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Hoechst

Hoechst Aktiengesellschaft
Pharma Research
Toxicology
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Mucosal tolerance to
50 % (w/w) isopropanol in aqueous solution
in the rabbit
Report No. 27/79

Summary

By testing mucosal tolerance in the rabbit according to FDA guide-lines, 50 % (w/w) isopropanol in aqueous solution proved to be slightly irritant to the mucosa.

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Method:

Mucosal tolerance was tested in 6 rabbits by single application of 0.1 ml of the 50 % (w/w) isopropanol/water mixture in the conjunctival sac of the left eye of the rabbit. The right eye served in each case as untreated control. The experiment was conducted according to the FDA guide-lines (Federal Register 38, No. 187, 27.09.1973, p 27019).

Evaluation was performed at 1, 7, 24, 48, and 72 hours after application by means of a magnifying-glass. After recording of the 24-hour result all eyes were rinsed with physiological saline solution. The 48- and 72-hour results were recorded after additional instillation of a drop of fluorescein-sodium in the dilution 1 : 10 000 = 0.01 %.

The experiment was carried out in the period 18.12. to 21.12.1978.

A numerical evaluation was undertaken according to the classification made in the 'Appraisal of the Safety of Chemicals in Food, Drugs, and Cosmetics', FDA, Austin, Texas, p 51, 1975 (Appendix 1).

Result:

The highest index of irritation of 20 was reached after one to seven hours. Acco ding to the FDA guide-lines the tested substance therefore has to be classified as a mild irritant.

Dr. Ma/Bo
9th February 1979

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Appendix
Evaluations

Scale for Scoring Ocular Lesions

(1) Cornea

(A) Opacity-degree of density (area most dense taken for reading)

No Opacity 0

Scattered or diffuse area, details of iris clearly visible 1

Easily discernible translucent areas, details of iris slightly obscured.....2

Opalescent areas, no details of iris visible, size of pupil barely discernible.....3

Opaque, iris invisible.....4

(B) Area of cornea involved

One quarter (or less) but not zero.....1

Greater than one quarter, but less than half.....2

Greater than half, but less than three quarters.....3

Greater than three quarters, up to whole area.....4

A X B X 5 Total maximum = 80

(2) Iris

(A) Values

Normal.....0

Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive).....1

No reaction to light, hemorrhage, gross destruction (any or all of these).....2

A X 5 Total maximum = 10

(3) Conjunctivae

(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Vessels normal.....0

Vessels definitely injected above normal.....1

More diffuse, deeper crimson red, individual vessels not easily discernible...2

Diffuse beefy red.....3

(B) Chemosis

No swelling.....0

Any swelling above normal (includes nictitating membrane).....1

Obvious swelling with partial eversion of lids.....2

Swelling with lids about half closed.....3

Swelling with lids about half closed to completely closed.....4

(C) Discharge

No discharge.....0

Any amount different from normal (does not include small amounts observed in inner canthus of normal animals).....1

Discharge with moistening of the lids and hairs just adjacent to lids.....2

Discharge with moistening of the lids and hairs, and considerable area around around the eye.....3

Score (A + B + C) X 2 Total maximum = 20

The scores for cornea (1), iris (2), and conjunctiva (3) obtained in each rabbit at the specific reading time are added to give the primary irritation score. The mean of the scores for all rabbits at the specific reading time is calculated. The highest score obtained at any of the reading times is used for the evaluation and the substance is categorized as follows:

0 - 10	Non-irritant	(nicht reizend)
11 - 25	Slightly irritant	(leicht reizend)
26 - 56	Moderately irritant	(mäßig reizend)
57 - 110	Severely irritant	(stark reizend)

Annex

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Schleimhautverträglichkeit / Eye irritation

Substanz / Substance	Konzentration / Concentration	Dosis / Dose	Tierart / Species
Isopropanol/water 50 % (w/w)	undiluted	0,1 ml	Albino Himalayan rabbit

Stunde / Hour		1						7						24						48						72					
Kaninchen Nr. / Rabbit No.		307	308	309	310	311	312	307	308	309	310	311	312	307	308	309	310	311	312	307	308	309	310	311	312	307	308	309	310	311	312
I Cornea	A Grad der Trübung / Opacity	1	0	1	1	1	0	1	0	1	1	1	0	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0
	B Betroffener Bereich / Area involved	1	0	1	1	1	0	1	0	1	1	1	0	0	0	0	2	1	0	0	0	0	1	0	0	0	0	0	0	0	0
	a – A x B x 5 (max 80)	5	0	5	5	5	0	5	0	5	5	5	0	0	0	0	10	5	0	0	0	0	5	0	0	0	0	0	0	0	0
II Iris	Bewertung / Value	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	b – Wert x 5 (max. 10)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III Conjunctiva	A Rötung / Redness	2	2	2	3	2	3	3	3	3	3	3	3	3	2	2	2	2	2	3	0	2	1	0	1	2	0	2	1	0	1
	B Schwellung / Chemosis	2	1	1	2	2	1	3	2	2	3	3	2	2	1	1	2	1	1	1	0	1	0	0	0	1	0	1	0	0	0
	C Absonderungen / Discharge	2	2	2	3	3	3	3	2	3	3	3	3	3	1	2	2	1	2	1	0	0	0	0	0	1	0	0	0	0	0
	c – (A+B+C) x 2 (max. 20)	12	10	10	16	14	14	18	14	16	18	18	16	16	8	10	12	8	10	10	0	6	2	0	2	8	0	6	2	0	2
	a + b + c (max. 110)	17	10	15	21	19	14	23	14	21	23	23	16	16	8	10	22	13	10	10	0	6	7	0	2	8	0	6	2	0	2
	$\bar{x}$	16						20						13						4						3					