EFFICACY AND SYSTEMIC TOXICOLOGY STUDIES OF DEBRIDING BIOGEL CREAM A NOVEL WOUND HEALING FORMULATION

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ABSTRACT
Swiss albino mice were treated with Debriding Biogel Cream for the wound healing activity and evaluate the toxic potential after systemic administration to male and female rabbits. The wound healing potential was determined using Comparison with Innovators Product and Systemic Toxicity Studies. That may results wound healing and Mean Wound Healing Time was also reduced. There was no pre-terminal mortality or morbidity during the study period and No adverse effects were noticed at the site of the drug administration. No effect on food intake, body weight, clinical signs and behavioral activity. All hematological parameters were found to be normal.

Keywords: Swiss albino mice, Debriding Biogel Cream, Innovators Product.

INTRODUCTION
Wound healing, is an intricate process in which the skin (or another organ-tissue) repairs itself after injury. In normal skin, the epidermis and dermis exists in a steady-state equilibrium, forming a protective barrier against the external environment. Once the protective barrier is broken, the physiologic process of wound healing is immediately set in motion. The model of wound healing is divided into four sequential phases: (1) hemostasis, (2) inflammatory, (3) proliferative and (4) remodeling. Upon injury to the skin, a set of complex biochemical events takes place to repair the damage. The speed of wound healing can be impacted by many factors, including the bloodstream levels of hormones such as oxytocin. The wound is made smaller by the action of myofibroblasts. When the cells’ roles are close to complete, unneeded cells undergo apoptosis. However, this process is not only complex but fragile, and susceptible to interruption or failure leading to the formation of non-healing chronic wounds.

Biogel is a white viscous topical application cream, particularly prepared for dermal usage. Biogel contains 0.2% of Hyaluronic Acid as an Active Pharmaceutical Ingredient. HA which is the main constituent of Biogel is a polysaccharide that guides the physiochemical process of cellular events in tissue repair and creates an optimal condition for proliferation and migration of cell. Biogel is indicated for the treatment of partial to full thickness dermal ulcers, wounds including cuts, irritation of the skin and superficial and deep burns.

MATERIALS AND METHOD
1) Evaluation of Wound-Healing Potential of Biogel in Comparison with Innovators Product

Experimental Protocol
Eight to ten weeks old female Swiss albino mice weighing 22 to 26 g was selected.

Group I: This group of animals was applied with placebo (saline).

Group II: The animals of this group received single applications of Biogel once daily until complete healing of the wounds.

Group III: The wounds of this group of animals were applied with Innovators ointment once daily until complete healing of the wounds.
Wound healing activity will be assessed by Morphological, Biochemical, Histopathological analysis.

Morphological and other Physical assessment

**Wound contraction**

Wound contraction was monitored by capturing the video images of each full-thickness wound with a charge coupled device camera connected to a computer.

Mean wound-healing time (Independent experiment each with 20 mice / group / 3 groups)

All animals in each group will be monitored until complete healing of wounds, and the day at which each wound healed will be as recorded. The mean of all healed wounds was determined and has been expressed as mean wound healing time.

**Biochemical Estimations**

The estimations will be carried out at different post-irradiation time periods for all groups. Estimation of Collagen, Estimation of Nitric oxide using a UV-visible spectrophotometer.

**Histopathologic studies**

The cross-sectional full-thickness skin biopsy specimens from each group will be collected on days 4, 8, and 12. Histopathology- Slides will be assessed for Fibroblast proliferation, Neovascularization and Collagen deposition.

2) Systemic (Acute) Toxicity Study Newzeland White Rabbits

Systemic toxicity study was conducted in eighteen rabbits (9 males + 9 females), which were divided into three groups viz. (i) Group-1 Vehicle Control (VC) (ii) Group-2 Test Group (TG I) and iii) Group-3 Test Group (TG II). Animals were conditioned for a period of 7 days after randomization. All the animals were randomized in to 3 groups and test compound administered to each group of 3 males and 3 females subcutaneously. Before the test compound administration hair at the site of the injection was removed by clipping. The animals were monitored for behavior, cage side activity, bio chemical and hematology during the experimental period. On 14th day all animals subjected to hematology, biochemistry and necropsy. Collected the vital organs and examined the same for histopathology including site of injection.

**RESULTS**

![Wound Day - 0](image1)
![Control Day - 4](image2)
![Bio-gel Day - 4](image3)
![Innovators Day 4](image4)

![Day - 14](image5)
![Bio-gel Day -14](image6)
![Innovators Day - 14](image7)

Fig. 1
Fig. 2: Wound healing effect

**ORGAN WEIGHT**

**Table 1: HEART**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameter</th>
<th>Day 7</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC</td>
<td>Heart</td>
<td>3</td>
<td>2.1</td>
</tr>
<tr>
<td>TG I</td>
<td>Heart</td>
<td>3.2</td>
<td>5.5</td>
</tr>
<tr>
<td>TG II</td>
<td>Heart</td>
<td>4.3</td>
<td>2.6</td>
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**Fig. 3**
### Table 2: LUNGS

<table>
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<th>Day 14</th>
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<tr>
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<td>Lung</td>
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<td>6.04</td>
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<tr>
<td>TG I</td>
<td>Lung</td>
<td>6.05</td>
<td>6.08</td>
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<tr>
<td>TG II</td>
<td>Lung</td>
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**Fig. 4**

### Table 3: LIVER

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**Fig. 5**
Table 4: KIDNEY

<table>
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<td>Kidney</td>
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<td>13</td>
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<tr>
<td>TG I</td>
<td>Kidney</td>
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<td>9</td>
</tr>
<tr>
<td>TG II</td>
<td>Kidney</td>
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Fig. 6

Table 5: BRAIN

<table>
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<th>Parameter</th>
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<th>Day 14</th>
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<tbody>
<tr>
<td>VC</td>
<td>Brain</td>
<td>6.7</td>
<td>6.2</td>
</tr>
<tr>
<td>TG I</td>
<td>Brain</td>
<td>6.3</td>
<td>6.4</td>
</tr>
<tr>
<td>TG II</td>
<td>Brain</td>
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Fig. 7
CONCLUSION
This study clearly demonstrated that wound healing potential of Biogel ointment and innovators ointment is proved to be similar, hence it can be concluded that both products can be used for same indications. Biogel is a topical application cream, particularly prepared for dermal usage. All the animals were observed for a period 14 days after the administration of the test compound. Parameters evaluated including clinical signs of toxicity, live phase of animals, cage side observations, and body weight and food consumption. Blood samples were collected on day 7 and 14 for hematological and clinical chemistry analysis. Animals were necropsied and vital organs were weighed and subjected to histopathological examination at the end of the study period.
In the 14 days of study period no mortality or morbidity was observed in any group. Statistically significant differences were not observed in control and test group animals. Histopathology observation of vital organs did not reveal any significant differences between the control and test group animals. Thus it can be concluded from this study that sub-cutaneous administration of Biogel cream is not exerted any systemic toxic effects in rabbits. Biogel cream is comparable with innovators product Bionect cream and it is safe to use as a topical application under the given experimental conditions.

REFERENCES
16. OECD guidelines for testing of chemicals; skin sensitization.