

Dehyton® MC

-Summary of toxicological information-

Summary

Dehyton® MC was not toxic or harmful in an acute toxicity test in the rat. It is a severe eye irritant for the rabbit. Data from a test in the rabbit do not indicate Dehyton® MC to be irritating to the skin. Dehyton® MC did not display any sensitizing effects in guinea pigs. From a subacute oral toxicity study in the rat a NOAEL of 1000 mg/kg bw / day can be deduced. No potential for gene mutations was detected in the Ames test.

Zusammenfassung

Dehyton® MC war weder giftig noch gesundheitsschädlich in einer Untersuchung zur akuten oralen Toxizität in Ratten. Am Kaninchen verursachte Dehyton® MC schwere Augenreizungen. Daten aus Untersuchung am Kaninchen geben keine Hinweise auf ein hautreizendes Potenzial. Am Meerschweinchen trat mit Dehyton® MC kein sensibilisierendes Potenzial zutage. Aus einer subakuten oralen Toxizitätsstudie mit Ratten ist ein NOAEL von 1000 mg/kg Körpergewicht/Tag abzuleiten. Aus dem Ames-Test gibt es keine Hinweise auf ein Potenzial für Genmutationen.

General

This evaluation refers exclusively to the product Dehyton® MC in the quality as specified and provided by BASF. Dehyton® MC (INCI: Sodium Cocoamphoacetate) is an amphoteric surfactant and suitable for the application in mild surfactant preparations.

1. Acute oral toxicity

Acute oral toxicity is the adverse effect occurring within a short time of oral administration of a single dose of a substance or multiple doses given within 24 hours. Generally rodents (rats, mice) are used as test animals. The test substance is applied by gavage once in graduated doses to various groups of test animals priorly fasted.

The acute oral toxicity of Dehyton® MC was investigated in ten male Wistar rats. Single doses of 5000 mg/kg body weight were administered orally by gavage to animals that had priorly been fasted. No adverse effects were observed during a 14 day post observation period. Although, due to historical reasons the test procedure does not comply with current methods (only one gender tested), the result is regarded as being valid nevertheless, since the LD₅₀ was > 5000 mg/kg and thus far exceeded the European classification limit of 2000 mg/kg ⁽¹⁾.

On the basis of this test a classification and labelling of Dehyton® MC is not necessary.

2. Dermal absorption

Dermal absorption is the process in which a substance is taken up through the skin and hence is systemically available.

Experimental determination of dermal absorption was omitted for the following analogous consideration: in general, invasion via the gastro-intestinal route renders a significantly higher bioavailability compared to the dermal route. As the substance or its homologue applied orally (a worst case condition compared to dermal application) up to the classification limit ((2000 mg/kg for the acute toxicity and 50 mg/kg/day for repeated dose toxicity)) did not cause any signs of systemic toxicity, this can be deduced also for the cutaneous route of application.

3. Dermal irritation

Dermal irritation / corrosion is the production of *reversible* / *irreversible* inflammatory changes in the skin following the application of the test substance. International standard test method is OECD guideline No 404 (consistent with EU guideline 84/449/EEC No B4): the test substance is applied to one flank of the shaved back skin of the rabbits. The untreated area of each animal serves as a control.

The acute dermal irritation of diluted Dehyton® MC (25 % active matter) was tested on the shaved skin of five New Zealand rabbits, strain Charles River. The contact time under occlusive conditions was 4 hours. The 24/48/72 hours scores under these conditions were 1.33 for the erythema and 0.93 for the oedema ⁽²⁾.

With regard to classification the patch test data in rabbits were obtained according to a protocol slightly deviating to the current OECD standard guideline No. 404. Dehyton® MC was tested undiluted on the shaved back skin of six New Zealand rabbits. The contact time under occlusive conditions was four hours. The 24/48/72 hours scores were < 0.25 for the erythema, no oedema were observed on the exposed skin area. Within 72 hours all skin reactions disappeared ⁽¹⁾.

The mode of contact was occlusive instead of semi-occlusive. With regard to this modification contributing to more stringent test conditions relatively mild effects were observed in the rabbit.

In light of the available data, a classification and labelling of Dehyton® MC is not necessary.

4. Mucous membrane irritation (eye irritation)

Eye irritation / corrosion is the production of *reversible* / *irreversible* changes in the eye following the application of a test substance to the anterior surface of the eye. International standard test method is OECD guideline No 405 (consistent with EU guideline 84/449/EEC No B5): the test substance is instilled into one eye each of at least three rabbits. The untreated eye of each animal serves as a control.

0.1 ml of diluted test substance (20 % active matter) was instilled by a single application and permanent contact into the eyes of six male New Zealand rabbits. The eyes were scored 2, 6, 24 and 72 hours and 7 days after application. 2 hours after instillation, only slight redness and of the conjunctivae and slight oedema was observed. The reversibility was complete in less than seven days. No cornea and irital reactions were observed between 2 and 72 hours time ⁽¹⁾.

Furthermore eye irritation for the group of Cocoamphoacetates were synopsized and evaluated:

In all tests, a 0.1ml sample of substance was instilled into the conjunctival sac of each rabbit, the other eye served as the untreated control. In some studies rinsing after instillation was used, in other not. Ocular irritation responses were scored according to Draize (max=110) on days 1, 2, 3, 4 and 7. Cocoamphoacetate at concentrations of 16 to 50 % active matter as well as solutions of unknown activity, were minimally to severely irritating when no rinsing took place ⁽³⁾.

A clear dose dependent decrease in the eye irritation potential can be expected based on those literature data. So for example with 16 % active matter only minimal irritation similar to the results seen with 20 % active matter in the in-house study are reported.

Nevertheless for reasons of precaution and data with 25% active matter ⁽⁴⁾ the undiluted product has to be classified and labelled as severe irritating to eyes (R 41).

5. Skin sensitization

Skin sensitization (allergic contact dermatitis) is an immunologically mediated cutaneous reaction to a substance. In the human, the responses may be characterized by pruritis, erythema, oedema, papules, vesicles, bullae or a combination of these. In other species the reactions may differ and only erythema and oedema may be seen. Generally guinea pigs are used as test animals. During the first phase of the test, the induction, the skin of the test animals is treated with a minimally irritating concentration of the test substance. After a lag time they are challenged with a maximally non-irritating concentration. Potential signs of hyperreactivity are evaluated 24 and 48 hours after finalization of the challenge.

A test slightly deviating from the Magnusson and Kligman method was performed with Dehyton® MC to investigate the sensitizing potential with female guinea pigs, strain Pirbright White. The test substance was applied as a 5 % dilution in aqua dest. for the intracutaneous and as a 5 % dilution for the epicutaneous induction. Concentration for the open epicutaneous challenge was 25 % in aqua dest. No skin reactions indicative for an immune response have been observed 24 and 48 hours after removal of the challenge patch ⁽⁵⁾.

On the basis of this test a classification and labelling of Dehyton® MC is not necessary.

6. Subchronic toxicity

Subchronic toxicity is the adverse effect occurring as a result of the repeated daily dosing of a chemical to experimental animals for a part (not exceeding 10 %) of the life span. International standard test method with respect to oral application is OECD guideline No 408. The test substance is applied orally once in graduated doses every day over a time period of 90 days to various groups of test animals (in case of an application time of 28 days the study is designated as "subacute" - see OECD-guideline No. 407). Animals are monitored daily for signs of intoxication. Furthermore food and water consumption, body weight development and in-life clinical chemistry and, after necropsy, organ weights and histo-pathological parameters are recorded.

A subacute toxicity study was carried out with Dehyton® MC. Groups of 10 male and 10 female Wistar rats received single daily doses of 0 (group 1), 250 (group 2), 500 (group 3) and 1000 (group 4) mg/kg bw Dehyton® MC (5 treatments/week) by gavage for 28 days. To study the reversibility of possible findings in addition to the groups 1 and 4, 5 male and 5 female animals respectively were used.

All doses, even the highest dose of 1000 mg/kg/day, were tolerated by all animals without lethality. The development of the mean body weights of each group (250, 500 and 1000 mg/kg/day) was normal in all male test groups and comparable to the control. At the end of the study all female test groups showed a slight increase in body weight, which was considered to be unrelated to the test compound. In all female test groups the hematological

examination revealed a slight increase in the number of thrombocytes, irrespective of the dose applied. This finding was considered not to be treatment related. The biochemical examination revealed some compound- and dose independent variations. Similar, non-dose-dependent variations were observed with regard to the absolute and relative organ weights such as the weights of kidney, hearts, brain, gonads and liver, which were considered not to be compound related. The macroscopical and microscopical examination of the organs of the high dose group revealed no indications of compound related organ damage. Thus, the additional groups were not examined microscopically. From this study a systemic NOAEL of 1000 mg/kg bw can be deduced⁽⁶⁾.

On the basis of the subchronic toxicity test results a toxicological classification and labelling of Dehyton® MC is not necessary.

7. Mutagenicity

Mutagenicity is the capacity to induce a relatively permanent change in the hereditary material of an organism involving changes in the genes ("gene mutations") or chromosomes ("chromosome mutations"). Gene mutations can be investigated in the *Salmonella typhimurium* reversion ("Ames") test. International standard test method is OECD guideline No 471 (consistent with EU guideline 84/449/EEC No B14). The mutation is detected by a reversion of histidine-auxotrophic bacteria towards prototrophy.

Dehyton® MC was tested with the bacterial tester strains *S. typhimurium* TA 100, TA 1535, TA 1537, TA 1538 and TA 98 in the presence and absence of enzymes obtained from the livers of Aroclor 1254 pre-treated rats (S9 mix) according to an in-house protocol similar to the OECD guideline No. 471. Solutions of the test compound were freshly made up in water just before use. The following concentrations were tested: 4, 20, 100, 500 and 2500 µg/plate.

Dehyton® MC did not induce reverse mutations in the tested strains of *Salmonella typhimurium* in this bacterial mutagenicity test, neither with nor without metabolic activation by S9 mix⁽⁷⁾.

Thus, Dehyton® MC is considered not to be mutagenic in this bacterial mutagenicity test *in vitro*.

References:

- 1 Internal data (1981); unpublished results, Rep. No. TBD 810145
- 2 Internal data (1987); unpublished results, Rep. No. TBD 870150
- 3 Journal of the American College of Toxicology , Vol. 9, No 2 (1990), p 121-142
- 4 Internal data (1987) unpublished results, Rep. No. TBD 870555
- 5 Internal data (1981) unpublished results, Rep. No. TBD 810177
- 6 Internal data (1989) unpublished results, Rep. No. TBD 890303
- 7 Internal data (1981) unpublished results, Rep. No. TBD 810050

This document and any information provided herein is for your guidance only. All information is given in good faith and is based on sources believed to be reliable and accurate at the date of publication of this document. BASF MAKES NO WARRANTY OF ANY KIND, EITHER EXPRESS OR IMPLIED, BY FACT OR LAW, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.

Confidential