

Neutrophils and monocytes are attracted to the site of injury by a variety of chemotactic factors produced in response to tissue damage. Both these cell types need to be activated on arrival at the wound site.
Activation of these cells takes place by factors in their local environment. Following activation neutrophils rid the wound of contaminating bacteria. Monocytes undergo a phenotypic change to the activated macrophage.
The macrophage produces growth factors (FGF, PGEF) that can start, accelerate or modify the healing process. They also produce cytokines (TNF, interleukin-6) that act as messengers between individuals and other cells. Macrophages phagocytose and kill pathogenic organisms and scavenge dead tissue and neutrophils.
After 72 hours the macrophage is the dominant cell type to be found at the wound site. The formation of new blood vessels occurs with the release of angiogenic growth factors (HGF) which stimulate endothelial cell proliferation and stimulates the growth of the new blood vessels.

Findings:

Although inflammation is a normal phase in the healing process, regulated inflammation is beneficial for better healing and for patient comfort. On the other hand, extreme inflammation leads to excessive exudates and definitely interferes with the healing process.

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Proliferation

The formation of new connective tissue (granulation tissue) is dependent on the formation of the new blood vessels within the wound. As the capillary loops of the new vessels form and oxygenated blood reaches the wound bed the wound becomes less hypoxic and less nutrient deficient. The macrophages recruit a new cell type the fibroblast which lay down a network of collagen fibres surrounding the neovasculature of the wound. Fibroblasts also produce proteoglycans, that coat the collagen fibres and binds them together, giving them greater flexibility. They also produce fibronectin which holds the collagen and cells together. Granulation tissue formation usually begins after about +/-80 hours. For this process to proceed there must be a good supply of oxygen and nutrients. Essential nutrients are important in this process as they are required in the hydroxylation of proline to hydroxyproline an amino acid found in collagen.
During the proliferation phase two other processes also occur - epithelialization & contraction.

Findings:

Permanent bandaging induces excessive suppuration or may alter granulation tissue formation because of the lack of sufficient oxygen supply.

Essential nutrients with a targeted activity are extremely beneficial in order to speed up this critical process.

Contraction

Where tissue damage is extensive with large tissue loss, regeneration occurs from the wound margins. The epithelium slowly migrating across the granulation tissue. Migration across the wound surface continues until other epithelial cells are met. The migration then ceases a complex process known as cell contact inhibition.

Wound contraction decreases the size of the wound and this is largely due to the myofibroblast cell (mature fibroblast). These create tension within the wound by pulling together collagen fibres across their cell surface thus aiding in wound contraction.

Once an open cavity wound has filled with new granulation tissue and epithelialization has occurred the proliferation phase of wound healing stops.

Maturation

This final phase of wound healing begins after the proliferation phase. It is the process of remodeling of the collagen fibres laid down in the proliferation phase. During this phase the type III collagen, a soft gelatinous collagen laid down in the proliferation phase is replaced with a more highly organised collagen type I. The differentiation of collagen is a dynamic process and although it takes place predominantly during the maturation phase it may continue to be remodeled indefinitely.
The process of remodeling continues with the fibroblasts migrating from the wound site. There is rationalization of the blood vessels resulting in a shrinking of the scar, minimizing it.