

DERMAL ABSORPTION AND TOXICITY STUDY OF ACETONE-BASED SKIN COATINGS IN MINIATURE SWINE

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INTRODUCTION

This study evaluated an acetone and polymer-based skin coating technology that has been developed as a combination barrier product and drug delivery system. The technology has the potential to address numerous distinct clinical applications by incorporating active ingredients to create dermatologicals, active skin care products, and cosmeceuticals.

The study evaluated both the potential for systemic absorption of acetone as well as dermal toxicity following acute and subchronic applications. Testing was performed on the basic vehicle (i.e., not containing any active ingredients).

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METHODS

Yucatan miniature pigs weighing 16-20 kg were topically administered a single dose of an acetone/polymer skin coating (3 animals per sex) or acetone alone (1 animal per sex) for acute evaluation. Acetone levels in blood were evaluated at regular intervals between 0 and 4 hours. After a washout period, a subchronic study was performed, with twice daily dosing (minimum of 6 hours between applications) of each treatment group for 5 days per week for 7 weeks, to both abraded and unabraded skin sites.

Blood was drawn at the beginning and the end of each week and acetone levels were quantified with gas chromatography and flame ionization detection. Clinical signs were monitored daily, 5 days/week. Body weights and food consumption were recorded weekly. Serum chemistry and hematologic parameters were evaluated at termination of the study. At necropsy, skin and major organs were collected, organs were weighed, and all tissues were processed for histopathological examination.

RESULTS

- No evidence of toxicity as determined by overt physical signs, body weight, food consumption, serum chemical or hematological analyses, organ weights, or gross pathological examination was seen with any of the treatment regimens.

- No perceptible elevation of acetone levels, or only slightly increased levels were observed after acute administration of any of the formulations tested. In addition, there was no evidence for elevated blood acetone levels after subchronic treatment.

- Histology showed that there were no significant microscopic differences between any treatment or control groups.

ACETONE LEVELS

Baseline (n=8)	= <0.9 µg/ml
Acetone (n=2)	= <6.0 µg/ml
Skin Coating (n=6)	= <6.0 µg/ml
NOEL (humans)	= >330 µg/ml

HISTOPATHOLOGIC FINDINGS

No significant differences were seen between untreated skin and skin treated with either acetone alone or the acetone/polymer mixture. No difference was seen between abraded and unabraded sites.

CONCLUSION

The results demonstrate that acetone alone or present in a mixture of acetone/ polymer coating is non-toxic and non-irritating to skin following either an acute or subchronic administration in miniswine. Furthermore, there is no evidence that blood acetone concentrations ever reach levels that would be considered toxic to humans. Only minimal amounts of acetone are absorbed after topical application.

REFERENCE

HW Haggard, LA Greenberg, and JM Turner. The physiological principles governing the action of acetone together with determination of toxicity. J. Indust. Hygiene. Toxicol. 26 (1944)133-151.

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