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Zusammenfassung der Produktdaten zur Toxikologie und Ökologie / Summary of Product Data with Reference to Toxicology and Ecology

Zur Bewertung der toxikologischen Eigenschaften wird auf literaturbekannte Daten und Publikationen für den Stoff/die Inhaltsstoffe des Produktes verwiesen (siehe Anlage). / For assessment of the toxicological properties there is referred to data published in literature about the product/components (see enclosure).

Es wird verwiesen auf / It is referred to

Final Report on the Safety Assessment of Stearyl Heptanoate, Journal of the American College of Toxicology 14 (6):498-510, 1995

Die Untersuchungsergebnisse zu / The results on

- **Acute Oral Toxicity, Acute Dermal Toxicity, Ocular Irritation, Sensitization, Comedogenicity, Mutagenicity**

sind zusammengestellt in dem Dokument / have been summarized in the document

STEARYL HEPTANOATE (Interne Bez. / Internal marking "stearhept_zs")

STEARYL HEPTANOATE

Literaturangaben zur Toxizität
Toxicological Test Results from Literature

Quelle / Reference:

Final Report on the Safety Assessment of Stearyl Heptanoate

Journal of the American College of Toxicology 14 (6):498-510, 1995

(Auszug / Excerpt)

Animal Toxicology

Acute Oral Toxicity

Five male and five female fasted albino Sprague-Dawley rats were given a single oral dose of 16 ml/kg Stearyl Heptanoate by gavage (Inveresk Research International, 1977). A control group was dosed with 16 ml/kg water by gavage. Clinical observations were made for 14 days and the rats were then killed. Body weights were measured prior to dose administration, on day 7, and at study termination. No animals died during the study. The only observations were mild piloerection and slight diarrhea on day 1. Body weight gains were comparable to control values. The oral LD_{50} of Stearyl Heptanoate for male and female albino Sprague-Dawley rats was > 16 ml/kg.

Five male and five female fasted albino Sprague-Dawley rats were given a single oral dose of 5.0 g/kg of a cosmetic formulation containing 0.7 % Stearyl Heptanoate in mineral oil USP by gavage (Hazleton Laboratories America, Inc., 1988a). (Dose volume was 10.0 ml/kg.) Clinical observations and mortality checks were made 1, 2.5, and 4 h after dosing and then once or twice daily, respectively, for 14 days. Body weights were measured prior to dose administration, on day 7, and at study termination. No animals died during the study and no clinical signs of toxicity were observed. The oral LD_{50} of a formulation containing 0.7 % Stearyl Heptanoate for male and female albino Sprague-Dawley rats was > 5.0 g/kg.

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Acute Dermal Irritation

Six albino rabbits, three per sex, were used to evaluate the primary dermal irritation potential of Stearyl Heptanoate (Inveresk Research International, 1977). The skin on the backs of the rabbits was clipped free of hair providing four application sites, two of which were abraded. Chromatography paper (1 sq. in.) wet with either 0.5 ml of the test material (undiluted) or sodium lauryl sulfate (a 10 % solution in water) was applied to an intact and an abraded site on each rabbit for 24 h under occlusive patches. The test sites were rinsed after patch removal. The sites were scored immediately and 48 h after patch removal for erythema and edema according to the Federal Hazardous Substances Labelling Act (F.H.S.L.A.) scoring system (16CFR 1500.41). The greatest average score for both erythema and edema produced by Stearyl Heptanoate was 1.00 for abraded skin after 24 h. The score for both erythema and edema for intact skin after 24 h was 0.83. The primary irritation score for Stearyl Heptanoate (determined by adding the erythema and edema scores for intact and abraded skin after 24 and 72 h and dividing each by 4) was 1.21/8. (The primary irritation score for Sodium Lauryl Sulfate was 3.51/8.) Stearyl Heptanoate was classified as mildly irritating.

Sensitization

Albino Dunkin Hartley guinea pigs were used to determine the sensitization potential of a cosmetic formulation containing 1.5 % Stearyl Heptanoate (Hazleton Laboratories America, Inc., 1987a). The animals were divided into a test group of 20 animals, 10 per sex, a negative control group of 10 animals, five per sex, and an irritation screen group of four animals, two per sex. During the irritation screen, which was used to determine the animals' irritation threshold for the material, the test article was applied undiluted or at concentrations of 25, 50, or 75 % w/v in deionized water to the backs of the animals. Each animal received two concentrations of the test material. The test sites were examined 24 and 48 h after exposure. (The site was depilated 3 h before the 24 h reading using a commercial depilatory.) It was determined from the results obtained during this screen that the test material was to be applied undiluted for the induction phase and as a 75 % w/v suspension in deionized water for the challenge. The dose volume for all applications was 0.3 ml. At induction, 0.3 ml of undiluted test material was applied to the shaved left shoulder of each animal using a Hilltop Chamber (25 mm diameter). The test site was wiped with a paper towel after 6 h of exposure. Each animal received one application per week for a total of three applications, and the application sites were examined and scored according to the Buehler scale 24 h after dosing and prior to the challenge application. The challenge was performed 2 wks after the third induction application. The challenge dose of 75 % w/v test material in

deionized water was applied to a previously un-patched site on the anterior right flank of the test group animals as well as to the previously untreated controls. The test sites were examined and scored 24 and 48 h after dose application. (The site was depilated 3 h before the 24 h reading using a commercial depilatory.) General observations were made daily. Body weights were measured at study initiation, weekly throughout the study, and at study termination.

Five of the 20 animals of the test group and three of the 10 animals of the negative control group had faint dermal reactions (scores of 0.5) to the challenge application; reaction scores of the test animals were not greater than the reaction scores of the negative control animals. The incidence of a positive response (the number of animals having responses of ≥ 1 at either the 24 or 48 challenge reading divided by the total number of animals tested) was 0/20 and 0/10 for the test and negative control groups, respectively. The severity of response (the sum of the test grades divided by the total number of animals tested) for animals of the test group was 0.1 after 24 h and 0.0 after 48 h. For animals of the negative control group, the severity was 0.2 after 24 h and 0.1 after 48 h. No significant clinical observations were made during the study. No significant differences in body weight gains were observed between the test and control groups.

Ocular Irritation

Six albino rabbits, three per sex, were used to determine the ocular irritation potential of Stearyl Heptanoate (Inveresk Research International, 1977). A volume of 0.1 ml of undiluted test material was placed in the conjunctival sac of the right eye of each rabbit; the eyes were not rinsed. Irritation was scored according to the F.H.S.L.A. scoring system (16CFR 1500.42) after 1, 24, 48, and 72 h and after 7 days. Ocular reactions were confined to the conjunctiva and persisted for several days. After 7 days, all eyes were normal except for very mild conjunctival erythema which occurred on day 1, was 1.7 and the PIIs were 0.7 after 1 h, 1.7 on day 1, 0.3 on day 2, and 0.0 on day 3. No corneal or iridal irritation was observed in any of the animals. A cosmetic formulation containing 0.7 % Stearyl Heptanoate was not considered a primary eye irritant.

Comedogenicity

Six male New Zealand White rabbits were used to examine the comedogenic potential of a cosmetic formulation containing 1.5 % Stearyl Heptanoate (Hilltop Biolabs, Inc., 1987a). The material was applied undiluted to the inner surface of the basal portion of the right ear of each rabbit using the tip of a 2.5 cc syringe. An empty

syringe rubbed across the left ear served as the negative control. Three rabbits were treated 5 days/wk for 2 wks while the other three rabbits were treated 5 days/wk for 4 wks. All ears were scored for comedone formation (on a scale of 0 to 4) after every fifth application and prior to study termination. The animals were killed at the end of the study and the ears were removed and processed so that the epidermal tissue could be examined microscopically. During the study, the following irritative effects were noted in the right ear of one or more animals: erythema; small scratches; slight to extreme desquamation; slight thickening; red or yellow appearance in colour; brown spots; and reddish-brown discoloration. No significant irritation was observed.

For animals dosed for 2 wks, the greatest average in-life comedone score was 3.33 on day 5, with one animal having a score of 4 (severe, confluent involvement) and the other two having scores of 3 (moderate [extensive] comedone formations). The average scores on days 12 and 15 were 2.67 and 2.0, respectively. The average scores for the control ear were 0, 0.67, and 0.67 on days 5, 12, and 15, respectively. For animals dosed for 4 wks, the greatest average in-life comedone score was 2.33 on day 5, with one animal having a score of 3 and the other two having scores of 2 (mild [several] comedone formations). The average score was 2.0 on days 12, 15, 22, and 26 and 1.33 on day 29 (a score of 1 corresponded to trace [few] comedone formations). The average control scores varied from 0 to 1.0 during the 4 wks of dosing. The average comedone scores in the processed tissues were 1.67 and 1.0 for the animals treated 2 and 4 wks, respectively; the average control score was 0 for both groups. The authors concluded that a cosmetic formulation containing 1.5 % Stearyl Heptanoate produced slight to moderate comedogenicity in rabbit ears.

Mutagenicity

The mutagenic potential of PCL-Solid 2/066220 was examined using the Ames *Salmonella*/microsome plate incorporation assay (Labor L+S GMBH, 1993a). PCL-Solid 2/066220 in dimethylsulfoxide (DMSO), 8.0-5000 µg/plate (concentration range determined using a preliminary study), was assayed with and without metabolic activation using *Salmonella* strains TA100, TA1535, TA98, TA1538, and TA1537. Positive and negative controls were used. Without metabolic activation, the positive controls were: Na-azide for strains TA100 and TA1535; 2-nitrofluorene for strains TA98 and TA1538; and 9-aminoacridine for strain TA1537. With metabolic activation, 2-aminoanthracene was the positive control for all the *Salmonella* tester strains. The vehicle served as the negative control for all strains with and without metabolic activation. Two trials were performed. PCL-Solid 2/066220, 8.0-5000.0 µg/plate, did not induce base pair or frame shift mutations with or without metabolic activation. The mutagenic potential of PCL-Solid 2/066220 was also examined using an *in vivo* micronucleus

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test (Labor L+S GMBH, 1993b). NMRI mice, five males and five females per group, were given a single oral dose of 500, 1500, or 5000 mg/kg PCL-Solid 2/066220 in corn oil at a volume of 10 ml/kg. Two negative control groups and a positive control group dosed with vehicle and cyclophosphamide, respectively, were used. Animals of the test and control groups were killed 24 h after dosing; mice of an additional group dosed with 5000 mg/kg PCL-Solid 2/066220 were killed 48 h after dosing. No clinical signs were observed for any of the test animals following dose administration. After 24 or 48 h, the number of polychromatic erythrocytes with or without micronuclei, the number of normochromatic erythrocytes, and the ratio of poly- to normochromatic erythrocytes observed for the test animals did not differ significantly from historical or negative control values. PCL-Solid 2/066220 did not have a clastogenic effect.