Diphoterine®: Review of the dermal toxicological data

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Poster n° 9119 presented at the XXIX International Congress of the EAPCCT, 12-15 May 2009, Stockholm, Sweden

Objective

To increase the knowledge concerning the toxicological data of Diphoterine® for immediate skin chemical splash decontamination and to determine whether or not it could be safely used for delayed patient management.

Methods

All available reports were reviewed and recently, new studies have been performed to determine the safety of Diphoterine® on both normal and damaged skin, as well as non-occlusive, semi-occlusive or occlusive application and blood.

Results

Test	Method	Results	Laboratory
Acute Dermal LD_{50}	OECD 402 on Sprague-Dawley CFY strain rat	Dermal LD_{50} > 2000 mg/kg No deaths, no toxic effects	Safepharm Laboratories Limited, Derby, UK
Cutaneous Irritation *in vitro*	*In vitro* Dermal Irritection®(1)	Human Irritancy Equivalent = 0.8 Non irritant	Integra Laboratory, Milan, Italy
Cytotoxicity in murine fibroblasts (3T3)	MTT test[a] following UNI EN ISO 10993-5, Sodium Lauryl Sulphate (SLS) used as positive control	IC_{50}>5 mg/l *versus* 0.08 mg/l (SLS) No cytotoxic effect up to 24 h.	Integra Laboratory, Milan, Italy
Skin sensitization in the guinea pig	OECD 406 Magnusson & Kligman Method	No sensitizing effect(2)	Laboratoire CERB, Baugy, France
Local tolerance on damaged/healthy animal skin – application 24 h	single, semi-occluded or non-occluded application to scarified / non-scarified skin in the rabbit(3)	Non-irritant and no toxic effects 48 h after the end of the application (or 72 h after the beginning of the experiment)	Laboratoire CERB, Baugy, France
Local tolerance on human normal skin – application 48 h	48 consecutive hours on 55 human volunteers (occlusive bandage)	IMM[b] average = 0.00 Non-irritant	Laboratoire IDEA, Martillac, France
Skin sensitization study in normal human volunteers	Marzulli-Maibach method (4) on 150 human volunteers with normal skin	Hypoallergenic	Laboratoire IDEA, Martillac, France
Mutagenesis	Ames Test – Bacterial reverse mutation test on *Salmonella typhimirium* TA1535, TA1537, TA98, TA100, TA102, *Escherichia Coli* WP2 uvrA	Non mutagenic	CIT, Evreux, France
Percutaneous diffusion and tolerability evaluation *in vitro*	Absorption tested on 3D epidermis with exposure up to 6 h. Skin cells viability evaluation by MTT test[a] method	87,6 % cell viability = high tolerability $c_{(Diphoterine®)}$ < 0.0035 %	Integra Laboratory, Milan, Italy
Haemocompatibility	Comparison with saline solution	From 80 % to 26.7 % in water 0.003 <Optical Density< 0.018 Haemocompatible	Laboratoire CERB, Baugy, France

Other Results

❖Irritation test on rabbit eyes (Safepharm Laboratories Limited, Derby, UK) as well as the *in vitro* evaluation of the eye irritation potential on human fibroblast cultures showed that Diphoterine® is not irritating to the eyes.

❖Oral toxicity on rats showed that Diphoterine® is non toxic (Oral LD_{50} > 2000 mg/kg).

❖No anti-inflammatory, cytotoxic or irritant effects observed on a 3D human epidermis model (MTT *in vitro* tests + pro-irritation potential IL-1α).

Conclusion

Diphoterine® showed no irritating, skin sensitizing, or toxic effects to normal or damaged skin. These results are in accordance with the lack of adverse effects observed in workers after immediate use of Diphoterine®. Further clinical comparative studies will be conducted in order to clearly show any benefits of its delayed use on the skin.

References

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[a]: Cell viability assay using MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide).
[b]: IMM is the average irritation index which allows the classification of the test product.