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Hoechst

Hoechst Aktiengesellschaft
Pharma Research
Toxicology
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Primary Skin Irritation of a preparation of
0.5 % Octopirox, 12.5 % Steinapol SBFA 30 (40 %),
0.11 % citric acid and 86.89 % water (pH 7.0)
in New Zealand rabbits (patch test).
Report No 763/79

Summary:

A patch test for skin tolerance carried out under the experimental conditions laid down in the FDA guide lines showed that this preparation was slightly irritant to the skin.

The Steinapol-water mixture used as a control proved also to be slightly irritant.

Materials and methods

Albino New Zealand rabbits (supplier: Erkrath) of 2.30 to 2.88 kg weight ($\bar{x}$ = 2.64 kg) were used as experimental animals. They were kept in cages on their own and received standard feed ERKA 8300 (Feeding material manufacturers Robert Koch OHG, Hamm/Westf.). Feed and water were offered in unlimited quantities.

The substance "Octopirox^{R}" - H 72 6146 A was supplied in a 0.5 % solution in 12.5 % Steinapol, 0.11 % citric acid and 86.89 % water (pH 7.0). The vehicle Steinapol SBFA 30, 40 % in water was used as a control on the same animals.

The experiment was carried out during the period 26.11 until 29.11.79.

Experimental procedure:

An area of at least 6 x 3 cm on both flanks of six rabbits was shaved with an electric razor. One half of each shaved area was, in addition, abraded with a scarifier.

The substance under test and the vehicle on its own were applied in 0.5 ml quantities on pieces of gauze sized 2.5 x 2.5 cm. They were attached to the prepared skin with strips of adhesive plaster and covered with inert, impervious PVC film 6 - 8 cm wide and an elastic bandage was then wound round the animals' trunks. The period of application was 24 hours, at the end of which time the bandage was removed and the first inspection carried out, followed by further assessment at 24 and 72 hours.

The findings were used to determine the primary irritation score according to para 1500.41 of Federal Register 38,No 187, 27.09.1973, p 27019 (Appendix 1).

Results:

The substance under test produced primary irritation score of 1.9. A single instance of definite erythema and oedema was noted, as was a dry, rough and coarsely scaly skin. Ocropirox^{R} 0.5 % in Steinapol-water mixture must, therefore, be judged to be slightly irritant to the skin.

Steinapol SBFA 30 (40 %) - water mixture used as a control produced similar erythema and oedema, though the skin was dry and rough in all rabbits. In one animal it was also indurated, scaly with an open ulcer with pink exudate and small areas of desquamation. The primary irritation score of 2.2, obtained after the application of the vehicle on its own, showed that the Steinapol-water mixture had slightly irritative properties to the skin.

Dr. L/Bo
11th December 1979

Pharma Research
Toxicology
Hoechst Aktiengesellschaft

Dr. Leist
Head of Laboratory

Dr. Weigand
Coordination
Industrial Toxicology

Appendix
Classification

Evaluation of Primary Skin Irritation
(Patch Test after FDA)

The table is reproduced from U.S. Code of Federal Regulations § 1500.41 "Method of testing primary irritant substances" as published in Federal Register 38, 27019 (1973).

	Value
1. Erythema and Eschar Formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
2. Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

"The 'value' recorded for each reading is the average value of the six or more animals subject to the test.

Add the values for erythema and eschar formation at 24 and 72 hours for intact skin to the values on abraded skin at 24 and 72 hours (four values). Similarly, add the values for edema formation at 24 and 72 hours for intact and abraded skin (four values). The total of the eight values is divided by four to give the primary irritation score."

Evaluation

0.0 - 0.5	Non-irritant	(nicht reizend)
0.6 - 3.0	Slightly irritant	(leicht reizend)
3.1 - 5.0	Moderately irritant	(mäßig reizend)
5.1 - 8.0	Severely irritant	(stark reizend)

Annex
Report No. 763/79
December 11th, 1979

DERMAL TOLERANCE - PATCH TEST

Study No.:

Substance: Steinapol SBFA 30, 40 % in water

Dose: 2 x 0,5 ml/g on 3 x 3 cm skin surface

Investigator: Vatter

Concentration: 12,5 %

Application 1 x intact h flank l scarif. f flank

Species: Albino New Zealand rabbit

Study start: 26.11.1979

Time after appl.		24 h						48 h						72 h					
Animal No.		527	528	530	531	532	533	527	528	530	531	532	533	527	528	530	531	532	533
scarified	Erythema	0	1	2	3	2	1	0	1	2	0	0	1	0	1	2	0	0	1
	Edema	2	2	1	2	1	1	3	2	0	0	1	0	2	1	0	0	0	0
intact	Erythema	0	1	2	3	2	1	0	1	2	4	1	1	0	1	2	2	0	1
	Edema	2	2	1	2	1	1	2	2	0	0	0	0	2	1	0	0	0	0
Sum		36						23						16					
Skin dry, rough														X	X	X	X	X	X
Skin with fine scales																			
Skin with coarse scales											X								
Skin hardened																	X		
Skin raised																			
Skin parchment-like																			
Skin chapped (superf.)																			
Skin chapped (deep)																			
Eschar formation											X						X		
Necrosis																			
Desquamation, small-sized											X						X		
Desquamation, large-sized																			
Open wound											X								
Exudation (clear)																			
Exudation (reddish)											X								
Scratch marks																			
Discolorations isolated																			
Discolorations extensive																			

primary irritation index: Sum of all rabbits, 24 + 72 h-value= 52 : 24= 2,2

Remarks: h = hindflank l = left
f = foreflank

Annex
Report No. 763/79
December 11th, 1979

DERMAL TOLERANCE - PATCH TEST

Study No.:

Substance: Octopirox - H 72 6146 A							Dose: 2 x 0,5 ml/g on 3 x 3 cm skin surface						Investigator: Vatter										
Concentration: 0,5 %ig in Steinapol SBFA 30, 40 %/water							Application 1 x intact h flank r scarif. f flank						Species: Albino New Zealand rabbit						Study start: 26.11.1979				
Time after apol.			24 h						48 h						72 h								
Animal No.		527	528	530	531	532	533	527	528	530	531	532	533	527	528	530	531	532	533				
scarified	Erythema	1	1	3	1	3	0	1	1	3	0	0	1	0	1	2	0	0	0				
	Ecema	2	1	2	0	0	1	2	2	1	0	1	0	2	1	0	0	0	0				
intact	Erythema	1	1	3	3	2	0	1	1	3	1	0	1	0	1	2	1	0	0				
	Edema	2	3	1	1	1	1	2	2	1	0	1	0	1	1	0	0	0	0				
Sum		34						25						12									
Skin dry, rough															X	X							
Skin with fine scales																							
Skin with coarse scales															X	X							
Skin hardened																							
Skin raised																							
Skin parchment-like																							
Skin chapped (superf.)																							
Skin chapped (deep)																							
Eschar formation																							
Necrosis																							
Desquamation, small-sized																							
Desquamation, large-sized																							
Open wound																							
Exudation (clear)																							
Exudation (reddish)																							
Scratch marks																							
Discolorations isolated																							
Discolorations extensive																							

primary irritation index: Sum of all rabbits, 24 + 72 h-value= 46 : 24= 1,9

Remarks:
h = hindflank
f = foreflank
r = right

$\bar{x}$ = 2,644

527 - 2 876
528 - 2 632
530 - 2 714
531 - 2 304
532 - 2 504
533 - 2 836