KALI-CHEMIE AG, SPARTE PHARMA

Biochemical Research and Development

- Transformation and Kinetics -

Resorption of ^{14}C-Salicylate after topical application of Algesal-Cream to the rabbit

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SUMMARY

The percutaneous resorption of the salicylate contained in Algesal-Cream is examined using the renal ^{14}C-excretion following intravenous injection of ^{14}C-salicylate and topical application of Algesal-Cream.

Within 72 hours after the intravenous application of ^{14}C-diethylamine-salicylate, 96.6 % of the applied radioactivity is eliminated via the urine.

144 hours after the application of ^{14}C-labelled Algesal-Cream 57.8 % of the applied radioactivity can be found in the urine of the rabbit. Therefore the resorption of Diethylaminesalicylate contained in Algesal-Cream is 59.6 %.

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(Dr. Hausleiter)

1. MATERIAL

1.1 Animals

Male New Zealand Rabbits

Weight: 2.3 - 2.9 kg

Breeder: Hermann Meyer, Creußen

1.2 Test substance

^{14}C-Salicylic acid

New England Nuclear NEC 263

Lot No. 1153-206

The galenic preparation of the test-substance was carried out in cooperation with the galenical department of Kali-Chemie AG.

2. METHOD

One day prior to the resorption study an area of 12 x 12 cm is carefully depilated on the rabbits backs, using an electric shaver for small animals. The test preparation in a dosage of 0.5 g cream/kg (corresponding to 50 mg/kg salicylate) is applied to a surface area of 10 x 10 cm of the depilated skin and is rubbed in for three minutes.

The area of skin which has been treated in this way is then covered with a thin, perforated aluminium foil which is kept securely in place by means of bandage and sticking plaster.

The rabbits are kept in metabolism cages for the collection of urine and faeces.

For the intravenous application 50 mg/kg of diethylamine-salicylate are dissolved in 0.6 ml/kg of physiological saline and injected into the ear-vein.

The ^{14}C-radioactivity of the urine is measured immediately in a Packard Instruments Liquid Scintillation Spectrometer type 3380, using Insta-Gel as the scintillator.

3. RESULTS

Within the first 24 hours period following the intravenous application of ^{14}C-diethylaminesalicylate, 95.8 % of the applied radioactivity are eliminated via the urine. The amount increases only slightly up to 96.6 % within the next two days.

As expected, the renal elimination of radioactivity following the epicutanous application of Algesal-Cream was slower. After 24 hours on average 41.4 %, after 48 hours 50.3 % and after 72 hours 56.3 % of the administered ^{14}C had been eliminated. At the end of the 144 hours observation period a total renal radioactivity elimination of 57.8 % had been measured.

The percutaneous resorption of diethylaminesalicylate is calculated to be 59.6 % from the ^{14}C-activities eliminated via the urine after intravenous and topical application of Algesal-Cream.

Time [hr]	i.v.-Injection			Algesal-Cream		
	N	$\bar{x}$	$s_{\bar{x}}$	N	$\bar{x}$	$s_{\bar{x}}$
0 - 24	7	95.8	5.8	6	41.4	6.8
0 - 48	5	96.4	5.2	6	50.3	4.0
0 - 72	5	96.6	5.2	6	56.3	5.7
0 - 96				6	57.0	5.1
0 - 120				6	57.6	6.1
0 - 144				5	57.8	6.1

Cumulative elimination of radioactivity in the urine of the rabbit following intravenous or epicutaneous application of ^{14}C-diethylaminesalicylate in % of the dose