

PENETRATION OF ^{65}Zn THROUGH THE SKIN OF RATS

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Abstract. A study has been made of the penetration of ^{65}Zn from various zinc chloride solutions, from a zinc oxide suspension and from a zinc tape containing zinc oxide through the intact skin of rats. ^{65}Zn rapidly appeared in the blood and other tissues. The maximum ^{65}Zn activity in serum occurred within or around the first hour after the application of both zinc chloride and zinc oxide almost completely independent of the zinc concentration applied and the pH. A greater total penetration of ^{65}Zn was found from a carrier-free ^{65}Zn -zinc chloride solution at pH 1 than from the same solution made less acidic (pH 4) and from a zinc oxide suspension at pH 8 (125 $\mu\text{g Zn/ml}$). The ^{65}Zn penetration from the carrier-free solution was slightly (though not significantly) higher than that from the same solution with zinc chloride added to bring the total zinc concentration to 125 $\mu\text{g/ml}$.

Autoradiographically, ^{65}Zn activity was seen in both dermis and panniculus carnosus. The activity was most concentrated on and near the epidermis and around hair follicles in dermis. No differences were observed between animals treated with zinc chloride (pH 1 and pH 4) and animals treated with a zinc oxide suspension.

It has been shown that wound healing is impaired in zinc-deficient animals and humans (5, 24). When zinc is administered orally to zinc-deficient humans, wound healing is accelerated (5). Supplementation of zinc has been shown to be an effective treatment for the skin lesions in acrodermatitis enteropathica (13, 21) and skin disease induced by parenteral nutrition (14). There is also evidence of a beneficial effect of oral zinc in the treatment of acne (19) and recurrent furunculosis (2).

Zinc oxide has been used for centuries in the topical treatment of skin disorders and in more recent years in a zinc tape for the treatment of venous leg ulcers (4) and a variety of wounds (7, 26). While it is possible that the zinc in these preparations has a direct, local pharmacological effect, it is also possible that topical zinc treatment merely reverses the local effects of a systemic zinc deficiency or, if an appreciable amount of zinc is absorbed into the body as a whole, alleviates the deficiency itself. Systemic absorption of zinc has been demonstrated

in rats with wounds treated with various zinc compounds (6, 8, 9, 11) as well as in humans with burns treated with zinc tape (7).

The purpose of the present study was to determine the penetration through intact skin of radioactive zinc from various formulations of zinc chloride and zinc oxide.

MATERIAL AND METHODS

Animals

Seventy-two male, albino rats of the Sprague-Dawley strain weighing 85-180 grams were used. The rats were housed in individual metabolism cages of acrylic resin and stainless steel. They were fed a standard laboratory diet containing 100 $\mu\text{g Zn/g}$ and tap water *ad libitum*.

Radioisotopes

A stock solution of carrier-free ^{65}Zn -zinc chloride (the Radiochemical Centre, Amersham, England; 0.5-1.1 mCi/ml, >100 mCi/mg Zn, pH 1) was either applied direct or made less acidic (pH 4) by the addition of NaOH or reduced in specific activity by the addition of 125 $\mu\text{g Zn/ml}$ as zinc chloride before being applied. ^{65}Zn -zinc oxide was used in a suspension (125 $\mu\text{g Zn}$ and 0.7 mCi $^{65}\text{Zn/ml}$, pH 8, NEN Chemicals GmbH, Dreieich, West Germany) and in a zinc tape. The ^{65}Zn -labelled zinc tape was prepared for the present experiment by irradiating zinc oxide powder in a quartz glass tube with thermal neutrons at a flux of approximately 2.2×10^{13} neutrons $\cdot \text{cm}^{-2} \cdot \text{sec}^{-1}$ for 72 hours (AB Atomenergi, Studsvik, Sweden). The specific activity was 11.8 nCi $^{65}\text{Zn}/\mu\text{g Zn}$. The irradiated zinc oxide was mixed mechanically for 3 hours with an adhesive substance composed of gum, resin and trichloroethylene to give a final concentration of zinc of 17% of the total dry weight. This mixture was then spread as evenly as possible on cotton gauze and dried. The range of ^{65}Zn activity was 5-10 $\mu\text{Ci/cm}^2$. The ^{65}Zn -labelled zinc tape was stored for one month in order to practically eliminate activity of other zinc radioisotopes before it was used in the present experiment.

Experimental design

The hair on the dorsal and lateral aspects of the backs of the animals was removed with electric shears after which the remaining hair was gently shaved (Braun electric shaver). The area to which the ^{65}Zn was to be applied was examined to make certain that no lesions had occurred.

Directly after shaving, either 25 µl of ^{65}Zn solution or suspension was applied to approximately 3 cm² of the shaved areas on both sides of the animals, or else an approximately 5 cm² piece of ^{65}Zn -labelled zinc tape was applied on both sides. The drop of ^{65}Zn solution or suspension was gently spread over the test area with a glass rod without injuring the surface. The test areas were then covered with a plastic film and a bandage of plastic coated tape was applied around the body.

Samples of blood from tails of the rats were taken at different intervals after application of ^{65}Zn , using 50-µl micropipettes or weighed, borosilicate tubes. The blood samples were allowed to coagulate and were then centrifuged if the ^{65}Zn activity in the serum and/or coagulum was to be measured. At the end of each experiment the animals were killed with an overdose of ether. In some experiments, small tissue samples of liver, heart and testis were taken, using special precautions to avoid contamination with zinc remaining on the skin surface and placed in weighed, borosilicate tubes. Wet weight was recorded for all tissue samples after which ^{65}Zn activity was measured by gamma scintillation. In those experiments in which whole-body counting was performed, the skin contaminated with ^{65}Zn was first carefully removed.

In the first experiment (series I) the absorption of carrier-free ^{65}Zn as ZnCl_2 , pH 1, into blood in 5 rats was compared with that of ^{65}Zn from zinc tape in 5 rats over a period of 4 days.

In the second experiment (series II) the absorption into serum and coagulum of carrier-free ^{65}Zn as ZnCl_2 , pH 1, as well as its distribution to selected tissues during the first day after application was determined. Six animals were killed at 10 min, 4 and 24 hours after application of the solution.

In the third experiment (series III) the effect of pH (1 and 4) on the absorption of carrier-free ^{65}Zn -zinc chloride solutions was tested. Both the absorption into blood and the distribution in the body of ^{65}Zn from these preparations were compared with those of the ^{65}Zn -zinc oxide suspension. The 19 rats used were divided into three groups and killed 2 hours after the application. The contaminated skin, the entire gastro-intestinal tract and the liver were removed and measured separate from the carcass (the remaining body) in a whole body counter. Skin samples were also taken for autoradiography.

In the fourth experiment (series IV) the effect of the specific activity in a ^{65}Zn -zinc chloride solution (pH 1) on the penetration of ^{65}Zn was tested. Thirteen rats were used, 6 with carrier-free (655 mCi/mg Zn) ^{65}Zn -zinc chloride and 7 with the same solution supplemented with 125 µg zinc/ml as zinc chloride (5.2 mCi/mg Zn), and killed after 2 hours. In this experiment only the skin to which the solution had been applied was removed before the ^{65}Zn activity was measured in a whole body counter. Skin biopsies were taken for autoradiography.

In the fifth experiment (series V) ^3H -thymidine was utilized to determine if any major damage, which could have facilitated the penetration of ^{65}Zn , was caused in the stratum corneum by the shaving procedure. In a preliminary experiment on guinea pigs, no ^3H -thymidine incorporation was observed in regional lymph nodes 1.5 hours after topical application of ^3H -thymidine without occlu-

sion, when the skin was shaved in the same way as in this experiment. However, when the stratum corneum was removed by stripping, a pronounced incorporation of ^3H -thymidine was seen in the regional (inguinal) lymph nodes and also to some extent in distant (neck) lymph nodes. In this experiment on rats, 12 animals were used, divided into two groups, and 25 µl of an aqueous solution of ^3H -thymidine (0.2 µCi/ml) at pH 1 or pH 4 was applied. The pH of the two solutions was adjusted immediately before the experiment and they were applied to an area of 3 cm² on both sides of the animals. Two hours later the animals were killed and samples of skin as well as regional lymph nodes (inguinal) were taken for autoradiography.

Gamma scintillation measurements

The ^{65}Zn activity in the small tissue samples was measured in a 7.4×8.4 cm NaI (TI) through-hole scintillation detector in a Packard 5320 single-channel analyzer calibrated to operate at the 1.116 MeV gamma peak of ^{65}Zn . A dilution of the application solution was used as a reference. The background counting rate was recorded on each occasion and subtracted from the sample and reference counting rates.

For the small tissue samples the relative activity (R.A.) was calculated:

$$\text{R.A.} = \frac{^{65}\text{Zn activity/g fresh weight of the sample}}{^{65}\text{Zn activity applied/gram body weight}}$$

The ^{65}Zn activity in the large samples was measured in a whole body counter with a 7.6×7.6 NaI (TI) scintillation detector and a single-channel analyzer (AE 3207, AB Atomenergi, Studsvik, Sweden) calibrated to operate at the 1.116 MeV gamma peak of ^{65}Zn . A dilution of the application solution was used as a reference. The samples were placed about 25 cm from the detector. For the large samples the ^{65}Zn activity absorbed was calculated:

$$\% ^{65}\text{Zn absorbed} = \frac{^{65}\text{Zn activity in carcass, liver, and gastrointestinal tract}}{^{65}\text{Zn activity in carcass, liver, gastrointestinal tract, skin, bandage}} \cdot 100$$

The small samples were not included in the calculation of ^{65}Zn absorbed because their activity was comparatively low.

Autoradiography

Punch biopsies, 3 mm in diameter, were taken from the ^{65}Zn -treated skin areas. The following techniques were used for light microscopic autoradiography with ^{65}Zn :

1. The skin biopsies were fixed in 10% neutral formaldehyde, embedded in paraffin, sectioned (~6 µm) and mounted on glass slides. The paraffin in the sections was removed with xylol, alcohol (99.5–70%) and deionized water, and the sections were dipped in fresh autoradiographic film emulsion (Eastman Kodak NTB 2). The emulsion was exposed in boxes containing silica gel at 4°C for 1 week and then developed (Eastman Kodak D19B) and fixed and the sections stained with haematoxylin.

2. The skin biopsies were either frozen using a liquid

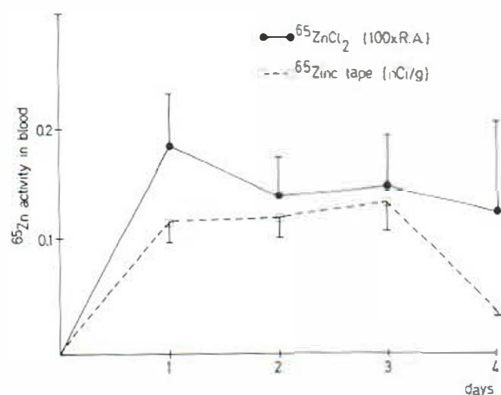


Fig. 1. ^{65}Zn activity in blood of rats of series I expressed as relative activity for zinc chloride treated animals and as nCi/g for zinc tape (zinc oxide) treated animals. The results are expressed as means $\pm$ S.E.M.

propane/propene mixture cooled with liquid nitrogen at -196°C , or else wrapped in plastic and frozen with isopentane cooled with carbon dioxide at -70°C . The biopsies were stored at -70°C . Glass slides were dipped in emulsion (Eastman Kodak NTB 2) and the emulsion allowed to dry. Cryostat sections taken under safe light conditions at -30°C were placed on the emulsion-coated slides which were kept at -5 to -15°C . Exposures were made for one week at -20°C (23). After exposure the slides were quickly thawed to room temperature, dried for 2 min in a gentle current of air, dipped in cellulose acetate, dried, developed (Eastman Kodak D19B) and fixed. The sections were then stained with haematoxylin.

For autoradiography with ^3H -thymidine, biopsies were taken from ^3H -thymidine treated skin and from regional (inguinal) lymph nodes. The biopsies were fixed in 10% neutral formaldehyde, embedded in paraffin, sectioned ($\sim 6 \mu\text{m}$) and submitted to autoradiography as described above in I.

Statistics

The differences between group means for various variables were tested using Student's *t*-test for unpaired observations. The test was modified when the variances differed significantly ($p < 0.01$, *F*-test).

RESULTS

Gamma scintillation measurements

In the animals of series I which were killed after 4 days, ^{65}Zn from zinc chloride (carrier-free) or zinc oxide (zinc tape) penetrated the skin and was found in blood. The highest ^{65}Zn activity in blood in the $^{65}\text{ZnCl}_2$ group was found at 24 hours, when the first blood sample was taken, after which only small differences were observed (Fig. 1). In the ^{65}Zn -

labelled zinc tape group the activity in blood was moderate by the end of the first day, increased very little during the second and third day and then decreased.

The animals of series II also received carrier-free ^{65}Zn as zinc chloride but with sampling at shorter intervals after application. A maximum activity in blood (Fig. 2) was observed at 1 hour. As early as 10 min after application a substantial ^{65}Zn activity was present in coagulum, serum, liver, and heart (Fig. 3) with an increase to 4 hours and thereafter decreases in all these tissues up to 24 hours. In testis the ^{65}Zn R.A. was low after 10 min but increased through 24 hours.

In the animals of series III a lower penetration of ^{65}Zn was found with both zinc chloride, pH 4, and zinc oxide suspension, pH 8, compared with that of zinc chloride, pH 1. This difference was found in serum, coagulum and whole blood (Fig. 4) as well as in the body as a whole (Table I) and in selected tissues (Table II). The maximum activity in serum had apparently occurred by 0.5 hour with zinc chloride, pH 4, and by 1 hour with zinc chloride, pH 1, and zinc oxide, pH 8. The variances were generally lower in the zinc oxide treated animals. The total retention of ^{65}Zn was almost equal in the zinc chloride pH 4 group and the zinc oxide pH 8 group (Table I). The most pronounced total retention, 4.1%, was found in the zinc chloride pH 1 group. The distribution of ^{65}Zn in the body was in principle the same in all three groups with regard to the proportion of the activity found in carcass, liver and gastrointestinal tract (Table I) as well as the relation between the R.A. in different tissues (Fig. 4, Table II).

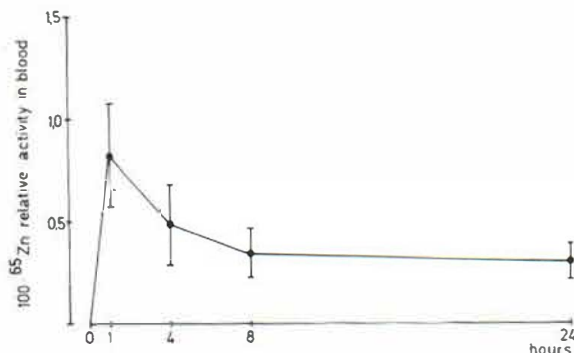


Fig. 2. ^{65}Zn relative activity of blood taken from rats of series II at various times after application. The results are expressed as means $\pm$ S.E.M.

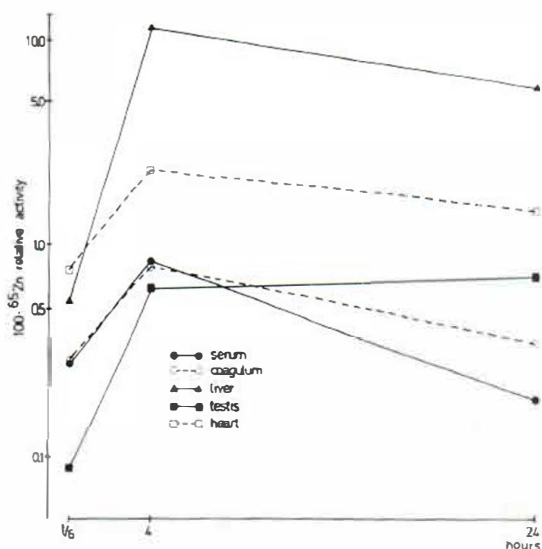


Fig. 3. ⁶⁵Zn relative activity at various times after application, as determined in serum, coagulum, liver, testis, and heart of rats of series II. The results are expressed as means $\pm$ S.E.M.

In the animals of series IV the ⁶⁵Zn activities in serum, coagulum and the body as a whole were higher in the carrier-free zinc chloride group (1.1 μ g Zn/ml, pH 1) than in the lower specific activity zinc chloride group (125 μ g Zn/ml, pH 1) (Table III).

Autoradiography

No damage due to the shaving technique was observed microscopically in the skin. However, when using routine histological techniques, it may be difficult to visualize changes in the stratum corneum due to trauma.

After fixation in formalin, impregnation with paraffin and dehydration with alcohol, a pro-

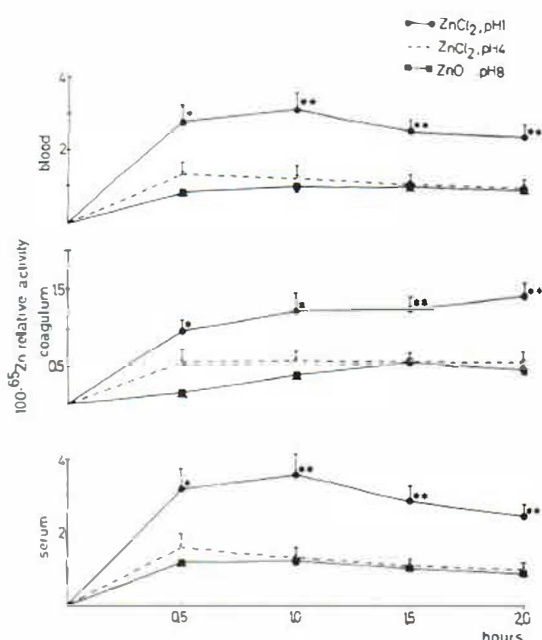


Fig. 4. ⁶⁵Zn relative activity of serum, coagulum, and whole blood taken from animals of series III at various times after application. The results are expressed as means $\pm$ S.E.M. Results of comparisons with the zinc chloride treated group, pH 4, (*t*-test) are indicated. **p* < 0.05, ***p* < 0.001.

nounced reduction in activity was seen within the section. When the biopsies were frozen and kept frozen throughout the exposure time, ⁶⁵Zn was preserved *in situ* in the biopsies. A high ⁶⁵Zn activity was seen in both dermis and panniculus carnosus in all biopsies. The activity was most concentrated on and near epidermis and around hair follicles in dermis (Fig. 5a and b). No differences were observed between animals in the zinc chloride pH 1 and pH 4

Table I. Absorption of ⁶⁵Zn from the skin of animals in series III and the proportion of the activity found in liver, gastrointestinal tract, and carcass

The results are expressed as means $\pm$ S.E.M. The results of comparisons with the zinc chloride, pH 4, group (*t*-test) are also indicated

	% absorbed activity	% absorbed by carcass	% absorbed by liver	% absorbed by gastrointestinal tract
Zinc chloride, 1.3 μ g Zn/ml, pH 1	4.1 $\pm$ 0.6**	50.2 $\pm$ 1.0	28.8 $\pm$ 0.9	21.0 $\pm$ 1.2
Zinc chloride, 1.3 μ g Zn/ml, pH 4	1.6 $\pm$ 0.3	53.5 $\pm$ 3.0	24.7 $\pm$ 2.0	21.8 $\pm$ 1.9
Zinc oxide, 125 μ g Zn/ml, pH 8	1.9 $\pm$ 0.2	52.0 $\pm$ 4.2	22.8 $\pm$ 1.6	25.2 $\pm$ 4.0

***p* < 0.01.

Table II. *Relative activity (R.A. $\times 100$) in selected tissues of animals in series III*

The results are presented as means $\pm$ S.E.M. The results of comparisons with the zinc chloride, pH 4, group (*t*-test) are also indicated

	Serum	Coagulum	Liver	Heart	Testis
Zinc chloride, pH 1	2.9 $\pm$ 0.4**	1.5 $\pm$ 0.2**	21.7 $\pm$ 2.8**	4.2 $\pm$ 0.6**	0.8 $\pm$ 0.1**
Zinc chloride, pH 4	1.4 $\pm$ 0.2	0.7 $\pm$ 0.1	9.0 $\pm$ 2.2	1.7 $\pm$ 0.4	0.4 $\pm$ 0.1
Zinc oxide, pH 8.5	1.2 $\pm$ 0.1	0.5 $\pm$ 0.1	8.0 $\pm$ 1.0	1.3 $\pm$ 0.2	0.3 $\pm$ 0.0

***p* < 0.01.

groups and the zinc oxide suspension group (series III and IV).

^3H -thymidine was incorporated into scattered cells of the basal layers of epidermis, cells in hair follicles near the surface as well as in deeper parts of the dermis, and also in some connective tissue cells located in the dermis (series V) (Fig. 6). No incorporation of ^3H -thymidine was observed in the regional lymph nodes and no differences were observed between pH 1 and pH 4 groups.

DISCUSSION

The very rapid appearance and continuous presence of ^{65}Zn in the blood and several tissues after topical application of ^{65}Zn -zinc chloride solution, ^{65}Zn -labelled zinc tape (zinc oxide) or ^{65}Zn -zinc oxide suspension demonstrate that zinc penetrates the skin barrier of rats, as has been demonstrated earlier in guinea pigs (25). It was previously established in rats that considerable amounts of zinc are absorbed through skin wounds treated with a ^{65}Zn -labelled zinc tape (11). If the procedure used in the present study for removing the rats' hair had caused slight injury to the epithelium, this would presumably facilitate the penetration of traces of zinc through the skin barrier. However, in a pre-

liminary study using guinea pigs, whose hair was removed in the same manner, the skin provided an effective barrier to an aqueous solution of ^3H -thymidine penetration, while stripping the epithelium with tape caused an appreciable amount of ^3H -thymidine to penetrate the skin and accumulate in regional lymph nodes. As no damage to the epithelium of the rats in the present experiment could be seen, either macroscopically or microscopically, it may be concluded that the ^{65}Zn in all likelihood penetrated the intact skin of the rats.

Zinc chloride is potentially toxic to tissues (20) and, in *in vitro* experiments using light microscopy, toxic effects have been observed in the epithelium of cat palatal mucosa cultivated in media containing zinc chloride at concentrations of 25 μg Zn/ml and above (10). However, it is unlikely that the zinc concentrations and/or amounts of zinc used in the present *in vivo* experiment were sufficiently high to cause damage to the epithelium which in turn would allow the penetration of zinc.

The use of an occlusive dressing increases the penetration of any substance and increases the surface area by causing folds to occur (12, 17). An increased penetration of ^{65}Zn can therefore be assumed in the present study and the occlusive dressing may be responsible for the penetration of ^3H -

Table III. *Absorption of ^{65}Zn from the skin of animals in series IV, to serum, coagulum, and whole body (except contaminated skin)*

The results are expressed as means $\pm$ S.E.M.

	100 $\times$ R.A.				
	Serum (0.5 hour)	Coagulum (0.5 hour)	Serum (2 hours)	Coagulum (2 hours)	% absorbed activity
Zinc chloride, 1.1 μg Zn/ml, pH 1	2.1 $\pm$ 0.8	0.8 $\pm$ 0.3	1.2 $\pm$ 0.3	0.7 $\pm$ 0.3	6.1 $\pm$ 1.5
Zinc chloride, 125 μg Zn/ml, pH 1	1.6 $\pm$ 0.4	0.5 $\pm$ 0.1	0.9 $\pm$ 0.3	0.6 $\pm$ 0.1	3.6 $\pm$ 0.9

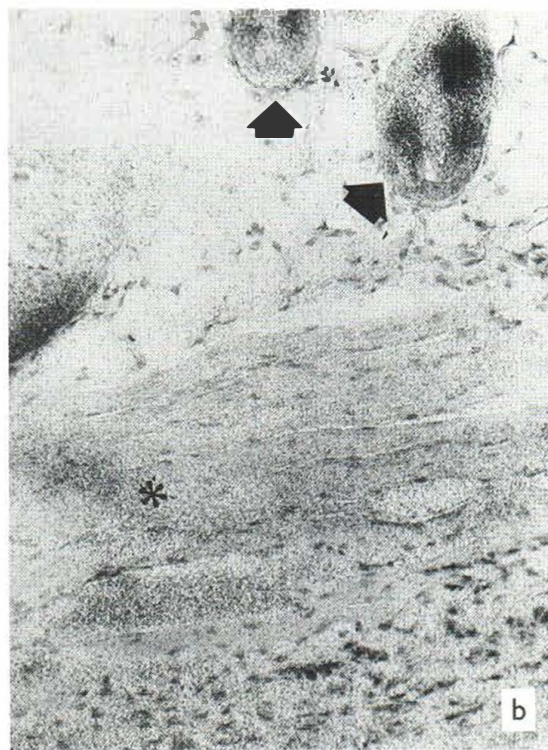
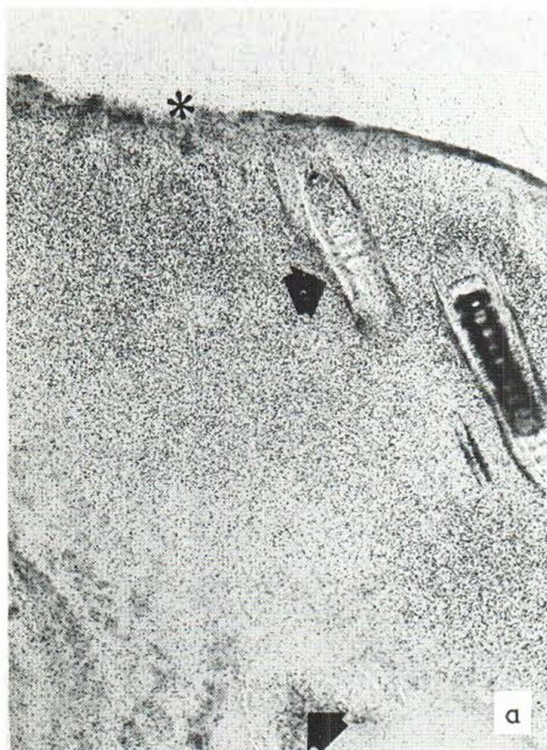


Fig. 5. (a) Autoradiography of skin. ^{65}Zn -zinc chloride, pH 4. Some unspecific activity is observed above epidermis (star). Within the dermis, heavy labelling is seen, especially around some hair follicles (arrows). Hematoxylin, $\times 280$. (b) Autoradiography of the deeper layers of dermis and panniculus carnosus. ^{65}Zn -zinc

chloride, $125 \mu\text{g Zn/ml}$, pH 1. In the dermis, heavy labelling is seen in the club-shaped ends of hair follicles (arrows). In panniculus carnosus (star) too, labelling is accentuated, compared with the connective tissue of dermis. Hematoxylin, $\times 165$.

thymidine into the skin—though not to regional lymph nodes—of the rats.

The amount of ^{65}Zn which penetrates the skin and is found in the body represents a mainly one-way movement of zinc. It may be that some of this penetration represents exchange between the applied zinc preparations and the tissue zinc, rather than net absorption. Net absorption would in that case be lower than that indicated by the present ^{65}Zn retention data.

A significantly higher penetration of ^{65}Zn was seen from a carrier-free ^{65}Zn -zinc chloride solution at pH 1 than at pH 4 or a ^{65}Zn -zinc oxide suspension at pH 8. The ^{65}Zn penetration from a carrier-free ^{65}Zn -zinc chloride solution was slightly but insignificantly greater than that from the same solution supplemented with zinc chloride to a final zinc concentration equivalent to that of the zinc oxide

suspension ($125 \mu\text{g Zn/ml}$). Thus the composition of the zinc compound and the zinc concentration appear to have less effect on the penetration of zinc than does the pH of the solution or suspension. If the penetration of zinc through rat skin obeys Fick's law of diffusion (27) then no difference is to be expected in the percentage ^{65}Zn penetrated per unit of time among solutions with different zinc concentrations. As a change in the skin's pH to either side of neutral pH causes an increased permeability (1), it is to be expected that a higher penetration of ^{65}Zn would be seen at pH 1 than at pH 4. What is surprising is the relatively high penetration of ^{65}Zn from a zinc oxide suspension, pH 8, as zinc oxide is relatively insoluble in water and dissociates to a far lesser degree than does zinc chloride. However, the components in stratum corneum may react with zinc oxide in such a way as to cause its solution

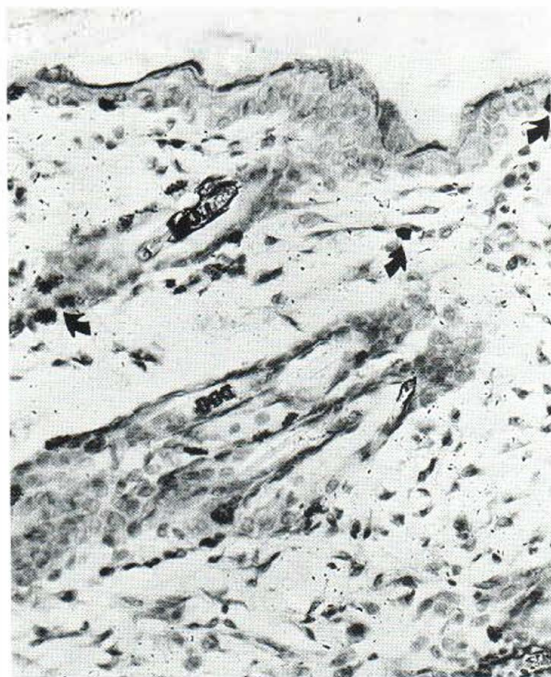


Fig. 6. Autoradiography with ^3H -thymidine, pH 4. Labeling (arrows) is seen in the basal cells of epidermis, cells of the adjacent hair follicles and some connective tissue cells. Hematoxylin, $\times 220$.

and/or dissociation and permit zinc penetration at a rate equivalent to that of the zinc ions from the zinc chloride solution. Zinc oxide may have a relatively higher solubility in epidermis than in the vehicle, which may cause it to be more readily released from its vehicle into the skin (17). The distribution in the body of ^{65}Zn from zinc oxide is similar to that from zinc chloride, which indicates that the ^{65}Zn in both cases is present in those forms which are originally found in the body and that zinc ions are probably liberated from the zinc oxide and absorbed into blood, as has been previously suggested (11).

^{65}Zn penetration of zinc through intact skin has been demonstrated previously in animals by Skog & Wahlberg (25) and Kapur et al. (13). In the latter investigation the penetration of ^{65}Zn from various zinc preparations through the skin of the shaved backs of three rabbits was studied. The ^{65}Zn activity in whole skin blocks excised after 6 and 24 hours was measured after fixation in alcoholic formalin. It was observed that most of the ^{65}Zn activity had disappeared from the skin surface 24 hours after

application and that the ^{65}Zn was located in the keratogenous zone of the hair shafts and in the subcutaneous muscle layers. The autoradiographic findings of the present study definitely indicate that most of the ^{65}Zn in the tissue is removed by formalin fixation, a finding which is in accordance with previous results (23), and thus the conclusions drawn by Kapur et al. are most likely not correct. With frozen section autoradiography, ^{65}Zn activity from a zinc chloride solution and a zinc oxide suspension was found in dermis, epidermis, and panniculus carnosus. Presumably high concentrations of zinc (not included in the present whole body absorption data) may be found in epidermis and dermis when high concentrations are applied to the skin surface, despite the fact that zinc ions are removed by blood circulation.

Skog & Wahlberg (25) measured the disappearance constant and percentage disappearance of ^{65}Zn from zinc chloride applied to the shaved backs of guinea pigs. Generally, a relatively low absorption was found ($<0.07\%/ \text{cm}^2 \cdot \text{hr}$) for solutions with various zinc concentrations (0.005–4.87 M) and pH (1.8–5.7). These figures are somewhat lower than those of the present study on rats (0.13–0.51%/ $\text{cm}^2 \cdot \text{hr}$). However, the permeability of the skin is greater in rats than in guinea pigs (27).

Recently, Keen & Hurley (15) demonstrated that a considerable penetration of zinc through rat epidermis can be achieved after treating the skin with a depilatory (keratinolytic) agent which dissolves the keratin of the highly differentiated keratinized cells of the stratum corneum, the most important skin barrier (27). When the ^{65}Zn -labelled zinc tape used in the present study was applied to skin wounds in rats for 4 days (11) approximately 50 times as much ^{65}Zn was absorbed into the blood.

The present autoradiographic results reveal that topically applied zinc is absorbed into dermis diffusely but that it also concentrates around hair follicles in the rat. The scintillation studies demonstrated that a small proportion of the zinc may be absorbed by the body as a whole. Zinc is an integral part of several metallo-enzymes (22), takes part at multiple sites in nucleic acid metabolism (16) and has an anti-inflammatory effect (3). Thus, while topically applied zinc may satisfy a locally increased need for zinc or relieve the local effects of a systemic zinc deficiency, it may also have a direct pharmacological effect on skin disorders which are not related to zinc deficiency.

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