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Research Article

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

Syed Muneer[1]*, Y. Narasimha rao[1], M. Prasad rao[1], Sivasankar R. Beeravalli[2]

[1]Department of Pharmacology, MAM College of Pharmacy, Narasaraopet, Guntur (Dt.), Andhra Pradesh, India.
[2]9703, Inkwood Drive, Frederickrs burg, Virginia, U.S.A.

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 Were 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

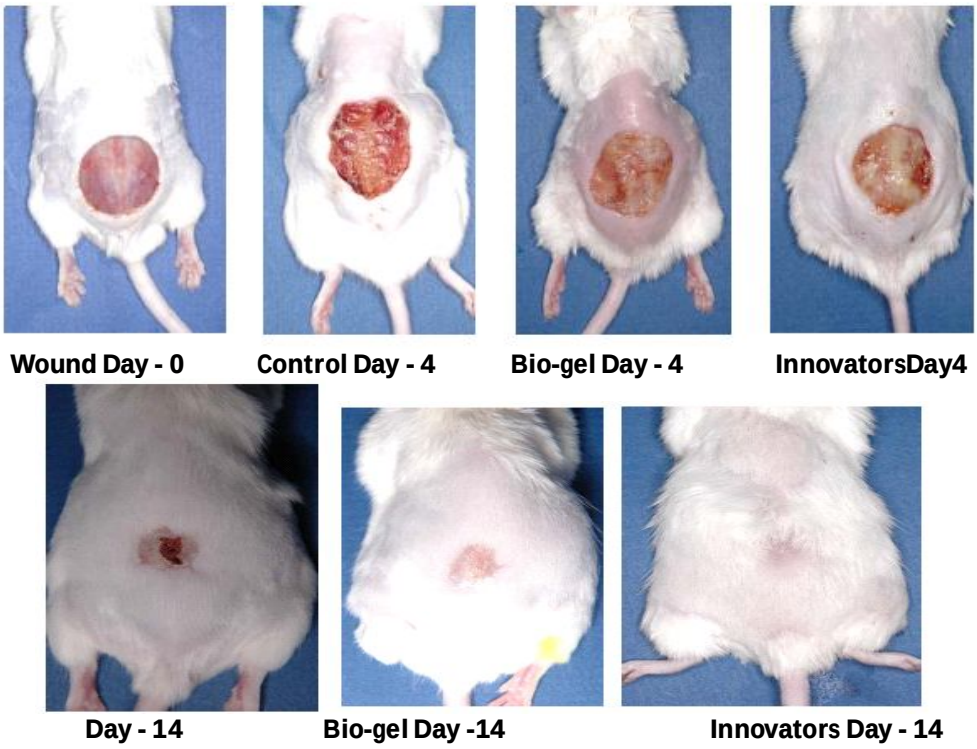

Fig. 1

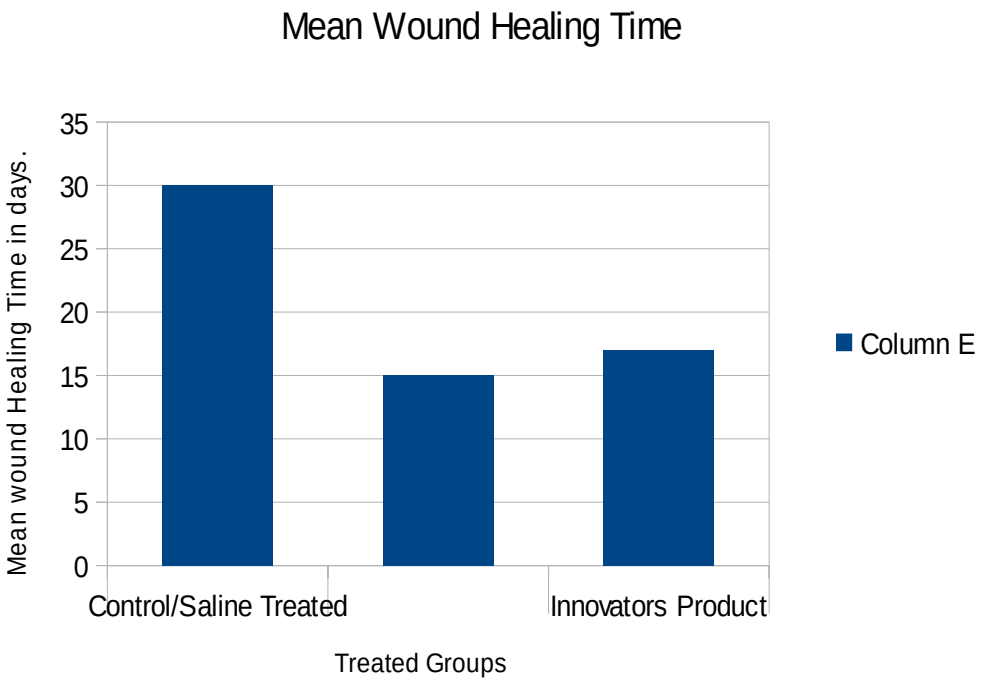

Fig. 2: Wound healing effect

ORGAN WEIGHT

Table 1: HEART

Groups	Parameter Heart	Day 7	Day 14
VC	Heart	3	2.1
TG I	Heart	3.2	5.5
TG II	Heart	4.3	2.6

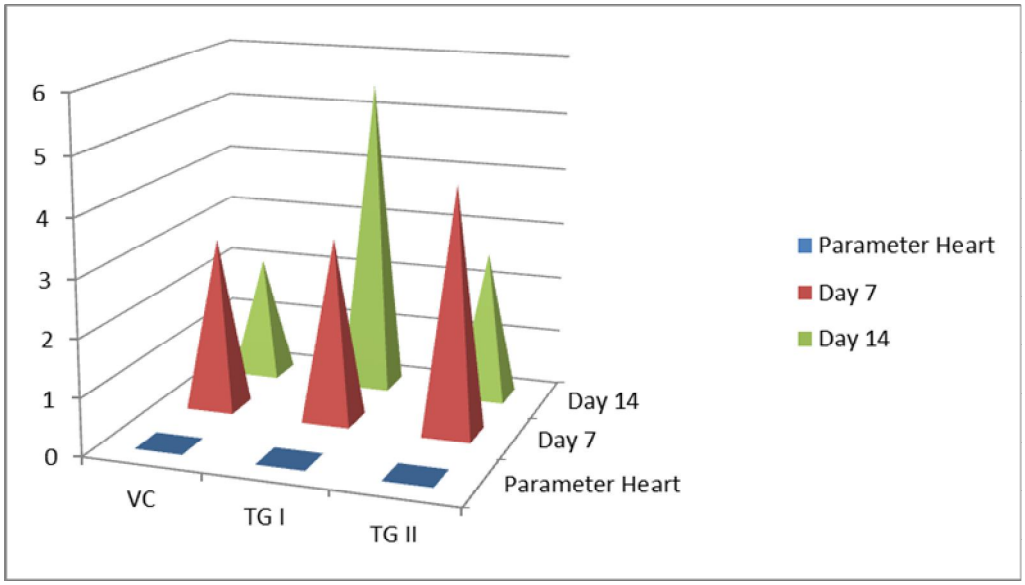

Fig. 3

Table 2: LUNGS

Groups	Parameter Lung	Day 7	Day 14
VC	Lung	5.02	6.04
TG I	Lung	6.05	6.08
TG II	Lung	6.04	7.02

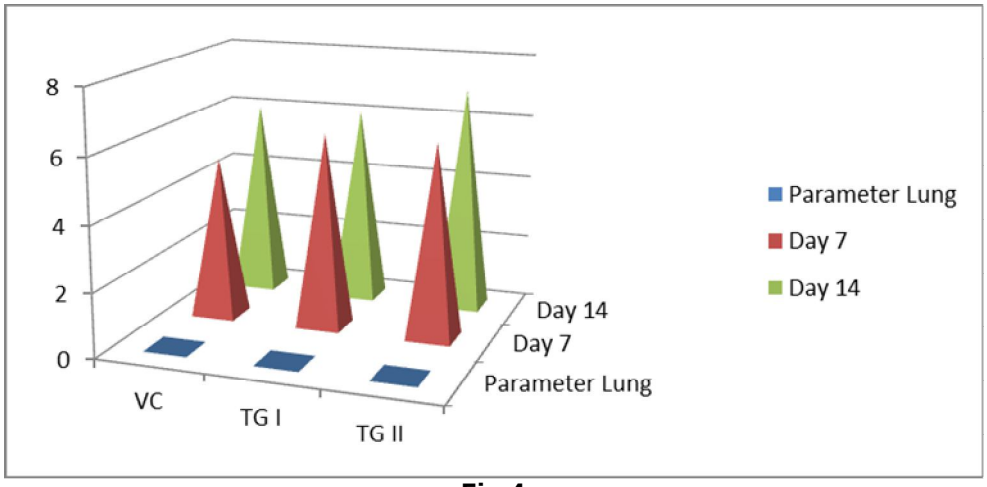

Fig. 4

Table 3: LIVER

Groups	Parameter Liver	Day 7	Day 14
VC	Liver	42.08	36.05
TG I	Liver	37.05	43.06
TG II	Liver	40	35.4

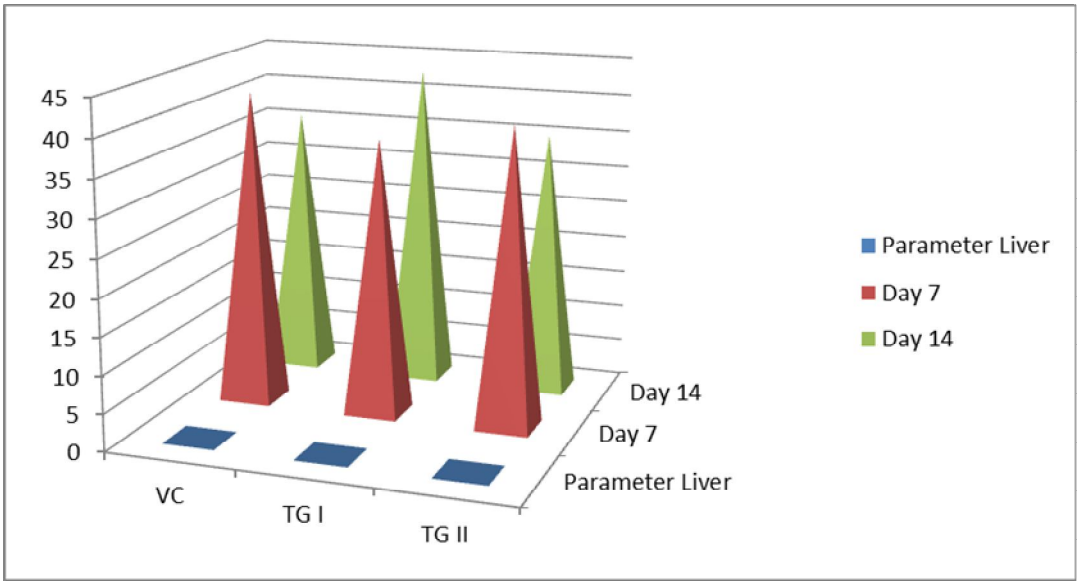

Fig. 5

Table 4: KIDNEY

Groups	Parameter Kidney	Day 7	Day 14
VC	Kidney	10	13
TG I	Kidney	11.4	9
TG II	Kidney	10	9.8

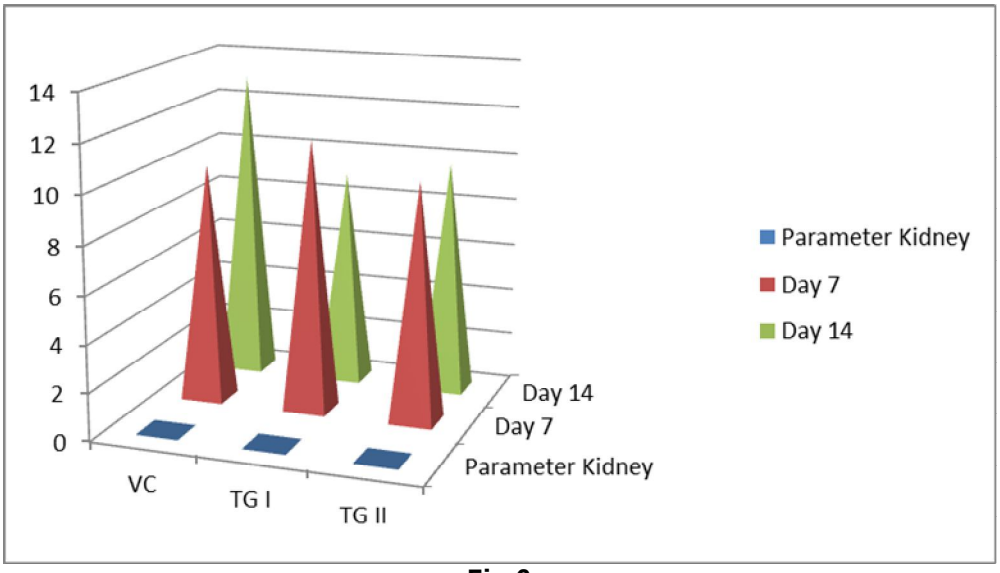

Fig. 6

Table 5: BRAIN

Groups	Parameter Brain	Day 7	Day 14
VC	Brain	6.7	6.2
TG I	Brain	6.3	6.4
TG II	Brain	6.8	5

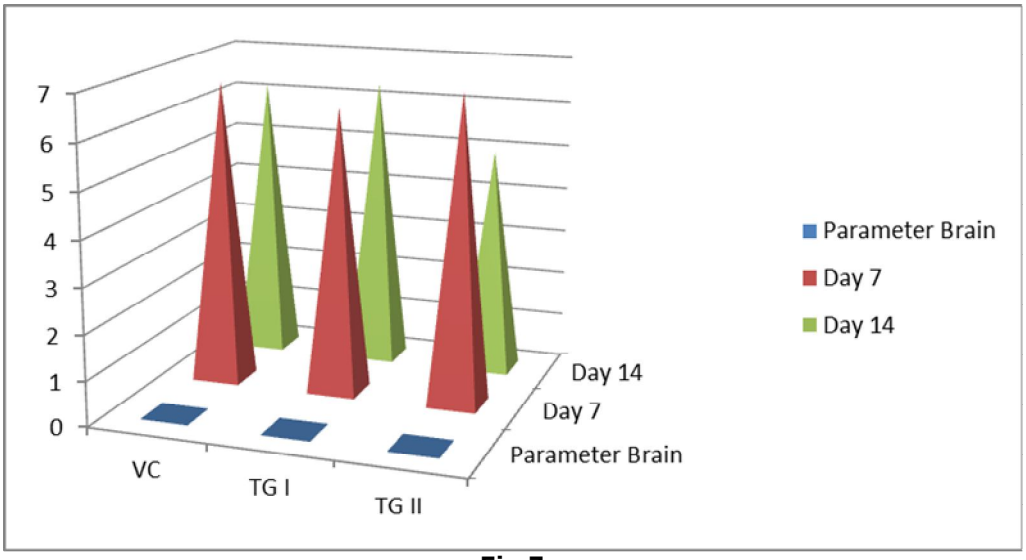

Fig. 7

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 hematology 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

1. King SR, Hickerson WL, Proctor KG.Beneficial actions of exogenous hyaluronic acid on wound healing. Surgery. 1991 Jan;109(1):76-84.
2. Frenkel JS The role of hyaluronan in wound healing Int Wound J. 2012 Aug 14. doi: 10.1111/j.1742-481X.2012.01057.
3. Yannas IV, Lee E, Orgill DP, et al. Synthesis and characterization of a model extracellular matrix that induces partial regeneration of adult mammalian skin. Proc Nall Acad Sci U S A. 1989; 86 (3): 933–7.
4. Harris PA, di Francesco F, Barisoni D, et al. Use of hyaluronic acid and cultured autologous keratinocytes and fibroblasts in extensive burns [letter]. Lancet. 1999; 353 (9146): 35–6.
5. Aigner J, Tegeler J, Hutzler P, et al. Cartilage tissue engineering with novel nonwoven structured biomaterial based on hyaluronic acid benzyl ester. J Biomed Mater Res. 1998; 42 (2): 172–8.
6. Barbucci R, Magnani A, Baszkin A, et al. Physico-chemical surface characterisation of hyalmonic acid derivatives as a new class of biomaterials. J Biomat Sci Poly Ed. 1993; 4 (3): 245–73.
7. Manna F, Dentini M, Desideri P, et al. Comparative chemical evaluation of two commercially available derivatives of hyaluronic acid (hyalaform (R) from rooster combs and restylane (R) from *Streptococcus*) used for soft tissue augmentation. J Fur Acad Dermatol Venereol. 1999; 13 (3): 183–92.
8. Stern R, McPherson M, Longaker MT. Histologic study of artificial skin used in the treatment of full-thickness thermal injury. J Burn Care Rehabil 1990; 11 (1):7-13.
9. Sattar A, Rooney P, Kumar S, et al. Application of angiogenic oligosaccharides of hyaluronan increases blood vessel numbers in rat skin. J Invest Dermatol. 1994; 103: 576–9.
10. Mast BA, Diegelmann RF, Krummel TM, et al. Hyaluronic acid modulates proliferation, collagen and protein synthesis of cultured fetal fibroblasts. Matrix. 1993; 13 (6): 441–6.
11. Locono JA, Krummel TM, Keefer KA, et al. Repeated additions of hyaluronan alters granulation tissue deposition in sponge implants in mice. Wound Repair Regen.
12. Paget and Barnes (1964) Evaluation of Drug activities: Pharmacometrices, Eds. Laurence and Bacharach Vol1 Acad. Press NY.
13. EFPIA/ECVAM paper on good practice in administration of substances and removal of blood, J Appl Toxicol 21 15-23,2001.
14. Magnusson B.and Kligman A.M (1969). The identification of contact allergens by animal assay.
15. The guinea pig maximization test. J.Invest.Dermatol, 52, 268.
16. OECD guidelines for testing of chemicals; skin sensitization.
17. ISO 10993-10; A Practical Guide to ISO 10993-10: Sensitization.
18. Gilmore MA. Phases of wound healing. *Dimens Oncol Nurs.* 1991;5(3):32-4.
19. Maxson S, Lopez EA, Yoo D, Danilkovitch-Miagkova A, Leroux MA. Concise review: role of mesenchymal stem cells in wound repair. *Stem Cells Transl Med.* Feb 2012;1(2):142-9.