The # 1
for intensive and rapid skincare

« ***It would seem that the time is now ripe for veterinarians to recognize that animal wounds can also be managed in more sophisticated and humane ways and to work towards the development of better methods for managing animal wounds*** ».

Blackwell Science, D.H. Lloyd, Veterinary Dermatology, vol. 8, 4, 1997.

www.derma-gel.com

Veterinus
Derma GeL®

Avoid **the use of…**

Traditional Sprays

Irritant and decreasing cell viability. In addition, some of them are mutagenic or cytogenotoxic, altering (proud flesh, keloids…), delaying or stopping the healing process.

Creams & Ointments

More slowly and only partially absorbed. Leaving unabsorbed greasy residues on the surface of the wound. These unabsorbed greasy residues oxidize with body temperature, favoring irritation of epithelial cells and delaying the healing process.

Dressings

Adhering to the wound bed and damaging the new layer of regenerative epithelial cells when removing the dressing from the wound. On the other hand, dressings can increase local temperature at wound level, favoring excessive suppuration and delaying the healing process because of the lack of air.

Topical antibiotics

On skin wounds, topical antibiotics favor infection because of destruction of the normal bacterial flora. Mutagenic, they alter or delay the healing process.

Alcoholic Solutions

Solutions with high content of alcohol have acute irritant/sensitizing effect on skin cells, delaying or altering the healing process.

Veterinus
Derma GeL®

☑ Product

available in **GeL** or **Fluid** form.

Both « 2 in 1 » formulas ensure an intensive and rapid skincare plus a protective barrier effect against foreign contaminants.
The GeL form is indicated as a multipurpose wound dressing. The Spray form is mainly indicated for an easy management of superficial lesions such as post operative traumas (spray on stitches),...

☑ Packaging

dispenser tube cont. 100ml - 3.4 fl.oz **GeL form**
spray bottle cont. 50ml - 1.7 fl.oz. **Fluid form**
Reclosable doses 10ml – 0.3 fl.oz. **GeL form**

Unlike traditional jars and containers in which you have to dip your fingers and thus contaminate the product with each use, the original device of the dispenser pump prevents air and impurities from entering the tube, thus guaranteeing optimal product stability and activity. Moreover, this hygienic and practical tube enables you to measure out a dose of gel, according to your needs.

☑ Research

using 3-dimensional reconstructed skin models

Veterinus Derma GeL® remains unique and ahead of the rest in terms of extensive scientific research performed on 3-dimensional reconstructed skin models in order to assess its efficacy, the cell viability, the absence of irritant/sensitizing effect on epithelial cells as well as the absence of mutagenicity and cytogenotoxicity, ensuring hair regrowth in the original color.

Veterinus
Derma GeL®

MEMORANDUM

We find the use of saline lavage of the wound to be of great value in achieving primary-intention healing of the wound. This is so because saline irrigation helps to decrease the degree of inevitable wound contamination. **Some clinicians favor the use of povidone-iodine solutions, but even mild solutions irritate tissue**. We find that the inclusion of an antiseptic in the lavage solution is of little value, and physiological saline or a polyionic is preferable."
"The use of **local antibiotic solutions, ointments and powders is to be avoided because they not only irritate wounds but also favor infection because of destruction of the normal bacterial flora.** (1)

◆

Wound gels are excellent for helping to create or maintain a moist environment Some hydrogels provide absorption, desloughing and debriding capacities to necrotic and fibrotic tissue.

Best Uses • Helps provide and maintain a moist wound environment by increasing moisture content, hydrogels have the ability to help cleans and debride necrotic tissue.

Advantages • Effective in hydrating wound surfaces and liquefying necrotic tissue on the wound surface. Non-adherent and can be removed without trauma to the wound bed. "Soothing" effect promotes patient acceptance. (2)

◆

Recent scientific research established the superiority of hydrogels compared to traditional greasy skincare products (e.g. creams, ointments, oil based liquids...). These greasy products are more slowly and partially absorbed leaving unabsorbed greasy residues on the surface of the skin. These greasy residues oxidize with body temperature, promoting irritation of epithelial cells, decreasing dramatically cell viability, favoring infection and interfering with the healing process or delaying it. (3)

(1) *Manual of Equine Practice - Dermatology - Skin Wounds by Prof. R. Rose and D. Hodgson*
(2) *The Wound Care Information Network by Dr. A. Freedline*
(3) *Maximilian Zenho & Co. - Comparative Study On Skincare Products*

Veterinus
Derma GeL®

Indications

Veterinus Derma GeL® is an isotonic formulation in gel or fluid form indicated for **intensive and rapid skin care**. *Veterinus* Derma GeL® ensures **a uniform porous barrier of protection against** bacterial attack, foreign contaminants, avoiding desiccation and maintaining an ideal percentage of moisture. Bandaging the affected area is therefore not required. Certified **non-mutagenic** and **devoid of cytogenotoxicity** or irritant and sensitizing effect on epithelial cells, *Veterinus* Derma GeL® maintains cell viability to a very high rate and consequently favors a rapid **hair regrowth in the original color**. Staying where it is applied, *Veterinus* Derma GeL® - in gel form - will not run off the treated surface.

Directions

Daily cleanse the affected area with warm water or a saline solution, so as to preserve epithelial cells from irritation. Apply *Veterinus* Derma GeL® generously two or three times a day, as needed. To help prevent skin proliferation, extend application to the surrounding area.

Caution

When needed, bandage over the gel. After 24 hours, leave surface uncovered as the product ensures a protective barrier (keeping surface moist). Avoid the use of this product on abnormal cell proliferation : warts, ringworm, mud fever (when fungal invasion is present or suspected) ,... Ensure cap is replaced after use. Avoid all contact to inside of cap or tip of tube/bottle to prevent product contamination.
For animal use only. Keep in a cool dark place away from heat, frost and toxic radiation. Keep out of the reach of children.

Safety

Veterinus Derma GeL® is devoid of toxic or prohibited molecules. It is safe to use in competition, during gestation, when licked...

Quality

Veterinus Derma GeL ® is formulated on the basis of an exclusive blend of titrated botanical extracts. Unlike plant tinctures or common extracts which have an active ingredients content that varies according to the period of harvesting, weather conditions, quality of soil,... , *Veterinus* Derma GeL ® contains titrated extracts.

Ingredients

Titr. Polysaccharides (Pyrus Sorbus extr.) ; Centella Asiatica (titr. extr.) ; Calendula Officinalis (titr. extr.) ; Salvia Officinalis extr. ; Thymus Vulgaris extr. ; Origanum Majorana extr. ; Lavandula Officinalis extr. ; Propylene Glycol ; Hydrogenated Castor Oil ; Sodium Bicarbonate ; Glycerin ; Alcohol ; Aqua Purificata ; Carbomer (gel form only).

Veterinus
Derma GeL®

STUDY ON CELL VIABILITY, LACK OF IRRITANT AND SENSITIZING EFFECT ON SKIN AND INFLAMMATION SYNTHESIS OF THE PRODUCT *Veterinus* Derma GeL®

An approved organization for controls and investigations - BIO-PHARMA & SIMON LABORATORIES (Wavre - Belgium) - which operates according to Standard Operating Procedures (S.O.P.), Good Laboratory Practices (G.L.P.), accredited to EN 45001 and other international standardization norms, has performed a series of tests in order to assess cell viability as well as the absence of irritant and sensitizing effect on epithelial cells, with the use of *Veterinus* Derma GeL®.

KEY WORDS

Cell Viability Test, Tumor Necrosis Factor alpha Induction (TNF-α Test), Interleukin-1 alpha Induction (IL-1α Test), Interleukin 8 Induction (IL-8 Test), Interleukin 10 Induction (IL-10 Test), Interleukin 12 Induction (IL-12 Test), Prostaglandin E2 - Inflammation Synthesis (PGE2 Test).

INTRODUCTION

In this study, the cell viability and the irritancy/sensitization potential of *Veterinus* Derma GeL® have been determined by comparison with well-known skin irritant substances and 1 dermal sensitizing agent, each decreasing the viability of epithelial cells.
The model used in this study consists of a 3-dimensional culture of keratenocytes composed of a fully differentiated epidermis with a coherent horny layer.
These *in vitro* cultures exhibit barrier function and metabolic activity which allows patch application of the product, thus simulating *in vivo* topical exposure.
This type of model has been used to evaluate the transcutaneous passage of pharmaceutical molecules (Coquette et al., 1996), in the immunological response of the skin (Reins et al., 1994) and to evaluate the irritant/sensitizing effect. The results of these studies have shown a close correlation with those obtained in *in vivo* studies (Slivka and Zeigler et al., 1993).

MATERIAL & METHODS

- These investigations have been performed in the Department of Biology of BIO-PHARMA by A. VANDENBOSCH, Dip. Chem., under the supervision of A. COQUETTE, Ph. D., Study Director.
- Reference substances used were respectively : Triton X 100 ; Benzalkonium chloride ; Dinitrochlorobenzene (DNCB) and Tween 80 as negative control.
- Researchers have performed a cell viability test and the quantification of Tumor Necrosis Factor alpha (TNF-α), Interleukin-1 alpha (IL-1α), Interleukin 8 Induction (IL-8), Interleukin 10 (IL-10), Interleukin 12 (IL-12) and Prostaglandin E2 - Inflammation Synthesis (PGE2) in the culture surrounding medium.
- Each standard concentration, reference substances and *Veterinus* Derma GeL®, were respectively tested in duplicate.
- Standard values were averaged and plotted versus concentrations of *Veterinus* Derma GeL® and reference substances.

RESULTS

The cell viability test shows a high rate of viability (*Figure 1*) using different concentrations of *Veterinus* Derma GeL®. Basically, and under the experimental conditions, the behaviour of the model correlates with *in vivo* data.
In conclusion, the product *Veterinus* Derma GeL® can be considered as maintaining cell viability to a high rate and as totally devoid of irritant and sensitizing effects on epithelial cells.

Veterinus
Derma GeL®

Figure 1

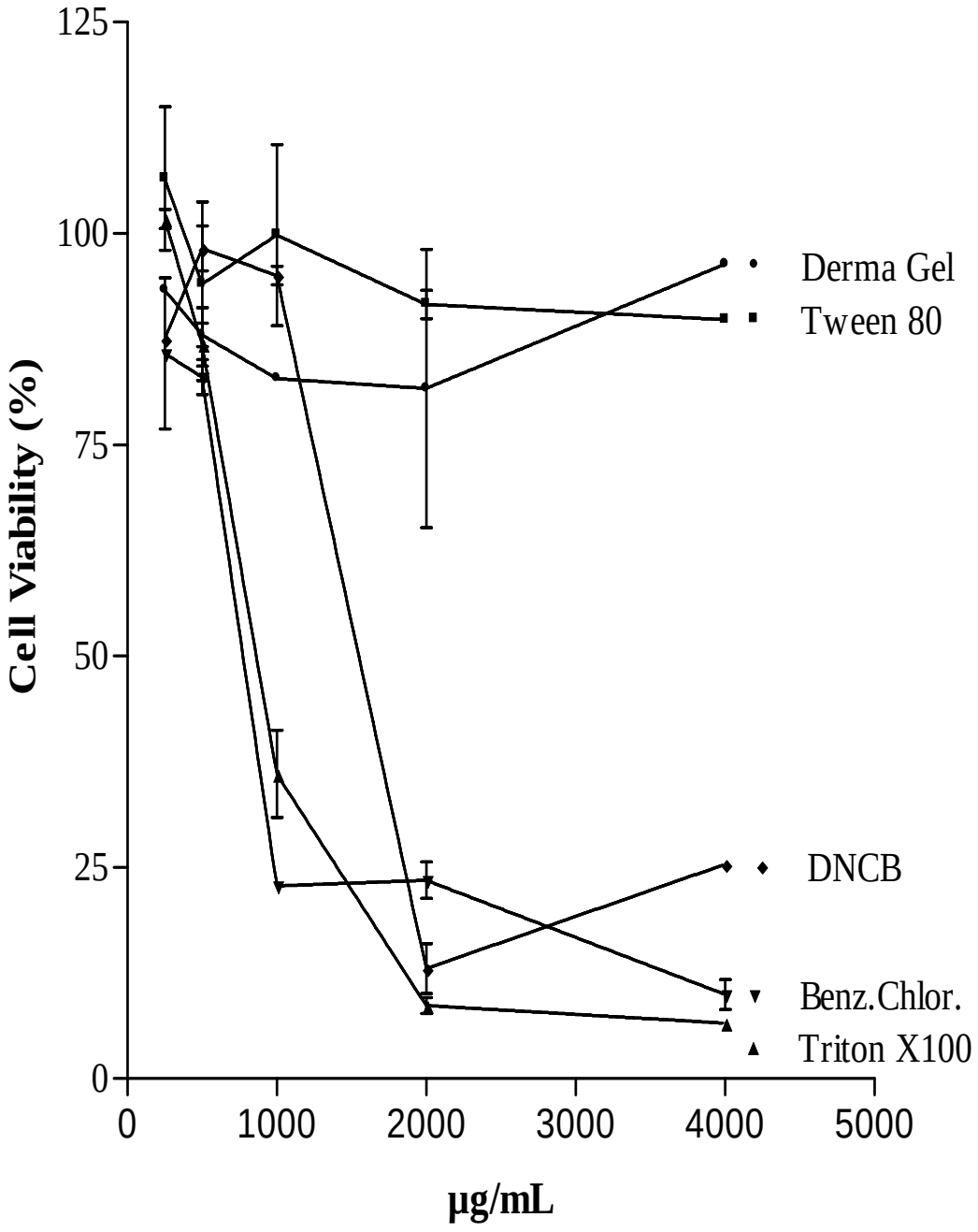

Fig 1 : Dose-response profile of Cell Viability conversion in skin equivalent model in vitro exposed to Benzalkonium Chloride, Triton X 100, Tween 80, Dinitrochlorobenzene (DNCB) and to the product VETERINUS DERMA GEL ®. The tissues were exposed to the different products for 20 hours at 37 °C (5 % CO_2) at which time Cell Viability conversion was assayed. Each point is the mean ± SD of 1 experiment performed in duplicate.

STUDY ON THE ABSENCE OF MUTAGENICITY AND CYTOGENOTOXICITY OF THE PRODUCT *Veterinus* Derma GeL®

An approved organization for controls and investigations - BIO-PHARMA & SIMON LABORATORIES (Wavre - Belgium) - which operates according to Standard Operating Procedures (S.O.P.), Good Laboratory Practices (G.L.P.), accredited to EN 45001 and other international standardization norms, has performed a series of tests in order to assess the absence of mutagenicity and cytogenotoxicity of the product *Veterinus* Derma GeL®.

KEY WORDS

Non mutagenic, no denaturation nor alteration of cells, no cytogenotoxicity.

INTRODUCTION

The aim of this study is to demonstrate the absence of mutagenicity / cytogenotoxicity of *Veterinus* Derma GeL®. The *Salmonella Typhymurium* histidine (his) reversion system is a microbiological assay which measures his^- $\rightarrow$ his^+ reversion which causes base substitutions of frameshift mutations in the genome of this organism.

MATERIAL AND METHODS

- This study has been performed in accordance with the OECD Guideline 471 - Genetic Toxicology - Reverse Mutation Assay.
- The four strains used for this assay are : TA 98, TA 100, TA 1535 an TA 1537. They originate from the Laboratory of Professor B. AMES, California University, Biochem. Department, US.A.
- The metabolic activation system used is a post-mithocondrial fraction (S9), prepared from cells treated with Aroclor at a concentration of 500mg/kg.
- A global statistical analysis (Anova Test at one criteria of classification) was carried out for each strain with or without metabolic activation system . A comparison of each test substance concentration versus negative controls (DMSO and phosphate buffer) was carried out for each strain - with and without metabolic activation system - by an individual statistical treatment (Dunnett Test).

  Every test and counting of the number of revertant colonies have been performed in triplicate by Dr. B. FRIH, Head of Biology Unit, and J.-M. GHYSEL, Pharmacist Director.

RESULTS

It has been observed through this study that - with or without metabolic activation - when compared versus negative controls (DMSO and Tph), there is no cytogenotoxic / mutagenic effect.
In conclusion, the absence of alteration or denaturation of cells favors an optimum activity of *Veterinus* Derma GeL®. Therefore, the efficacy of its active ingredients - responsible of cell viability (see Figure 1) - remains ideal. This explains why - when *Veterinus* Derma GeL® is applied as recommended - epithelial traumas are covered by cells genetically and completely identical to the cells that were initially available (= hair regrowth in the original color).

Veterinus
Derma GeL®

MAIN SCIENTIFIC REFERENCES

1. *Vandenbosch, A. Coquette - Biopharma - Maximilian Zenho & Co. - Assessment of the product Derma GeL on a 3-dimensional in vitro skin model. Analytical Report No. 197508 - March 1997*
2. *Coquette, B. Frih, J.-M. Ghysel, Biopharma - Maximilian Zenho & Co. - Cytogenotoxicity evaluation of the product Derma GeL - Final Assay Report No. 23171 - March 1997*
3. *Rose, R.J., Hodgson D.R., W.B. Saunders - Manual of Equine Practice - Dermatology, Skin Wounds, 1993, p. 340-341*
4. *Abraham C., Amoros M., Firre L. : Etude de l'activité antifongique des plantes supérieures : action de 39 plantes indigènes sur 4 champignons phytopathogènes. Annales pharmaceutiques françaises, 1983*
5. *Adzet T., Vila R., Ibanez C., Canigueral S. - Essential Oils of Some Iberian Thymus, Planta Medica, 54, 1988, 369-371*
6. *Allegrini J., De Buochberg S. - Une technique d'étude du pouvoir antibactérien des Huiles Essentielles, Laboratoire de Microbiologie, Faculté de Montpellier, 1972*
7. *Andary P., Roussel J.L., Motte M.E., Rascol J.P., Privat G. - Activité antifongique comparée de divers esters de l'acide dihydroxy-3,4 cinnamique. Crytogamie, Mycologie, 1982*
8. *Avramova S., Portarska F., Apostolova B., Petkova S., Konteva M., Tsekova M., Kapitanova K. - MBI Med Biol Inf, S.28, 1988, 28-33*
9. *Avvot B.J., Coll. : Screening data from the cancer chemotherapy national. Service center screening laboratoires. Plants extract. Cancer Res. 1996, 26, supp. Part 2 (2 volumes).*
10. *Bellon G., Malgras A., Randoux A., Borel J.P., - Further improvement of the fluorometric assay for hydroxyproline. J. Chromaogr., 1983. 278. 167-172*
11. *Bonté F., Dumas M., Chaudagne C., Meybeck A., - Activité comparée de l'asiaticoside et du madecassoside sur la synthèse des collagènes I et III par des fibroblastes humains en culture, Ann. Pharm. Fr., 1995, 53, 38-42*
12. *Bonte F., Dumas M., Chaudagne C., Meybeck A., (1994), - Infl. of Asiatic Acid, Madecassic Acid, and Asiaticoside on human collagen I synthesis, Planta Med. 60, 133-135*
13. *Borel J.P., Monboisse J.C., CR Soc Biol 1993, 187, 124-142*
14. *Bosse J.P., Papillon J., Frenette G., Dansereau J., Cadotte M., Le Lorier J. - Clinical study of a new antikeloid agent; Ann. Plastic Surg. 1979. 3. 13-21*
15. *Brenner D.A., Chojkier M., - Acetaldehyde increases collagen gene transcription in cultured human fibroblasts, J. Biol. Chem. 1987, 262, 17690-17695*
16. *Brun G. - Les Huiles essentielles en tant qu'agent de pénétration tissulaire, Thèse Pharmacie Strasbourg, 1952*
17. *Buckley A., Hill K.E., Davidson J.M. - Collagen metabolism in: Methods in Enzymology 1988, Academic Press, 674-694*
18. *Chemli R. - Thèse Doctorat de Sciences Pharmaceutiques, Université d'Aix-Marseille, 1986*
19. *Chemli R., Toumi A., Balansard G., Boukef K., Zouaghi H. - Third Symposium on Inflammation Markers, Lyon, June 1985*
20. *Chen Y.Q., Mauvier R., Tan E.M., Uitto J., J Invest dermatol 1993, 100, 535*
21. *Cheung K.Y., Xie J.X. - But PPH - J Ethanopharmacol 15, 1986, 1-44*
22. *Chushenko VN., Zhukov GA., Karanova OE., Obolentseva GV. - Khim Prir Soedim, 1988, 585-586 zit. nach: CA 109, 1988, 226748*
23. *Darias V., Bravo L., Barquin E., Martin Herrera D., Fraile C. - J Ethanopharmacol 15, 1986, 169-193*
24. *De Tommasi N., Conti C., Stein M.L., Pizza C. - Planta Med 57, 1981, 250-253*
25. *De Tommasi N., Pizza C., Conti C., Orsi N. - J Nat Prod 53, 1987, 830-835*
26. *Dehaut - Pouvoir antibactérien du Thymol, Thèse Pharmacie, Toulouse, 1945*
27. *Della Loggia R., Tubaro A., Becker H., Saar St., Isaac O. - The Role of Triterpenoids in the Topical Anti-Inflammatory Activity of Calendula officinalis Flowers, Planta Med, 60, 1994, 516-520*
28. *Derkach AI., Komissarenko NF., Chernobai VT. - Khim Prir Soedin 777, 1986, zit. ncha: CA 106, 1987, 135330k*
29. *Dumas, M. Chaudagne, C. Bonte, F., Meybeck, A. (1993) Mech. Ageing Dev. accepted for publication*
30. *Duquenois P. - Les antibiotiques des plantes supérieures, bull Soc Bot Fr, 1955*
31. *Freshney R.I., - Culture of animal cells. A manual of basic techniques, New York, Alan R. Liss Inc., 1983, 99-106*
32. *Freundlich B., Bomalaski J.S., Neilson E., Jimenez S.A. - Regulation of fibroblast proliferation and collagen synthesis by cytokines. Immunol Today, 1986, 7, 303-307*
33. *Genaust H.-Etymologisches Wöterbuch der botanischen Pflanzennamen, 2, Aufl., Birkhäuser, Basel Boston Stuttgart, 1983*
34. *Grimaud, J. P., Druguet, M., Peyrol, S., Guerret, S. (1986) in: Methods of Enzymatic Analysis, (Bermeyer, H. U., ed.) VCH Publishers, Weinheim, pp. 186-201*
35. *Herriset A., Jolivet J. - A propos de la chromatographie en phase gazeuse des essences de thymus, Pl Med et Phyt, 1973, 7*
36. *Hladon B., Drozdz B., Holub M., Bobkiexwiecz T. - In vitro studies on cytotoxic properties of sesquiterpene lactones in tissue cultures of human and animal malignant cells, Arch Immun. Ther. Exp. 23, 1975, 845-855*

… + M.S.D.S. → www.derma-gel.com

Maximilian Zenho & Co.

Animal Healthcare Department
Louise Tower
Avenue Louise, 149 / 24
B-1050 Brussels
Kingdom of Belgium

International Head Office

Tel. +32 2 535 76 50
Fax +32 2 535 75 75

sales@maxzenco.com
www.derma-gel.com

Veterinus
Derma GeL®