TEGOSOFT® CR MB

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

Zur Bewertung der toxikologischen bzw. der ökotoxikologischen Eigenschaften wird auf literaturbekannte Daten und Publikationen für den Stoff/die Inhaltsstoffe des Produktes verwiesen (siehe Anlagen). / Regarding evaluation of the toxicological and ecotoxicological properties we refer to relevant publications and data on the single substance / the product components (see attachments).

Hinweis / Comment

Das Produkt TEGOSOFT® CR MB (Cetyl Ricinoleate) ist nicht auf seine toxikologische und ökotoxikologische Wirkung überprüft worden. Es liegen jedoch Ergebnisse für Verbindungen vor, die wesentliche Fragmente des Cetyl Ricinoleates beinhalten. Die entsprechenden Strukturfragmente, d. h. der Cetyl- bzw. der Ricinoleate-Rest können durch Cetyl Alkohol sowie Glyceryl Ricinoleate definiert werden. Auf der Basis der vorhandenen Daten für diese Rohstoffe, lässt sich in vertretbarem Umfang auch für TEGOSOFT® CR MB ein ähnliches gesamttoxikologische Verhalten ableiten. / The product TEGOSOFT® CR MB (Cetyl Ricinoleate) has not been tested for its toxicological and ecotoxicological properties. However, test results are available for compounds which contain essential fragments alike in structure to the Cetyl Ricinoleate. The corresponding structural fragments, i.e. the Cetyl and the Ricinoleate radical are described by Cetyl Alcohol and Glyceryl Ricinoleate. On the basis of the data being available for those raw materials, it may be justified that a similar total toxicological profile for TEGOSOFT® CR MB can be deducted.

Die Ergebnisse sind zusammengestellt in den Dokumenten / The results are summarized in the documents

CETYL ALCOHOL	(Interne Bez. / Internal marking "cetal_zs")
GLYCERYL RICINOLEATE	(Interne Bez. / Internal marking "glyric_zs")

CETYL ALCOHOL

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Prüfung Test	Methode Method	Ergebnis Result	Datum Date
Basic toxicokinetics	[1]	Following skin application of lauryl alcohol about 2.84 % of the administered dose was absorbed. Of this absorbed dose > 90% was excreted in expired air (CO_2)	1987
Basic toxicokinetics	[2]	Substance was incompletely absorbed with 20% of the dose recovered unchanged from the faeces. Faecal excretion was complete within 48 h. About 6% of the dose was in the form of glucuronic acid conjugate in the urine	1958
Acute dermal toxicity (rat)	OECD 401	LD_{50} > 2,000 mg/kg bw	04/1996
Acute inhalation toxicity	No guideline followed	EL (1h) > 1.5 mg/L air [3]	
Acute dermal toxicity	No guideline followed	LD_{50} = 8,000 mg/kg bw [3]	
Acute dermal irritation/corrosion (rabbit)	OECD 404	not irritating	03/1996
Acute eye irritation (rabbit)	OECD 405	not irritating	04/1996
Skin sensitisation (guinea pig)	OECD 406	not sensitising	06/1996
90 day repeated dose toxicity (rat)	No guideline followed	NOAEL > 4,257 mg/kg bw based on highest dose tested	1973
90 day repeated dose toxicity (rat)	No guideline followed	NOAEL = 1,127 mg/kg bw/day (males) NOAEL = 1,243 mg/kg bw/day (females) (highest doses tested) [4]	
Gene toxicity (Ames)	OECD 471	not mutagenic	06/1996
In vitro mammalian cell gene mutation test	OECD 476	not mutagenic [5]	
Chromosomal aberration	OECD 473	non clastogenic [5]	
Toxicity to reproduction (rat)	No guideline followed	A repeated oral dose NOAEL of 1,822 mg/kg/day for males and 4,567 mg/kg/day (the highest dose tested) in females was determined for effects on reproductive organs in the rat	1966
Toxicity to reproduction (repeated dose 28-day oral toxicity in rats)	OECD 407	NOAEL for effects on reproductive organs = 1,000 mg/kg bw/day	1985

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Biodegradation aerobic	OECD 301 B	82.4 % (28 d) readily biodegradable	1993
Bioaccumulation aquatic / sediment	QSAR	BCF = 45.300 L/kg	2005
Absorption/desorption	QSAR	Log Koc (TGD hydrophobics method) = 5.487	2005
Acute fish toxicity	OECD 203	LC_{50} (96h) is greater than limit of solubility	03/1996
Acute daphnia immobilisation	QSAR	EC_{50} (48h) > 100 mg/L	2009
Algae growth inhibition test	DIN 38412 part 9	EL50 (96h) is > 0.01 mg/L (> limit of solubility)	02/1992

[1] Publication: Percutaneous absorption of aliphatic compounds. Iwata Y, Moriya Y, Kobayashi T. 1987, Cosmet. Toiletries 102(2): 53-68
[2] Publication: The metabolism of spermaceti W.A., McIsaac W M, Williams R T, 1958, Journal Biol. Chem. 2(2): 42-44
[3] Read-across from myristyl alcohol
[4] Read-across from 1-hexanol
[5] Read-across from behenyl alcohol

* Full Robust Study Summaries can be checked under the ECHA Registered Substance website and with the following registration number: 01-2119485905-24

Video instruction for use is available on the personal care website.

GLYCERYL RICINOLEATE

Literaturangaben zur Toxizität
Toxicological Test Results from Literature

Quelle / Reference:

Final Report on the Safety Assessment of Glyceryl Ricinoleate

Journal of the American College of Toxicology, Vol. 7, Number 6, 1988
Seiten/pages 721 - 739

(Auszug / Excerpt)

Animal Toxicology

Acute Oral Toxicity

Glyceryl Ricinoleate was evaluated for acute oral toxicity in mice. A preliminary range-finding study was performed using doses of 5.0, 10.0, 20.0, and 25.0 ml/kg, administered by cannula, on groups of two mice each. The mice were observed from the time of dosing until the end of a 7 day period. The results of this test were used to determine doses to be used for the final study. In a preliminary study, none of the mice died. The doses of Glyceryl Ricinoleate used in the final study were 12.5, 20.0, and 25.0 ml/kg. Test groups consisted of 10 mice each. Over the 7 day period, none of the mice at the lowest dose level died. In the 20.0 ml/kg group one mouse died within 24 h of dosing, and two mice died between days 4 and 7 in the 25.0 ml/kg group. The two mice that died in the high-dose group previously had a loss of body weight, as did others of the test animals (especially on day 7). Other signs noted in the test animals were piloerection within 30 minutes after dosing and inactivity within 2 h after dosing. All surviving animals appeared to be asymptomatic after day 7. It was concluded that the LD50 value for Glyceryl Ricinoleate exceeded 25.0 ml/kg.

The acute oral toxicity of products containing Glyceryl Ricinoleate was tested in rats. In the first test, five rats were dosed by oral intubation with 15.0 g/kg of a product containing 5.6 % Glyceryl Ricinoleate. The product was administered in corn oil, with a final Glyceryl Ricinoleate test concentration listed as 33.3 %.

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None of the rats died, and all gained weight over the 7 day observation period. The second test was identical to the first, except that a different unspecified product was used. As in the first test, none of the five rats died when dosed with 15.0 g/kg of the product in corn oil, and all gained weight over the 7 day observation period. The third test was performed in the same manner as the first two, once again the exception being the product type tested. As the previous tests indicated, the product was non-toxic when ingested, and the five rats all gained weight during the study.

Skin and Tissue Irritation

Four New Zealand white rabbits were used in a Draize skin test of Glyceryl Ricinoleate. A 0.5 ml sample of the test substance was placed on the clipped and intact and clipped and abraded skin of each rabbit. An occlusive patch was then placed over each test site, where it remained for 24 h. The test sites were scored by the method of Draize upon the removal of the patches and 48 h later (24 and 72 h readings). The average of the two scores was the primary irritation index (PII). Two of the rabbits had very slight erythema at both the intact and abraded sites at the 24 h reading, and the reaction of the abraded site of one of these rabbits persisted through the 72 h reading. A third rabbit had well-defined erythema at both sites at the 24 h reading, with the reaction at the abraded site again persisting with the same intensity through the 72 h reading. This same rabbit also had a slight edema at the abraded site at the 72 h reading. The fourth rabbit tested had no reactions. The PII was determined to be 0.75, and it was concluded that the Glyceryl Ricinoleate was mildly irritating.

A primary irritation study with rabbits was performed on Glyceryl Ricinoleate using the solid product, undiluted, as it was supplied by the manufacturer. The Glyceryl Ricinoleate, 5.0 g, was applied to the clipped and intact (left flank) and clipped and abraded (right flank) skin of six albino New Zealand white rabbits. Composite patches were placed over the test sites, remaining in place for 24 h. The sites were graded at 24 h and again at 72 h according to the method of Draize. All rabbits had scores of 0 for both erythema and edema formation resulting in a group total mean score and a primary irritation score of 0.0. Glyceryl Ricinoleate was thus classified as a non-irritant to the skin.

The primary skin irritation of various unspecified products containing 5.6% Glyceryl Ricinoleate was tested in rabbits using an occlusive patch single-insult test procedure. The maximum obtainable PII was 4. In the first test, the nine rabbits had scores of 0 at 2 and 24 h after removal of the patch, resulting in a group PII score of 0.00.

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The results of the second, third, and fourth tests were identical, the group PII being 0.00, indicating that the test products were non-irritating.(79-81) In another test, rabbit 9 had a score of ½ at the 2 h grading, but this had reduced to 0 by the 24 h grading.

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The other eight rabbits all had scores of 0 at both grading times. The group PII was 0.06, indicating that the test material was minimally irritating.(82) In the final test, all rabbits had scores of 0 at both grading times, resulting in a group PII score of 0.00, indicating that the product tested was non-irritating.

In a study of tissue irritation, injections of 0.5 ml of Glyceryl Ricinoleate were administered bilaterally into the pectoral muscle of six male Hubbard crossbred chickens weighing 3-4 pounds. On days 1, 3, and 7 post-injection, two chickens were killed and examined for the determination of gross lesions at the injection site. Sites were examined for inflammation and necrosis (scale of 1-5). Scores of 1 (three of six chickens) and 3 (two of six chickens) were reported. The right pectoral muscles of two chickens had necrotic foci (grade 5) on days 1 and 7. Glyceryl Ricinoleate caused moderate irritation and was not absorbed (i.e., the compound was visible at the treatment of sites of all six chickens).

After intravenous administration of a bolus of 0.1 ml/kg technical-grade ricinoleic acid into the inferior venae cavae of eight dogs, five dogs developed tachypnea (increase of at least five breaths per minute over the basal rate) and two dogs died from circulatory arrest. No other clinical signs, such as erythema, hives, edema, or defecation, were noted. Ricinoleic acid regularly produced an immediate decrease in blood pressure occasionally followed by a second hypotensive response that was not associated with histamine release. Increased histamine ranging from 0.6 to 15.3 ng/ml in the blood of seven dogs was observed within 2 minutes of administration of ricinoleic acid.

Eye Irritation

A 0.1 ml sample of Glyceryl Ricinoleate was placed into one eye of each of nine New Zealand white rabbits. Three of the rabbits had the test material rinsed from their eyes with 20 ml of lukewarm water 2 s after instillation, three rabbits had their eyes rinsed 4 s after instillation, and 3 rabbits did not have their eyes rinsed. In all the rabbits, the contralateral eye served as an untreated control. The eyes were graded for damage according to the Draize system for scoring ocular lesions at 1, 2, 3, 4, and 7 days after instillation of the test material. No irritation was observed in the eyes that had been rinsed, and only mild irritation of the conjunctiva, lasting no longer than 24 h, was noted in the eyes that were not rinsed. Into the conjunctival sac of the right eye of each of six albino New Zealand white rabbits was instilled 0.10 g undiluted Glyceryl Ricinoleate. The left eye of each rabbit served as the untreated control. The eyes were examined at 24, 48, and 72 h after instillation of the test material, and irritation was scored according to Draize and the Federal Register 1973. An opthalmo-scope was used to examine the eyes, and ultraviolet light and fluorescein dye were used to determine the incidence of corneal opacities. All test animals had scores of 0 throughout the 3 day observation period,

resulting in a group mean 3 day score of 0.0. Glyceryl Ricinoleate was classified as negative for irritation or a non-irritant to the eye.

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A group of unspecified products, all but one containing 5.6 % Glyceryl Ricinoleate (the exception contained 6.2 % Glyceryl Ricinoleate), was tested for eye irritation. In the first six tests, the protocol was the same and is summarized here. The product was applied to 100 % concentration to the eyes of six rabbits (per product tested). The product was applied three times, the eyes were not rinsed, and anesthesia was not used. With one exception, the eyes were scored daily for 3 days after application of the test product; in the other case, the eyes were scored for the first 4 days and again on day 7. The irritation was scored by the Draize classification of eye irritation. In test 1, all rabbits scored 0 at all times, the resulting conclusion being that the product tested did not have the potential for eye irritation. In test 2, rabbit 3 had corneal opacity, iritis, and redness, swelling, and discharge of the conjunctiva (scores of 5, 5, and 4, respectively) on day 1. This resulted in a total score of 3 for the day. On days 2 and 3, all rabbits scored 0, leading to the conclusion that the product tested had a minimal irritation potential. In test 3, rabbit 3 scored a 2 for conjunctival redness, swelling, and discharge on day 2, resulting in a total score of 1 for the day. On days 1 and 3, the scores were 0, leading to the conclusion that the product tested had a minimal irritation potential. In test 4, the total score for day 1 was 2, with rabbit 3 having scores of 5 and 6 for corneal opacity and conjunctival redness, swelling, and discharge, respectively. On days 2 and 3 all scores were 0, and it was concluded that the product tested had a minimal irritation potential. In test 5, the concentration of Glyceryl Ricinoleate in the product tested was 6.2 %. On day 1, rabbit 6 scored 2 for conjunctival redness, swelling, and discharge, for a group total score of 1. The same situation occurred with rabbit 2 on day 2, and the condition with this rabbit persisted into day 3. Also on day 3, rabbit 3 scored 5 for corneal opacity and 10 for conjunctival reactions. The group total score for day 3 was 3. On day 4, a conjunctival score of 2 remained for rabbit 3. By day 7, all rabbits were scored as 0. The conclusion reached was that the product tested had a mild irritation potential. In test 6, rabbits 1-3 scored 1 for conjunctival reactions on day 2, resulting in a group total score of 1 for that day. For days 1 and 3 the group total scores were 0, and the conclusion was that the product tested had a minimal eye irritation potential. In test 7, the product was tested at a concentration of 50 % in corn oil, and all scores for all rabbits were 0, indicating that the product tested did not have a potential for irritation.

In test 8, the product was also tested at a concentration of 50 % in corn oil. On day 1, rabbits 1, 4, and 5 scored 2 for conjunctival reactions, and rabbits 2 and 6 scored 4 for the same category. The group total score for day 1 was 2. On day 2, rabbits 3 and 4 scored 2 for conjunctival reactions, and rabbits 2 and 6 remained in the same condition as the previous day. The group total score for day 2 was 2. On day 3, all rabbits scored 0. The conclusion was that the product tested had a minimal irritation potential.

A final report on the "toxicity testing" of castor oil is expected from the National Toxicology Program.

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Mutagenicity and Carcinogenicity

Castor oil was negative for mutagenicity when tested by the Ames assay by the National Toxicology Program. A volume of 0.1 ml of a 2 % ricinoleic acid preparation in gum tragacanth was injected intra-vaginally into 20 BALB/c female mice twice weekly for a total of 100 injections. No tumors were seen in the 20 treated or in the 30 untreated mice. Of the 20 positive control mice treated with 0.3 % 7,12-dimethylbenz(a)anthracene, also in gum tragacanth, 15 developed squamous cell carcinomas of the vagina and/or perineal skin. Castor oil is currently being evaluated for carcinogenicity by the National Toxicology Program.

Clinical Assessment of Safety

Skin Irritation and Sensitization

The skin irritation potential of Glyceryl Ricinoleate was evaluated in 20 human test subjects. An unspecified product containing 5.6 % Glyceryl Ricinoleate was applied at full strength to occlusive patches, which were then applied in a single insult to the test subjects. The PII of the test product was 0.0, indicating that the product containing 5.6 % Glyceryl Ricinoleate was not an irritant. In a second irritation potential test, the PII for an unspecified product containing 5.6 % Glyceryl Ricinoleate was also 0.0. In this test, the number of panelists was 19, and as before, the product was applied on an occlusive patch as a single insult. Again the conclusion was that the product containing 5.6 % Glyceryl Ricinoleate was not an irritant.

Castor beans, the source of castor oil from which ricinoleic acid is isolated, contain a toxic polypeptide, ricin, at an approximate concentration of 3%.(100,101) Clinical cases of castor bean skin allergy and asthma have been associated with ricin or "a protein component, not within the ricinoleic acid component of the castor bean. A few cases of lipstick dermatitis have been reported. A 3 + positive reaction to castor oil, an ingredient in a makeup remover, was observed upon series testing of cosmetics and their ingredients after a 23-year-old woman reported acute facial dermatitis. After testing with ingredients of lipsticks and lip creams, a 22-year-old woman who had developed dry and painful cracking of the lips reacted with a 2 + response 48 and 72 h after application of castor oil. In follow-up testing, this subject had similar reactions to purified castor oil, ricinoleic acid, and a 3% preparation of ricinoleic acid in petrolatum. Tests with other fatty acids ingredients of castor oil were negative.

A 29-year-old female with a history of dermatitis to deodorant developed an acute edematous dermatitis of the lips and perioral area spreading to the entire face and neck after a few weeks of use of a lipstick product.(108)

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In a series of three patch tests, the subject had 2 + reactions to a standard test series (20% colophony in petrolatum) and to the lipstick formulation in the first test, 2 + reactions to castor oil and 1 % octyl-dimethyl-p-aminobenzoic acid in petrolatum, and a 3 + reaction to 0.5 % aqueous allantoin in the second test. The third test resulted in a 3 + reaction to castor oil, a severe (3 +) spreading reaction to 30% ricinoleic acid in petrolatum, and negative responses to the p-aminobenzoic acid derivative and allantoin preparations. Other cases of dermatitis resulting from the same lipstick formulation were reported previously. A 53-year-old male with no history of skin disease developed periorbital and facial edema with lesions on the lips and in the nose. A 36-year-old male with no history of skin disease developed a severe dermatitis on the lips and around the mouth. A 37-year-old female with a family history of psoriasis and hand eczema developed severe, vesicular dermatitis on the lips and around the mouth. All three subjects had 2 + reactions to the lipstick formulation and to "a microcrystalline wax" ingredient of unknown composition.

Summary

Glyceryl Ricinoleate is the monoester of glycerol and ricinoleic acid. It is an oily liquid with a characteristic odour. Castor oil contains 87-90 % Glycerol Ricinoleate. Glyceryl Ricinoleate is most frequently used in cosmetic as a base ingredient in lipsticks and as a pigment binder in eye shadows. Its use in cosmetic formulations has been reported at concentrations between 0.1 and 50 %. In 1986, it was used in a total of 34 cosmetic formulations. Monoglycerides of edible fats and oils are generally recognized as safe for use as emulsifying agents and food additives. Glyceryl Ricinoleate is listed by the FDA as an inactive ingredient in drug preparations. Castor oil is used as an active ingredient in some OTC wart-removing products, and ricinoleic acid is used in some OTC vaginal contraceptives. Castor oil is also considered a safe and effective laxative when taken orally as a single dose. Upon ingestion, Glyceryl Ricinoleate is absorbed into the intestinal mucosa. Increased doses of castor oil result in decreased absorption by the intestine. Ricinoleic acid appears to be preferentially incorporated into the triglycerides rather than the phospholipids. Metabolically, ricinoleic acid may be degraded by ß-oxidation into acetyl-CoA and a dodecanoyl-CoA. This dodecanoic acid may be further metabolized either by hydration followed by oxidation and cleavage or by isomerisation of the double bond. Another metabolic pathway involving the a-oxidation of a carbon unit from the carboxyl terminus of the fatty acid has also been observed. Acute oral toxicity tests indicated that Glyceryl Ricinoleate has an LD_{50} greater than 25.0 ml/kg in mice and that products containing 5.6 % Glyceryl Ricinoleate were not toxic when ingested. The feeding of castor oil to rats results in the presence of hydroxystearic acid in the faeces. The hydroxystearic acid is probably formed by bacterial hydrogenation of ricinoleic acid. The hydrolysis of castor oil and Glyceryl Ricinoleate in the small intestine releases ricinoleic acid; ricinoleic acid is the active cathartic ingredient in castor oil. The mechanisms of the cathartic action of ricinoleic acid are currently being studied.

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Glyceryl Ricinoleate, when evaluated by a Draize skin test, was a mild irritant to rabbits. In a primary skin irritation test in rabbits, Glyceryl Ricinoleate was classified as a non-irritant. When rabbits were tested with products containing 5.6 % Glyceryl Ricinoleate in a single-insult occlusive patch test, the products had either no (four of five tests) or mild (one of five tests) irritation potentials. Injection of Glyceryl Ricinoleate into the pectoral muscles of chickens caused mild irritation at the site of injection, but no Glyceryl Ricinoleate was absorbed. Glyceryl Ricinoleate was non-irritating to rabbit eyes in a primary eye irritation test, and in a Draize test, it was mildly irritating to rabbit eyes from which it was not rinsed but non-irritating to rabbit eyes from which it had been rinsed 2 and 4 s after instillation. Various products containing Glyceryl Ricinoleate were tested for irritation potential in rabbit eyes. Of eight tests, two products demonstrated no irritation potential, five products had a minimal irritation potential, and one product had a mild irritation potential. Castor oil was non-mutagenic by the Ames test. Carcinogenicity testing in female mice using ricinoleic acid, a possible constituent ingredient of spermicidal preparations, yielded negative results. In human single-insult occlusive patch tests no indication of skin irritation potential was observed in the two products tested (each contained 5.6 % Glyceryl Ricinoleate). There have been several reported instances of lipstick dermatitis, and castor oil and ricinoleic acid have been implicated in clinical patch test studies on patients experiencing dermatitis, and occasional facial edema, from the use of lipsticks.

Discussion

Section 1 Paragraph (p) of the CIR Procedures states that "A lack of information about an ingredient shall not be sufficient to justify a determination of safety." In accordance with Section 30(j)(2)(A) of the Procedures, the expert panel informed the public of its decision that the data on Glyceryl Ricinoleate were insufficient to determine that this ingredient, under each relevant condition of use, was either safe or not safe. The panel issued a "Notice of Insufficient Data" on January 29, 1987, outlining the data needed to assess the safety of Glyceryl Ricinoleate. The types of data required included: 1. Guinea pigs 28 day chronic dermal toxicity. 2. Clinical sensitization and photosensitization studies (or an appropriate ultraviolet spectrum instead of the photosensitization data). There has been no response or indication of intent to supply the aforementioned information.

Conclusion

The CIR Expert Panel concludes that the available data are insufficient to support the safety of Glyceryl Ricinoleate as used in cosmetics.