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8EHQ-91-1210
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November 29, 1993

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89948888129

Dear Sir or Madam:

Enclosed is a report entitled "The Absorption of Hydroquinone (HQ) Through Rat and Human Skin *In Vitro*". This report is being submitted as a follow-up to our original submission on hydroquinone of April 2, 1991 (EPA Document Control Number 8EHQ-0491-1210).

Please contact me if additional information is required.

Sincerely,

R. Hays Bell

R. Hays Bell
(716) 722-5036

RHB:JAF
Enc.

R. Hays Bell, Ph.D., Vice-President and Director, Corporate Health, Safety, and Environment
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STUDY TITLE

THE ABSORPTION OF HYDROQUINONE (HQ)
THROUGH RAT AND HUMAN SKIN *IN VITRO*

HAEL No. 87-0113
CIN 10000356

KAN 900356
CAS No. 123-31-9

AUTHORS

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TESTING FACILITY

Biochemical Toxicology Section
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Eastman Kodak Company
Rochester, New York 14652-3615

STUDY SPONSOR

Eastman Chemical Company
Kingsport, TN

October 6, 1993

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QUALITY ASSURANCE INSPECTION STATEMENT
(21 CFR 58.35(B)(7), 40 CFR 792.35(B)(7), AND 40 CFR 160.35(B)(7))

STUDY: 87-0113-7 **STUDY DIRECTOR:** BARBER, E.D.
ACCESSION NUMBER: 900356

PAGE 1
09/21/93

STUDY TYPE: IN VITRO METABOLISM: PERCUTANEOUS ABSORPTION

M. L. J. am
(AUDITOR, QUALITY ASSURANCE UNIT)

9/23/93
DATE

TO THE BEST OF MY KNOWLEDGE, THIS FINAL REPORT ACCURATELY DESCRIBES THE METHODS AND STANDARD OPERATING PROCEDURES, AND THE REPORTED RESULTS ACCURATELY REFLECT THE RAW DATA. THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY ASSURANCE UNIT OF H&L, EASTMAN KODAK COMPANY ROCHESTER, N.Y. AND WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES:

<u>INSPECTION DATES</u>	<u>PHASE(S) INSPECTED</u>	<u>STATUS REPORT DATES</u>
06/05/91	SAMPLE COLLECTION DAY 2 - 4 HR COLLECTION	06/05/91
06/12/91	PROTOCOL SUBMISSION	06/12/91
07/30/91	CONTROL ARTICLE APPLICATION TO TEST SYSTEM SAMPLE COLLECTION ZERO HOUR SAMPLE DAY 1 - TRITIATED WATER	07/31/91
07/31/91	SAMPLE COLLECTION DAY 2 - 2 HR COLLECTION CONCENTRATION DETERMINATION	07/31/91
08/03/93	FINAL REPORT REVIEW	08/03/93
08/18/93	FINAL REPORT REVIEW	08/18/93
09/17/93	FINAL REPORT REVIEW	09/17/93

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**THE ABSORPTION OF HYDROQUINONE (HQ)
THROUGH RAT AND HUMAN SKIN *IN VITRO***

**HAEL No. 87-0113
CIN 10000356**

**KAN 900356
CAS No. 123-31-9**

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

This report presents data compiled during the investigation of hydroquinone. The sponsor, test compound, study type, test species, study dates, and personnel responsible for the study are detailed in the protocol and appendices. All aspects of this study were performed in accordance with Good Laboratory Practice (GLP) Standards of the U.S. Environmental Protection Agency (40 CFR Part 792(TSCA) as revised August 17, 1989), the United States Food and Drug Administration (21CFR Part 58 as revised September 4, 1987), and Annex 2 of the Organization for Economic Cooperation and Development Guidelines for the Testing of Chemicals (C(81)30(Final)) as required by Council Directive 87/18/EEC of December 1986. To the best of the signer's knowledge and belief, there were no known deviations from the GLP standards that significantly affected the quality of this study.

Eugene D. Barber

Eugene D. Barber, Ph.D., DABT
Study Director

10-6-93

Date

**THE ABSORPTION OF HYDROQUINONE (HQ)
THROUGH RAT AND HUMAN SKIN *IN VITRO***HAEL No. 87-0113
CIN 10000356KAN 900356
CAS No. 123-31-9**ABSTRACT**

The rates of percutaneous absorption of hydroquinone (HQ) through human stratum corneum and full-thickness rat skin have been measured *in vitro* using approximately 5% aqueous solutions of HQ as the donor solutions. The measured absorption rate (mean \pm SD) of HQ through human stratum corneum was found to be $0.522 \pm 0.13 \mu\text{g}/\text{cm}^2/\text{hr}$ while that for full-thickness rat skin was $1.09 \pm 0.65 \mu\text{g}/\text{cm}^2/\text{hr}$. The ratio (rat/human) of the permeability constants (K_p) was 2.36.

The integrity of each skin sample was determined by measuring its permeability to tritiated water ($^3\text{H}_2\text{O}$) in Phase 1 of each study. The values for the permeability constants (mean \pm SD) for $^3\text{H}_2\text{O}$ were $(2.34 \pm 1.54) \times 10^{-3} \text{ cm}/\text{hr}$ for rat skin and $(0.967 \pm 0.24) \times 10^{-3} \text{ cm}/\text{hr}$ for human stratum corneum. These values were in good agreement with the historical values of these parameters from this laboratory. The mean damage ratios, calculated from the rates of absorption of $^3\text{H}_2\text{O}$ before and after exposure of the skin to HQ, were similar to the saline control values, indicating that aqueous solutions of HQ did not damage rat skin or human stratum corneum during the 8-hr exposure.

Using the definitions suggested by Marzulli, Brown and Maibach (1969), HQ would be classified as "slow" with respect to its absorption through human stratum corneum.

These data allow the estimation of HQ uptake in man following dermal exposure to a 5% aqueous solution of the pure chemical. If it is assumed that skin absorption in man is similar to that observed for human stratum corneum *in vitro*, and that the total surface area of the hands represents about 720 cm^2 , then $376 \mu\text{g}$ of HQ would be absorbed by the immersion of both hands for 1 hr. Assuming a 70 kg body weight, the dose from the 1 hr exposure would be $5.37 \mu\text{g}/\text{kg}$.

INTRODUCTION

The present study was designed to determine the rate of absorption of hydroquinone (HQ) through full thickness rat skin and human stratum corneum *in vitro* and to assess the damage to the skin caused by contact with this chemical. For a large number of compounds, good agreement has been found between the results of *in vivo* and *in vitro* skin permeability studies (Bronaugh *et al.*, 1982; Bronaugh and Stewart, 1984; Bronaugh, 1985; Franz, 1975; Franz, 1978). The procedure followed in this study employed Franz-type glass diffusion cells, in which the skin sample formed a membrane between two chambers, one of which contained an excess of donor solution, and another which acted as a receptor for the chemical after skin penetration.

MATERIALS AND METHODS

Materials

Franz-type diffusion cells (Figure 1) were fabricated in the Glass Fabrication Department, Eastman Kodak Company (Rochester, NY). The internal volume (approximately 5.5 mL) of each receptor chamber was determined gravimetrically and a calibration mark was made on the side arm as a constant volume indicator. Nine cells were housed in a cell drive unit/mounting assembly (Crown Glass Company). The receptor solution was stirred with a magnetic stirring bar and maintained at a constant temperature by the circulation of water at 30 °C.

Chemicals

HQ was obtained from the Eastman Chemical Company, Kingsport, TN. Uniformly labeled ¹⁴C-HQ was purchased from Wizard Laboratories, Davis CA at a specific activity of 22.2 mCi/mmole. The labeled HQ was analyzed for radiochemical purity using high performance liquid chromatography (hplc) with radiochemical detection. Unlabeled HQ was obtained from Eastman Chemical Company, Kingsport, TN. In studies conducted subsequent to those reported here, the structure of the unlabeled HQ was confirmed by mass spectrometry. Tritiated water was obtained from New England Nuclear Corp. (Boston, MA) while Volpo-20™, polyethoxy (n=20) oleate, was purchased from Croda, Inc., Mill Hall, PA.

Dulbecco's phosphate buffered saline and concentrated solutions of an antibiotic-antimycotic mixture (penicillin/streptomycin/amphotericin) were purchased from Grand Island Biological Co., Grand Island, NY. Ready-to-Use III™ scintillation

fluid was obtained from Kodak Laboratory and Research Products, Rochester, NY.

Skin Preparation

Human abdominal skin specimens were obtained from the National Disease Research Interchange, Philadelphia, PA. Patient records were obtained to ensure that the tissues had not been adversely affected by any clinical condition or disease. Skin samples used for these studies were frozen as soon as possible following their procurement to ensure that no physical or biological degradation would occur (Maibach *et al.*, 1971). Each skin sample was identified by a unique identification number. Stratum corneum was separated from whole skin specimens by immersing each sample in a 60 °C water bath for 45-60 seconds (Dugard *et al.*, 1984) and removing the outermost layer. Stratum corneum samples were re-frozen until the day of use in the experiment. Stratum corneum from three human donors was used in the absorption studies of HQ.

The integrity of each skin sample was determined by measuring its permeability to tritiated water ($^3\text{H}_2\text{O}$, approximately 1 mCi per skin sample). Full-thickness rat skin was obtained from male Fisher 344 CDF[®] (F-344)/CrIBR rats weighing 160 ± 1 g. Skin samples were obtained from euthanatized animals by carefully shaving the abdominal area to remove hair and then surgically removing the shaved skin. Excess fat and connective tissue were removed from the skin and pieces cut so as to cover the opening of the Franz-type skin cells. The entire procedure was conducted just prior to beginning the skin study thereby assuring that the specimens were fresh for each experiment.

Receptor Solution

The receptor solution used in these studies was Dulbecco's phosphate buffered saline (pH adjusted to 7.1) containing:

Penicillin, 100 Units/mL
Streptomycin, 100 $\mu\text{g}/\text{mL}$
Amphotericin B as Fungizone[™], 0.25 $\mu\text{g}/\text{mL}$
Volpo-20[™], 60 mg/mL

Liquid Scintillation Spectrometry (LSS)

Amounts of tritium or ^{14}C were determined by adding 50 μL samples of receptor solution to 10 mL of Ready-to-Use III[™] scintillation cocktail and counting in a Packard

Tricarb™ Model 460 CD liquid scintillation spectrometer.

Experimental Design

Each study consisted of a single experiment, as follows:

- Phase 1: determination of the permeability to $^3\text{H}_2\text{O}$;
- Phase 2: determination of the permeability to HQ;
- Phase 3: determination of the permeability to $^3\text{H}_2\text{O}$.

A total of nine cells was used in the experiment. These consisted of three groups of three cells: one control and two test cells for each skin sample. The cell, depicted in Figure 1, consists of two chambers. The upper, or donor, chamber is separated from the lower, or receptor, chamber by the skin specimen under study. The donor chamber of each cell designated as a control contained saline on Day 2, rather than HQ test solution.

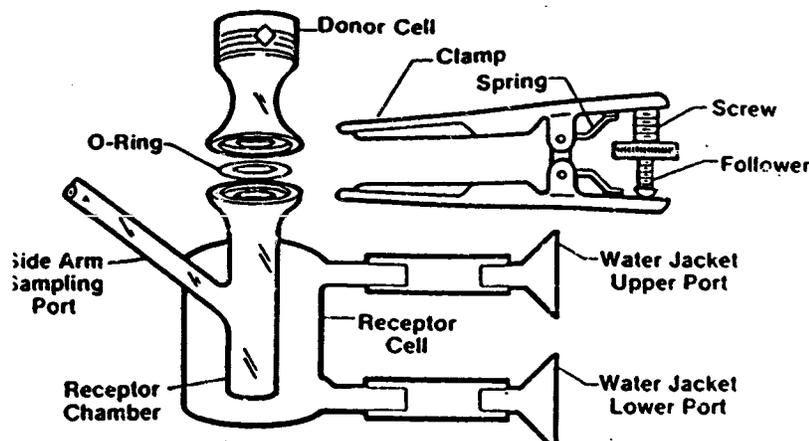
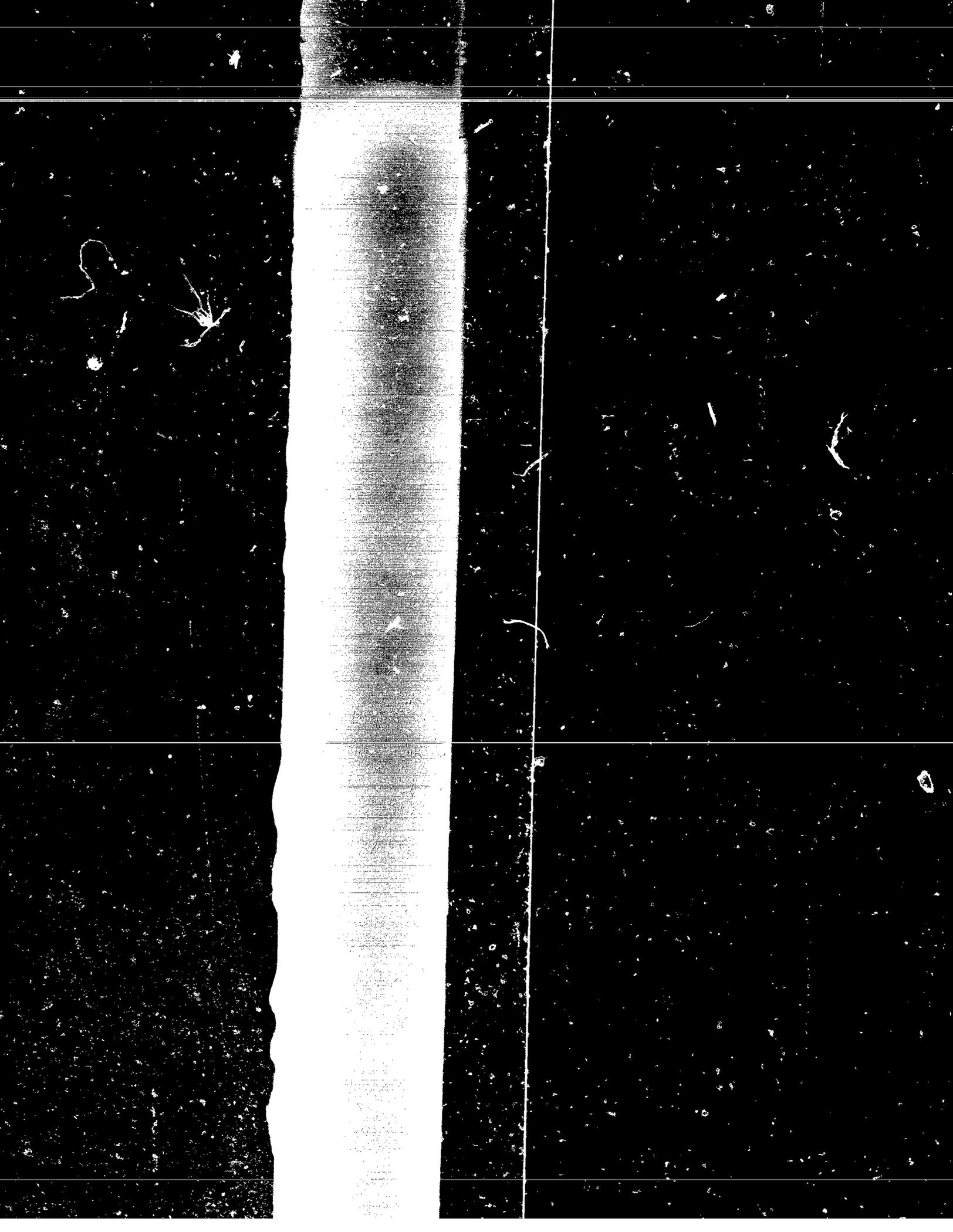


Figure 1. Illustration of a Franz-type diffusion cell used in these *in vitro* percutaneous absorption studies



For each phase of the experiment the receptor chambers were filled with isotonic saline containing an antibiotic-antimycotic solution (Penicillin, Fungizone and Streptomycin, GIBCO Laboratories, Grand Island, NY) and 6% Volpo-20™. Duplicate 50 µL background (0-hr) samples were taken from each receptor chamber using the sampling port (Figure 1). The donor solution, 300 µL of ³H₂O or HQ test solution, was applied in excess to ensure steady state absorption kinetics. Duplicate 50 µL samples were taken from each receptor chamber hrly for 8 hrs and assayed for radioactivity by LSS. The receptor chambers were refilled after each sampling.

At the conclusion of Phases 1 and 2, the donor and receptor chambers were rinsed three times with saline, the donor chambers filled with saline and the receptor chamber filled with antibiotic-antimycotic mixture in saline. The cells were left filled and stirred overnight. The following morning, they were emptied, and refilled with the appropriate solutions.

Calculation of the Permeability Constant, Absorption Rate, and Damage Ratio

The data from each phase of the study were entered into an IBM PS/2 model 70 computer system using data analysis software based in the Microsoft Excel™ environment and calculations were performed. The rate of increase in the concentration of radioactivity (DPM per cell) in the receptor chamber was calculated by linear regression analysis.

The permeability constant and absorption rate were calculated for each cell using the slope of the linear plot of "concentration of HQ or ³H₂O in the receptor chamber versus time". The equation describing the relationship between these two parameters for any test substance is:

$$\text{Permeability Constant} \times \text{Concentration in Donor} = \text{Absorption Rate}$$

The following equation was used to derive the permeability constant for ³H₂O or HQ:

$$\text{Permeability Constant (cm/hr)} = \frac{\text{slope (DPM per hr)}}{\text{donor count (DPM/mL) x skin area (cm}^2\text{)}}$$

The absorption rate for each cell was then found by multiplying the permeability constant by the concentration of ³H₂O or HQ in the donor chamber (mg/mL). The permeability of each skin sample to ³H₂O was determined a second time, on the

day following exposure to HQ. The rates of $^3\text{H}_2\text{O}$ permeability after 8-hr exposure to HQ and that obtained prior to exposure to HQ were used to derive a "damage ratio" as follows:

$$\text{Damage Ratio} = \frac{\text{Permeability constant after exposure}}{\text{Permeability constant before exposure}}$$

This value provided a means to assess any alteration to the epidermal membrane resulting from contact with HQ test solutions.

Stability Studies

In the study with rat skin, the HQ donor solution was removed from the donor cells at the conclusion of the 8-hr exposure and was assayed by hplc. In the human skin study, an aliquot of the donor solution was incubated at room temperature for 24 hrs and assayed by hplc.

Study Dates

The protocol for these studies received final approval on May 20, 1991. The rat skin study was conducted on June 4 through June 6, 1991 and the human skin study was initiated on July 30, 1991 and ended on August 1, 1991.

RESULTS

The data and calculations from these studies are presented in the Appendix to this report. The data are presented by phase of the experiment ("Day" 1, 2, or 3) and cell number (1 through 9) for that phase. Each table header gives the cell parameters for that cell and the scintillation counts from the experiment are presented in tabular form. Each table is followed directly with a graphical presentation of the data from that cell along with the calculated best fit line and regression parameters. The data set from each experiment is preceded by a "summary" table in which data from all nine cells and all three Days are presented and summarized.

The donor solution was analyzed by hplc prior to and following the rat skin study on June 5, 1991. The donor solution was found to contain 49.19 ± 0.04 mg/mL HQ and no benzoquinone could be detected prior to the skin absorption study. Following the skin absorption study, the donor solutions from cells 2, 3, 5, 6, 8, and 9 were collected and pooled together. The solutions, which had been colorless at the

beginning of the experiment, were brown in color. Re-analysis gave a value of 42.27 mg/mL HQ and 0.30 ± 0.018 mg/mL benzoquinone. Thus the stability of HQ for the 8-hr duration of the skin absorption study was 85.9%. The radiochemical purity of the HQ donor solution was determined by hplc with the use of a radiochemical detector. HQ was the only detectable radiochemical peak on these triplicate chromatograms.

For the study using human stratum corneum, the HQ dosing solution was determined to be 55.94 ± 0.41 mg/mL HQ with benzoquinone present at a concentration of 0.258 ± 0.04 mg/mL. The stability of the solution was determined after 24 hrs of standing at room temperature at which time the HQ concentration was found to be 36.15 ± 0.26 mg/mL. Thus, the stability of HQ in an unused portion of the the dosing solution was 64.6%. The benzoquinone concentration at 24 hrs was determined to be 0.176 ± 0.064 mg/mL.

A summary of the data from the rat skin study is presented on page B1 of the appendices to this report. In the rat skin study, the permeability constant (mean \pm SD, n=9) for $^3\text{H}_2\text{O}$ from the pre-exposure experiment was found to be $(2.34 \pm 1.54) \times 10^{-3}$ cm/hr (n=9). This value is in reasonable agreement with the historical value for this parameter of $(2.11 \pm 0.50) \times 10^{-3}$ cm/hr. The absorption rate for HQ on Day 2 of the study was determined to be 1.09 ± 0.65 $\mu\text{g}/\text{cm}^2/\text{hr}$ (n=5, cell number 9 eliminated as outlier), giving a corresponding permeability constant of 2.26×10^{-5} cm/hr. The mean damage ratio calculated from the Day 3 absorption rates of $^3\text{H}_2\text{O}$ was 0.935 ± 0.18 for the six specimens exposed to HQ donor solution whereas the value was 0.972 ± 0.13 for the three control cells exposed only to physiological saline on Day 2.

In the human skin study (data presented on page C1 of the appendices to this report), the permeability constant (mean \pm SD, n=7, cells 4 and 6 eliminated as outliers) for $^3\text{H}_2\text{O}$ from the pre-exposure experiment was determined to be $(0.967 \pm 0.24) \times 10^{-3}$ cm/hr. This value is in reasonable agreement with the historical value for this parameter of $(1.82 \pm 0.83) \times 10^{-3}$ cm/hr. Note that the permeability constant for human stratum corneum is less than that determined for full thickness rat skin by a factor of 2.18. The absorption rate for HQ on Day 2 of the study was determined to be 0.522 ± 0.13 $\mu\text{g}/\text{cm}^2/\text{hr}$ (n=5, cell 6 eliminated as an outlier), giving a corresponding permeability constant of 9.33×10^{-6} cm/hr. The ratio of the permeability constant values (rat/human) is 2.42, in good agreement with ratios determined for other water soluble permeants. The mean damage ratio calculated from the Day 3 absorption rates of $^3\text{H}_2\text{O}$ was 1.18 ± 0.10 for the specimens exposed to HQ donor solution (cell 6 eliminated from calculation) whereas the value was 1.26

for two control cells (cell number 4 eliminated as an outlier) exposed only to physiological saline on Day 2.

DISCUSSION

The mean absorption rate of HQ through human stratum corneum was found to be $0.522 \pm 0.13 \mu\text{g}/\text{cm}^2/\text{hr}$ with a corresponding permeability constant of $9.33 \times 10^{-6} \text{ cm}/\text{hr}$. According to the definitions of Marzulli *et al.* (1969), HQ would be considered a "slow" penetrant relative to other chemical species. This relationship is depicted in Figure 3.

The absorption rate and permeability constant for HQ using rat skin were found to be approximately two times the values found for human stratum corneum. This observation is in agreement with those for many other chemicals in this and other laboratories (Barber *et al.* 1992).

The mean damage ratio, defined as the rate of tritiated water absorption following exposure to HQ divided by the corresponding value prior to exposure, was determined to be 1.18 for human stratum corneum and 0.935 for full thickness rat skin. These mean damage ratios are not different from those calculated from the control cells in each experiment. It can be concluded from these numbers that an approximately 5% aqueous solution of HQ produces no skin damage following exposure for 8 hrs.

These experiments allow the estimation of HQ uptake after skin exposure in humans, assuming that the rate of skin absorption for man is similar to that determined *in vitro*. The body surface area of a 70 kg man is about 18,000 cm^2 (Schleien and Terpilak, 1984), of which about 4% is the surface area of the hands. Therefore, if both hands were immersed in an aqueous solution containing 5% HQ for 1 hr, the total amount of HQ absorbed would be 376 μg , or a dose of about 5.37 $\mu\text{g}/\text{kg}$. This dose of HQ is approximately the same as that contained in three cups of brewed coffee (Deisinger, unpublished data) and is approximately four orders of magnitude less than the dose required to produce nephrotoxicity in the rat (NTP, 1989).

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The Health Physics and Radiological Health Handbook, Table 9.23. Nucleon
Lectern Associates, Inc.

PERMEABILITY THROUGH HUMAN STRATUM CORNEUM

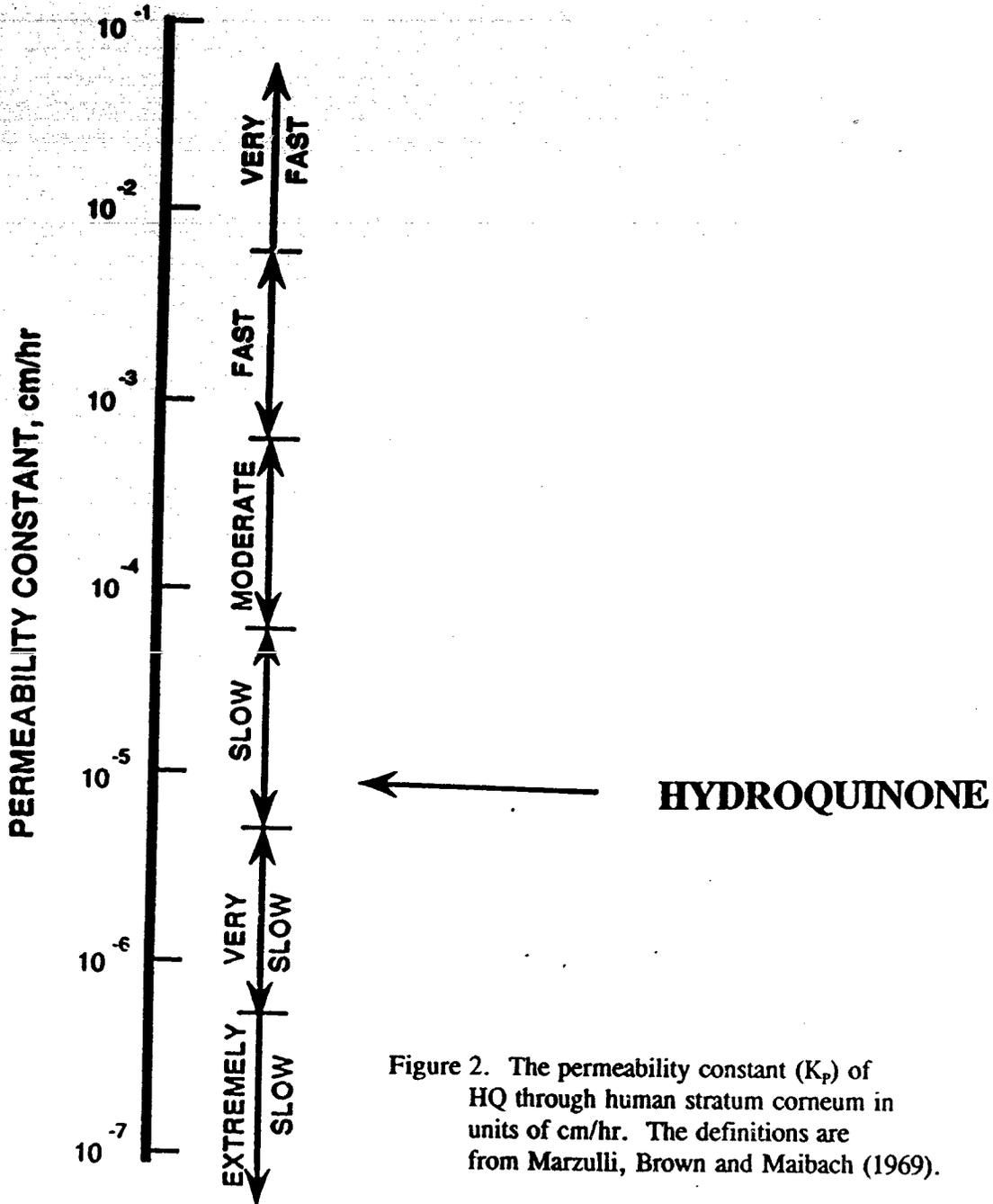


Figure 2. The permeability constant (K_p) of HQ through human stratum corneum in units of cm/hr. The definitions are from Marzulli, Brown and Maibach (1969).

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THE ABSORPTION OF HYDROQUINONE (HQ)
THROUGH RAT AND HUMAN SKIN *IN VITRO*

HAEL No. 87-0113
CIN 10000356

KAN 900356
CAS No. 123-31-9

FINAL REPORT

Eugene D. Barber
Study Director

10/6/93
Date

Walter L. C.
Manager, Biochemical Toxicology Group

9/23/93
Date

Douglas C. Joppa
Acting Unit Director, Biochemical Toxicology Section

9/28/93
Date

John P. ...
Director, Corporate Health and Environment Laboratories

10/13/93
Date

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APPENDICES

**THE ABSORPTION OF HYDROQUINONE (HQ)
THROUGH RAT AND HUMAN SKIN *IN VITRO***

**HAEL No. 87-0113
CIN 1000356**

**KAN 900356
CAS No. 123-31-9**

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PROJECT DETAILS

I. Sponsor: Eastman Chemical Company
Kingsport, TN

II. Materials:

1. Test Compound

A. Hydroquinone (HQ) was obtained from Eastman Chemical Company, Kingsport, TN

SRID :	A13B
HAEL:	87-0113
KAN:	900356
CAS No.	123-31-9

2. Uniformly labeled ^{14}C -Hydroquinone

Obtained from Wizard Laboratories, Davis, CA at a specific activity of 22.2 mCi/mmoie.

SRID 081187

Acquisition No. C-110

3. Standards

Tritiated Water ($^3\text{H}_2\text{O}$) was obtained from New England Nuclear. The amount received was 1000 mCi at a specific activity of 18 mCi/mmoie.

Lot No.: 2109-149

Acquisition #: T-09

III. Study Type:

In vitro percutaneous absorption of HQ through human stratum corneum and full-thickness rat skin.

IV. Laboratory Study Dates:

Rat skin study: June 4-6, 1991

Human skin study: July 30-August 1, 1991

V. Study Personnel:

Study Director: Eugene D. Barber, Ph.D., DABT

Principal Investigators: Daniel B. Schum, B.S., and Tammie Hill, A.A.S.

Unit Director, Biochemical Toxicology Section: Derek Guest, Ph.D.

VI. Testing Facility:

Biochemical Toxicology Section
Toxicological Sciences Laboratory
Corporate Health and Environment Laboratories
Eastman Kodak Company
Building 320, Kodak Park
Rochester, NY 14652-3615.

VII. Analysis of HQ Test Solution for Stability:

The donor solution was analyzed by high pressure liquid chromatography prior to and following the rat skin study on June 5, 1991. The donor solution was found to contain 49.19 ± 0.04 mg/mL HQ and no benzoquinone could be detected prior to the skin absorption study. Following the skin absorption study, the donor solutions from cells 2, 3, 5, 6, 8, and 9 were collected and pooled together. The solutions, which had been colorless at the beginning of the experiment, were brown in color. Re-analysis gave a value of 42.27 mg/mL for HQ and 0.30 ± 0.018 mg/mL benzoquinone. Thus the stability of HQ for the 8-hr duration of the skin absorption study was 85.9%.

For the study using human stratum corneum, the HQ dosing solution was determined to be 55.94 ± 0.41 mg/mL HQ and benzoquinone was detected at a concentration of 0.258 ± 0.04 mg/mL. The stability of the solution was determined after 24 hrs of standing at room temperature at which time the HQ concentration was found to be 36.15 ± 0.26 mg/mL. Thus, the stability of HQ under these conditions was 64.6%. The benzoquinone concentration at 24 hrs was determined to be 0.176 ± 0.064 mg/mL.

VIII. Calculations of Permeability Constant, Absorption Rate and, Damage Ratio:

1. Subtract the background DPM from the sample DPM.
2. Calculate the average sample DPM (X) for that time.
3. Divide the X for a given time by the aliquot volume (in mL) to get the DPM/mL.
4. The total DPM for the receptor chamber is found at each time point, using the following formulae:

$$t_1 = C_1V$$

t_1 = DPM per total volume at the time of first sample.
 C_1 = X DPM/mL. (DPM/mL) at time of first sample.
 V = volume of the receptor chamber (in mL).

$$t_2 = C_2V + C_1S$$

t_2 = DPM per total volume at the time of second sample.
 C_2 = X DPM/mL at time of second sample.
 S = total volume sampled at the respective sample time.

$$t_3 = C_3V + C_2S + C_1S$$

or in general,

$$t_n = C_nV + C_{n-1}S + C_{n-2}S + C_{n-3}S \dots C_1S$$

5. Plot the DPM per total volume vs. time.
6. By linear regression, determine the slope of the plot DPM per total volume vs. time, not incorporating the "lag phase" of the absorption, usually 1 or 2 hrs. The correlation coefficient and intercept are also determined by linear regression.
7. Use the following formula to determine the Permeability Constant:

$$\text{Permeability Constant (cm/hr)} = \frac{\text{slope (DPM per hr)}}{\text{donor DPM (DPM/mL) x skin area (cm}^2\text{)}}$$

8. Use the following formula to determine the Absorption Rate:

$$\begin{array}{l} \text{Absorption} \\ \text{Rate} \end{array} = \frac{\text{slope (DPM per hr)}}{\text{donor DPM (DPM /mg) } \times \text{skin area (cm}^2\text{)}} \quad \begin{array}{l} \text{(mg/cm}^2\text{/hr)} \end{array}$$

9. Use the following formula to determine the Damage Ratio:

$$\text{Damage Ratio} = \frac{\text{Permeability Constant (Day 3)}}{\text{Permeability Constant (Day 1)}}$$

SKIN SOURCE SUMMARY

Human Stratum Corneum

CELL NUMBER

SKIN ID NUMBER

1-3
4-6
7-9

20434
20368
20431

Rat Skin

CELL NUMBER

RAT EARTAG NUMBER

1-3
4-6
7-9

J7280
J7278
J7277

Test Compound: Hydroquinone
 Date: begun: 4-Jun-91
 completed: 6-Jun-91
 Test Species: Fisher 344
 Lab Notebook Ref.: LN668

Day 1 Summary (Tritiated water)

Cell #	Slope (M)	R ²	Permeability - Constant (cm/hr)	Absorption Rate (mg/cm ² /hr)
1	18836.1	0.9928	3.02E-3	3.02E+0
2	5025.5	0.9975	8.06E-4	8.06E-1
3	10784.2	0.9997	1.73E-3	1.73E+0
4	11561.1	0.9947	1.85E-3	1.85E+0
5	6381.3	0.9983	1.02E-3	1.02E+0
6	7900.6	0.9968	1.27E-3	1.27E+0
7	18676.0	0.9991	3.00E-3	3.00E+0
8	15797.5	0.9982	2.53E-3	2.53E+0
9	36318.8	0.9991	5.83E-3	5.83E+0

Day 2 Summary (Hydroquinone)

Cell #	Slope (M)	R ²	Permeability Constant (cm/hr)	Absorption Rate (mg/cm ² /hr)
1	64.0	0.6296	3.65E-7	1.76E-5
2	1578.1	0.9631	8.99E-6	4.33E-4
3	6322.9	0.9947	3.60E-5	1.74E-3
4	26.9	0.5059	1.53E-7	7.39E-6
5	3503.9	0.9829	2.00E-5	9.62E-4
6	1846.8	0.9464	1.05E-5	5.07E-4
7	78.3	0.6341	4.46E-7	2.15E-5
8	6557.2	0.9894	3.74E-5	1.80E-3
9	38861.1	0.9949	2.21E-4	1.07E-2

Day 3 Summary (Tritiated water)

Cell #	Slope (M)	R ²	Permeability Constant (cm/hr)	Absorption Rate (mg/cm ² /hr)
1	16959.6	0.9994	2.72E-3	2.72E+0
2	5389.7	0.9945	8.65E-4	8.65E-1
3	8882.9	0.9985	1.43E-3	1.43E+0
4	12973.9	0.9977	2.08E-3	2.08E+0
5	5952.5	0.9994	9.55E-4	9.55E-1
6	7164.0	0.9997	1.15E-3	1.15E+0
7	16719.6	0.9997	2.68E-3	2.68E+0
8	10824.0	0.9990	1.74E-3	1.74E+0
9	43206.4	0.9995	6.93E-3	6.93E+0

Skin Damage Summary

Cell #	Designation	Permeability		Damage Ratio
		Day 1 Constant (cm/hr)	Day 3 Constant (cm/hr)	
1	Control	3.02E-3	2.72E-3	9.00E-1
2	Test	8.06E-4	8.65E-4	1.07E+0
3	Test	1.73E-3	1.43E-3	8.24E-1
4	Control	1.85E-3	2.08E-3	1.12E+0
5	Test	1.02E-3	9.55E-4	9.33E-1
6	Test	1.27E-3	1.15E-3	9.07E-1
7	Control	3.00E-3	2.68E-3	8.95E-1
8	Test	2.53E-3	1.74E-3	6.85E-1
9	Test	5.83E-3	6.93E-3	1.19E+0