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Journal of the Society of Cosmetic Chemists

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VOLUME 25 • NUMBER 12

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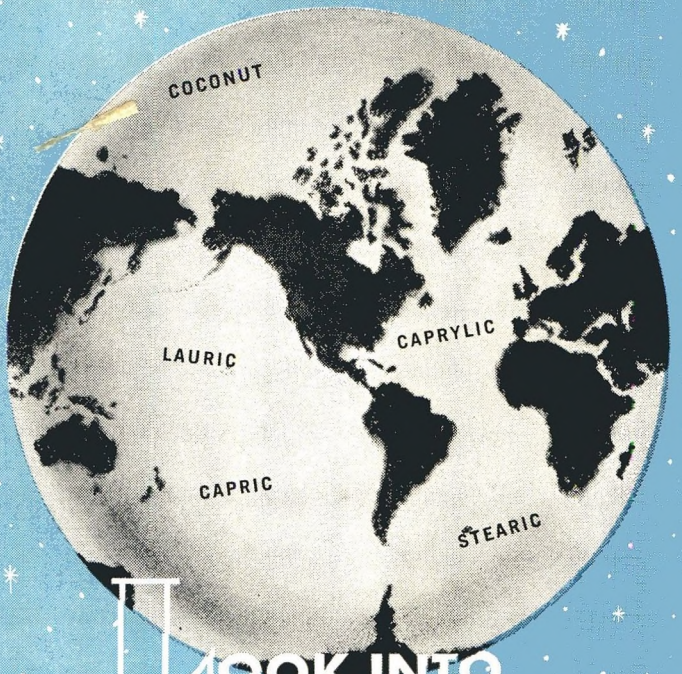

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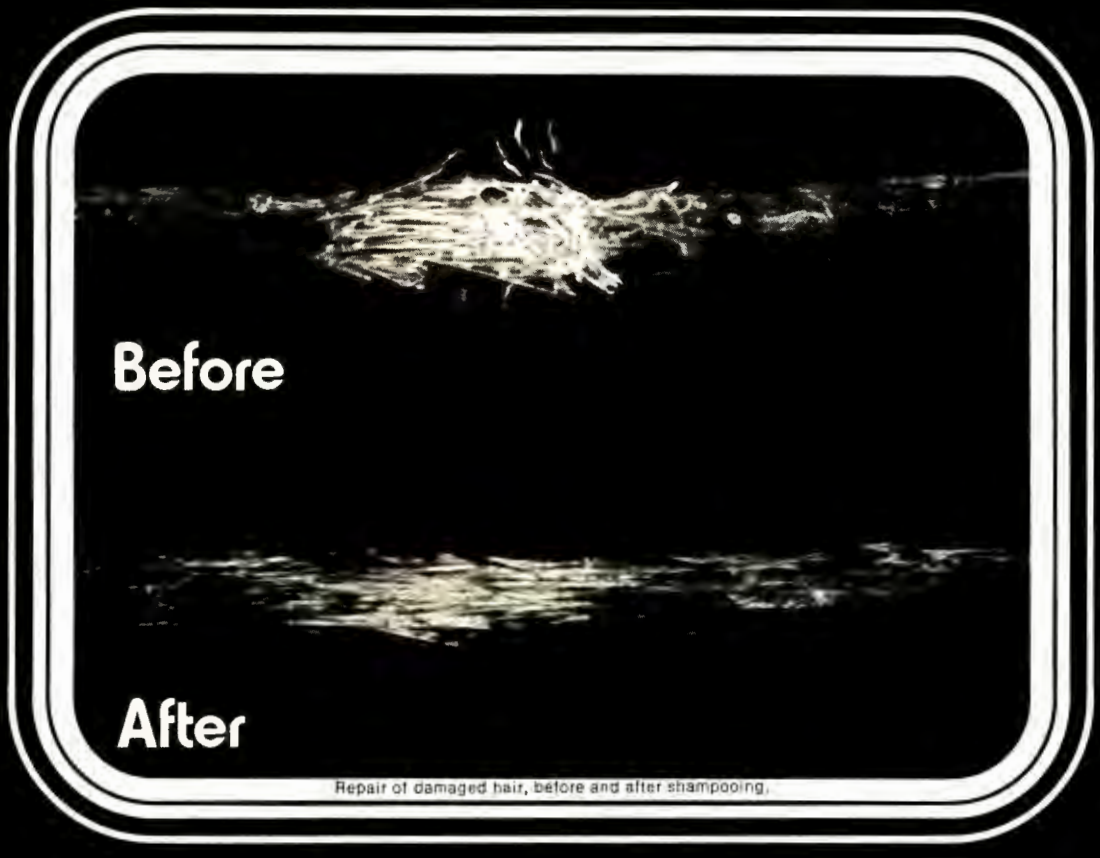

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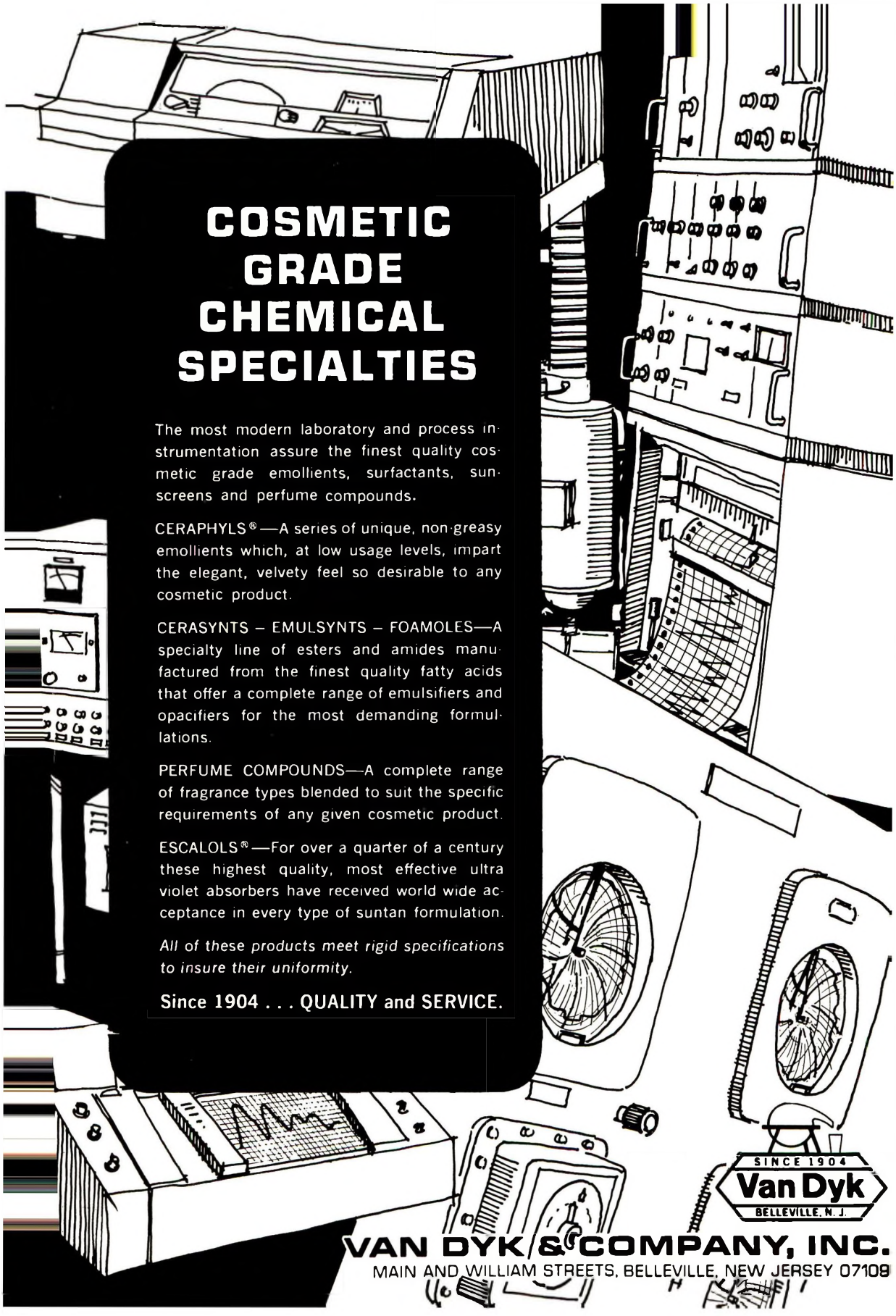

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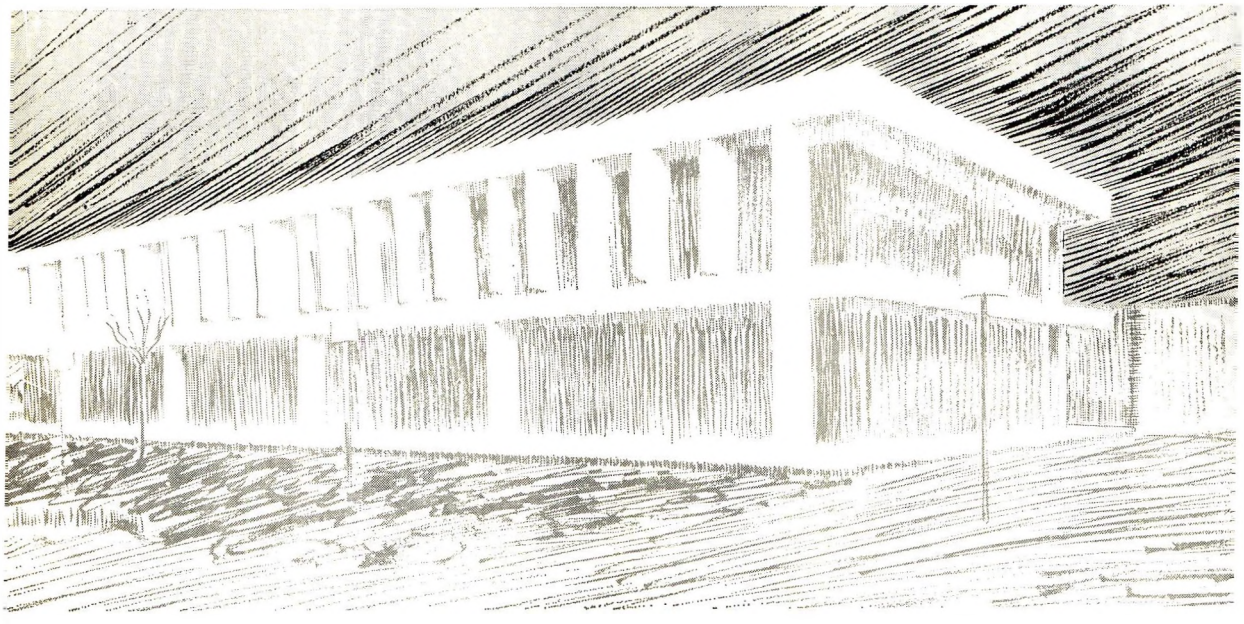

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SYNOPSES FOR CARD INDEXES

The following synopses can be cut out and mounted on 3 x 5 in. index cards for reference, without mutilating the pages of the Journal.

The hairless mouse as an experimental model for evaluating the effectiveness of sunscreen preparations: Hanna Wolska, Andrzej Langner, and Francis N. Marzulli. *Journal of the Society of Cosmetic Chemists* **25**, 639 (November 1974)

Synopsis—Skin reactions were observed in hairless mice (4 to 6 months old) which were administered different amounts of ultraviolet (UV) irradiation with a solar simulator. An identical minimal erythema dose (MED) was found in all animals, demonstrating a highly reproducible dose-effect response in this species. The skin of this species appears to be more responsive to UV irradiation than human skin. Additional mice were similarly irradiated 30 minutes after eight commercial sunscreens were applied separately. In unprotected animals these UV exposures would have been equivalent to up to 10 MED. The best protection was obtained with two sunscreens, one of which contained 5.4% *p*-dimethylaminobenzoic acid, the other 2.7% alkyl *p*-aminobenzoate. The least protection was provided by one containing 4.4% homomenthyl salicylate and one containing 1.6% alkyl *p*-dimethylaminobenzoate. The results obtained on hairless mice are consistent with those reported on man, suggesting that this species is likely to prove useful in evaluating the *in vivo* effectiveness of sunscreen preparations.

The uptake, distribution, and excretion of a commercial aerosol antiperspirant by the monkey: Paul Finkelstein and Ronald J. Wulf. *Journal of the Society of Cosmetic Chemists* **25**, 645 (December 1974)

Synopsis—Four monkeys were exposed to the spray of an aerosol antiperspirant in a head-only exposure chamber by directing the stream directly at the face for 5 seconds. One ingredient of the formulation, isopropyl myristate, was radiolabeled with carbon-14. Following exposure, two animals were sacrificed immediately and two others were allowed to live for 24 hours before necropsy. The distribution of carbon-14 in several tissues, as well as in the exhaled breath, was determined.

The results indicate that only about 0.025% of the dose sprayed at the animals reached the lower respiratory tract. In 24 hours about 85% of the carbon-14 had been eliminated.

Fluorometric determination of formaldehyde-releasing cosmetic preservatives: E. Patricia Sheppard and Clifton H. Wilson. *Journal of the Society of Cosmetic Chemists* **25,** 655 (December 1974)

Synopsis—The preservatives, 2-nitro-2-bromo-1,3-propanediol, 1-hydroxymethyl-5,5-dimethylhydantoin, and methane bis[*N,N'*-(5-ureido-2,4-diketotetrahydroimidazole)-*N,N'*-dimethylol] contain hydroxymethylene functional groups which oxidize to formaldehyde under mild conditions of temperature and pH. Formaldehyde released was reacted with 2,4-pentanedione and ammonia to produce 3,5-diacetyl-1,4-dihydrolutidine which was measured by fluorometry. Using this technique, the three preservatives were determined in cosmetics with average recoveries ranging from 96 to 106%.

Formaldehyde was released quantitatively from 1-hydroxymethyl-5,5-dimethylhydantoin. About 50% of the theoretical yield was obtained from methane bis-[*N,N'*-(5-ureido-2,4-diketotetrahydroimidazole)-*N,N'*-dimethylol]. Formaldehyde derived from 2-nitro-2-bromo-1,3-propanediol was highly dependent on temperature and at 60°C an average value of 28% of theoretical was obtained.

Photostability and skin affinity—two criteria for cosmetic light protective substances, e.g., naphthalene-1,5-bisureas: Udo Hoppe. *Journal of the Society of Cosmetic Chemists* **25,** 667 (December 1974)

Synopsis—The assessment of ultraviolet light absorbers for sunscreening products includes not only practical utility and absence of toxicity, both of which play an important role, but the equally important aspects of photostability and skin affinity. With the aid of a simple illuminator it is shown that—with or without the addition of dihydroxyacetone as a photosensitizer—some light protective substances in hydroalcoholic solution show varying photostability. New naphthalene-1,5-bisureas are described which are stable and, depending on their substitution, can be used as UV-B or UV-A absorbers. Rinse tests have shown that these compounds adhere well to pigskin. Furthermore, they exhibit the remarkable and unusual property of forming gels in hydrophobic solvents.

J. Soc. Cosmet. Chem., **25**, 639–644 (December 1974)

The Hairless Mouse as an Experimental Model for Evaluating the Effectiveness of Sunscreen Preparations*

HANNA WOLSKA, M.D.,† ANDRZEJ LANGNER, M.D.,† and FRANCIS N. MARZULLI, Ph.D.‡

Synopsis—SKIN REACTIONS were observed in HAIRLESS MICE (4 to 6 months old) which were administered different amounts of ultraviolet (UV) IRRADIATION with a solar simulator. An identical minimal erythema dose (MED) was found in all animals, demonstrating a highly reproducible dose-effect response in this species. The skin of this species appears to be more responsive to UV irradiation than human skin. Additional mice were similarly irradiated 30 minutes after 8 commercial SUNSCREENS were applied separately. In unprotected animals these UV exposures would have been equivalent to up to 10 MED. The best protection was obtained with two sunscreens, one of which contained 5.4% *p*-dimethylaminobenzoic acid, the other 2.7% alkyl *p*-aminobenzoate. The least protection was provided by one containing 4.4% homomenthyl salicylate and one containing 1.6% alkyl *p*-dimethylaminobenzoate. The results obtained on hairless mice are consistent with those reported on man, suggesting that this species is likely to prove useful in evaluating the *in vivo* effectiveness of sunscreen preparations.

Introduction

During the past decade, dermatologists have been vigorous in alerting the public about the destructive potential of solar radiation for skin (1). Kligman (2) and others pronounce sunlight a greater threat to the skin's integrity than

*Supported by Project 05-607-4, PL-480 Agreement Apr. 1972, May 1974, between the Food and Drug Administration, U.S. Department of Health, Education, and Welfare, and Warsaw Medical Academy, Warsaw, Poland (Prof. S. Jablonska, Director).
†Department of Dermatology, Warsaw Medical Academy, Warsaw, Poland.
‡Division of Toxicology, Bureau of Foods, Food and Drug Administration, Washington, D.C.

ageing. The term solar or actinic elastosis is considered more descriptive of the changes observed in skin damaged by time and the elements than the more classical term senile elastosis.

This increased attention has produced a more critical assessment of sunscreens which are marketed to protect the skin from the damaging effects of solar radiation and the techniques used for their evaluation. A cursory review of the subject reveals that the requirements for sunscreens under use conditions are not easily satisfied. In addition to the obvious need that they have a proper absorption spectrum and be nonirritating, nontoxic, reasonably stable, and not easily dissipated or removed by sweat or bathing, the manufacturer must consider marketing factors among which are included easy application, cosmetic acceptability, and suitable price. Fulfilling all these requirements provides a stimulus to further research.

Most investigations on sunscreens have been carried out on human subjects (3). Although man is the ultimate user of these products, the possibility of producing hyperpigmentation on large areas of skin, together with problems of obtaining human subjects, suggests the need for a suitable animal model, at least for the exploratory phases of sunscreen development. MacLeod and Frain-Bell (4) report that *in vitro* studies are frequently unreliable in determining the *in vivo* efficacy of sunscreen preparations. The present study involves the use of the hairless mouse in evaluating one aspect of the efficacy of sunscreens, namely, their photobiologic protection potential for skin.

Materials and Methods

Exploratory studies were conducted on 30 male and 30 female hairless mice 4 to 6 months of age. They were irradiated (3000 $\mu W/cm^2$) with a 150-W Xenon lamp* with WG-320 Schott filter in 20 groups of 3. The distance from final filter to skin was 7 cm. Intensity of irradiation was monitored with a long-wave UV-meter.† Four skin areas each about 1 cm^2 were exposed to solar simulating spectrum (which includes the erythema spectrum, 290–320 nm) for periods ranging from 15 sec to 3 min in 15-sec increments to find the minimal erythema dose (MED). Skin reactions were observed and recorded for 10 days at 1-hr intervals during the first 12 hr and then at 24-hr intervals. The mice gave uniform responses.

After completion of the exploratory studies, 8 commercial sunscreens were tested to evaluate their protection potential. Each preparation was applied to a 1-cm^2 area of skin of 10 hairless mice (about 4 mg for creams and 60 μl for liquids) and 30 min later the mice were irradiated with 2.5, 5, 7.5, or 10 MED. Control animals were irradiated without sunscreen protection with 1.5, 2.5, 5, 7.5, and 10 MED (3, 5, 10, 15, and 20-min exposure, respectively).

*Solar Light Co., Philadelphia, Pa.
†Ultraviolet Products Inc., San Gabriel, Calif., J-221.

The following preparations were tested°:

A: Contains 5.4% *p*-aminobenzoic acid.

B: Contains 7.7% homomenthyl salicylate.

C: Contains 2.7% alkyl *p*-dimethylaminobenzoate (declared as isoamyl-*p*-*N*,*N*-dimethylaminobenzoate); analysis of standards showed a mixture of amyl and isoamyl isomers.

D: Contains 11.2% 2-hydroxy-4-methoxybenzophenone†.

E: Contains 4.4% homomenthyl salicylate.

F: Label declaration 8% 2,2-dihydroxy-4,4-dimethoxybenzophenone plus 6% sodium 3,4-dimethoxyphenylglyoxylate (not analyzed).

G: Contains 4% menthyl anthranilate plus 5% 2-ethoxyethyl *p*-methoxycinnamate.

H: Contains 1.6% alkyl *p*-dimethylaminobenzoate (declared as amyl *p*-dimethylaminobenzoate); analysis of standards showed a mixture of amyl and isoamyl isomers.

Results and Discussion

The minimal erythema dose (1 MED) in unprotected animals, a 2-min exposure, produced erythema in about 3 hr. In addition, the following grades of skin damage were seen.

+ = mild reaction (1–1.5 MED); moderate edema followed by desquamation at 8 days.

++ = moderate reaction (2.5 MED); edema followed by superficial erosion in the center of the exposed area. Changes disappeared within 10 days, leaving small scars.

+++ = strong reaction (5–7.5 MED); sharply limited pale edema at 24 hr; an inflammatory halo around the swollen area at 72 hr with punctate hemorrhages and erosion in the center followed by extensive necrosis with desquamation beginning at the periphery. The process of cicatrization was completed after 12–13 days.

++++ = very strong reaction (7.5–10 MED); sharply limited pale edema of the exposed area at 24 hr; inflammatory halo around swollen area and punctate hemorrhages and erosion in the center at 48 hr; prominent inflammatory halo with greater confluent erosion in center at 72 hr; extensive necrosis in the area of exposure with desquamation at periphery; cicatrization complete on 11–16th day (Fig. 1, 10 MED, 3 days after 20-min exposure).

In the present studies, preparations A and C protected hairless mouse skin against up to 10 MED compared to 7.5 MED for preparations D and F,

°One container of each lot of all samples except preparation F was chemically analyzed to identify the amount and type of UV absorber by chemists of Cosmetic Technology Division, Food and Drug Administration, under the direction of Henry Davis.

†A similar product by the same manufacturer contains the 5-sulfonic acid.

Figure 1. Response of unprotected hairless mouse (++++ reactions) three days after 20-min exposure to 10 MED ultraviolet irradiation

5 MED for preparation G, and 2.5 MED for preparation B. Preparations E and H were ineffective in protecting mouse skin under all test conditions (Table I). Thus 5.4% *p*-aminobenzoic acid (A) and 2.7% alkyl *p*-dimethylaminobenzoate (C) in commercial sunscreen preparations appeared to be superior under these test conditions to 6 preparations containing other active ingredients or concentrations. Preparations D containing 11.2% 2-hydroxy-4-methoxybenzophenone, and F, containing a combination of a benzophenone and a phenyl glyoxylate, though effective, were not as efficient as A and C. Preparation B, containing 7.7% homomenthyl salicylate, showed some advantage over preparation E, which contained only 4.4% of this active ingredient. Preparation H, containing 1.6% alkyl *p*-dimethylaminobenzoate, was ineffective. Yet preparation C, containing 2.7% of the same ingredient, was highly effective, suggesting the importance of concentration as a factor in effectiveness. The results obtained on hairless mice are consistent with certain results reported in the literature involving human subjects. For example, Pathak *et al.* (5) found 5% PABA and 2.5% isoamyl *p-N,N*-dimethylaminobenzoate most protective when compared with 24 other preparations under practical field conditions involving human subjects. They pointed out the importance of skin substantivity as a factor in a sunscreen's effectiveness under use conditions as contrasted with *in vitro* effectiveness. As in the present study on mice, Langner and Kligman (6) found PABA effective and menthyl anthranilate

Table I

Grades of Skin Reactions[a] Observed in Hairless Mice Protected Against Various Amounts of UV with 8 Commercial Sunscreens

Preparation	Exposure Conditions[b]			
	20 min (10 MED)	15 min (7.5 MED)	10 min (5 MED)	5 min (2.5 MED)
A	−	−	−	−
B	++++	+++	++	−
C	−	−	−	−
D	+	−	−	−
E	++++	+++	++	+
F	+	−	−	−
G	+++	++	−	−
H	++++	+++	++	+
Control	++++	+++/++++	+++	++

[a]Skin reactions: − = none; + = mild; ++ = moderate; +++ = strong; ++++ = very strong.
[b]MED = minimal erythema dose.

relatively ineffective when tested on man. Willis and Kligman (7) reported that homomenthyl salicylate (concentration not stated) was protective for humans against 5 MED using a Xenon light as UV source. In the present experiments, 7.7% homomenthyl salicylate protected mice against 2.5 MED but failed against 5 MED. Furthermore, these investigators reported that 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid (concentration not stated) provided protection against 9 MED in humans. In the present experiments 11.2% of this agent protected mice at 7 MED but failed at 10 MED. Finally, Willis and Kligman reported protection against 12 MED with a mixture of 2,2-dihydroxy-4-methoxybenzophenone and 2-hydroxy-4-methoxybenzophenone. In the present studies a related sunscreen preparation (F) protected mice at 7 MED but failed at 10 MED.

That there is not complete agreement in the matter of sunscreen protection is seen when the results of Katz (8) are compared with both those of Pathak *et al.* (5) and the work reported here. Katz (8) reported that 5% PABA in 70% ethanol, a cream with benzophenone derivatives of oxybenzone and dioxybenzone, and 3% 2,2-dihydroxy-4-methoxybenzophene in a cream base were superior to preparation C containing 2.5% isoamyl *p*-N,N-dimethylaminobenzoate in 65% ethanol, when tested on buttocks or suprapubic skin for protection against Florida midday sun.

At this point, comments are in order with regard to the response of mice and humans to UV irradiation. The clinical impression is that erythema develops and clears more slowly in humans than in mice. Mouse skin appears to be more extensively damaged, and the damage often involves subcutaneous

tissue. Pronounced edema and an inflammatory halo with necrosis were not observed in humans at UV doses which produce these effects in hairless mice. The greater vulnerability of the mouse skin is thought to be related to the thinner horny layer, thinner epidermis, and lack of epidermal pigment. This greater sensitivity may enhance the value of this species as a model for humans.

Conclusions

1. Skin reactions were reproducible and virtually the same minimal erythema doses were obtained repeatedly when hairless mice were exposed to identical amounts of solar simulating UV irradiation.

2. In hairless mice, the best protection against UV irradiation (10 MED) was obtained with 2 commercial sunscreens, one containing 5.4% PABA, the other 2.7% alkyl *p*-dimethylaminobenzoate. A preparation containing 1.6% alkyl *p*-dimethylaminobenzoate and one containing 4.4% homomenthyl salicylate were ineffective.

3. Although not compared directly, the response of hairless mouse skin to UV irradiation appeared to be more intense and may involve deeper (subcutaneous) tissues than the response of humans under similar conditions of exposure; nevertheless, comparative (sunscreen) results for the two species appear to be consistent with one another.

4. The hairless mouse appears to be a promising model for providing a basis for comparing the effectiveness of sunscreen preparations on skin *in vivo*.

(Received April 4, 1974)

References

(1) Epstein, J. H., Fukuyama, K., and Dobson, R. L., *Ultraviolet Light Carcinogenesis*, in F. Urbach, ed., *The Biologic Effects of Ultraviolet Radiation*, Pergamon Press, Oxford, 1969, p. 551.

(2) Kligman, A. M., Early destructive effect of sunlight on human skin, *J. Amer. Med. Ass.*, 210, 2377 (1969).

(3) Harber, L. C., Clinical evaluation of quantitative differences in ultraviolet absorption of compounds containing the substituted benzoic acid nucleus, *J. Invest Dermatol.*, **23**, 427 (1954).

(4) MacLeod, T. M., and Frain-Bell, W., The study of the efficacy of some agents used for the protection of the skin from exposure to light, *Brit. J. Dermatol.*, **84**, 266 (1971).

(5) Pathak, M. A., Fitzpatrick, T. B., and Frank, E., Evaluation of topical agents that prevent sunburn. Superiority of *p*-aminobenzoic acid and its ester in ethyl alcohol, *N. Engl. J. Med.*, **280**, 1459 (1969).

(6) Langner, A., and Kligman, A. M., Further sunscreen studies of aminobenzoic acid, *Arch. Dermatol.*, **105**, 851 (1972).

(7) Willis, I., and Kligman, A. M., The evaluation of sunscreens by human assay, *J. Soc. Cosmet. Chem.*, **20**, 639 (1969).

(8) Katz, S. J., Relative effectiveness of selected sunscreens, *Arch. Dermatol.*, **101**, 466 (1970).

J. Soc. Cosmet. Chem., **25**, 645–654 (December 1974)

The Uptake, Distribution, and Excretion of a Commercial Aerosol Antiperspirant by the Monkey

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Presented December 11, 1973, New York City

Synopsis—Four monkeys were exposed to the spray of an AEROSOL ANTIPERSPIRANT in a head-only exposure chamber by directing the stream directly at the face for 5 seconds. One ingredient of the formulation, ISOPROPYL MYRISTATE, was RADIOLABELED with carbon-14. Following exposure, two animals were sacrificed immediately and two others were allowed to live for 24 hours before necropsy. The distribution of carbon-14 in several tissues, as well as in the exhaled breath, was determined.

The results indicate that only about 0.025% of the dose sprayed at the animals reached the lower respiratory tract. In 24 hours about 85% of the carbon-14 had been eliminated.

Introduction

For many years the most widely used active ingredients in commercial antiperspirant products have been aluminum salts. They have been formulated and sold in a variety of vehicles and applicators, including simple aqueous solutions, lotions, creams, and sticks. More recently, the aerosol sprays have been introduced and have assumed a leading role in the marketplace. These formulations usually contain a suspension of an aluminum salt in a nonaqueous vehicle which is propelled by fluorocarbons.

With the introduction of these aerosol spray products, the possibility of inhalation hazards had to be considered. The usual procedures for testing for such hazards include acute inhalation exposures of rats and 30- or 90-day exposures of rabbits or rats and, more recently, monkeys. These tests are conducted under exaggerated conditions of exposure compared to the normal use of the product. Examination of toxicologic symptoms, as well as physiologic, histologic, and chemical alterations, is made in the animals. However, no attempt is made to determine what fraction of the spray is actually ab-

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sorbed by the animals. This is governed by several factors, among which is the particle or droplet size when the sprays contain partially volatile or suspended materials.

The studies reported here were an attempt to estimate the amount of antiperspirant spray inhaled by monkeys exposed to an exaggerated dose of the test product (5 sec of spray) directed at the face. This was done by labeling the major ingredient of the nonaqueous vehicle, isopropyl myristate (IPM), with carbon-14. No beta-emitting isotope of aluminum was convenient or practical to use as a label, although this might have been desirable. The only other ingredients in the formulation were perfume and the anticaking agent Bentone®-34.*

The monkeys were sacrificed immediately after exposure to minimize metabolic uptake and translocation. Since it was also desirable to look at the pattern of distribution of the absorbed spray, some of the monkeys were allowed to live for 24 hours before being sacrificed.

Experimental Methods

The antiperspirant spray formulation was radiolabeled by adding a very small quantity of carboxyl ^{14}C-IPM† with a high specific activity to a sample of concentrate in a spray can. Propellants were then added and the can was sealed. The formulation was shaken overnight to insure uniform distribution. Approximately 1 millicurie of ^{14}C was thus dispersed in 90 g of formulation.

Adult male rhesus monkeys weighing about 2.5 kg were used. The animals were allowed to accommodate to the laboratory environment for four weeks or longer. All received a general physical examination with special attention to the respiratory system. Only animals in good health were placed on the study.

A special chamber was constructed to permit a head-only exposure of the animals to the spray. Each animal was placed in a standard primate restraining chair with his head in the chamber. The system is shown in Fig. 1.

The acrylic chamber measured 6 in. x 6 in. x 18 in. One end of the box had an opening for admitting the spray, while air was drawn out from a port at the other end. A membrane filter (0.45-μ pore size) was positioned in front of this exit port to trap any airborne particles. Air was pulled through the chamber at 4 l./min.

A 5-sec burst of the aerosol spray was directed at the face of each animal. This released a mean of 53.05 μc of activity into the chamber. The animal was allowed to take 30 breaths, which took 1 to 2 min. Two animals were sacrificed immediately and two others were fitted with a face mask covering the nose and mouth to collect the exhaled breath for 24 hours.

*Bentone®-34, a magnesium aluminum silicate proprietary composition from National Lead Corp., Hightstown, N.J.

†Carboxyl ^{14}C-IMP, synthesized by New England Nuclear Corp., Boston, Mass.

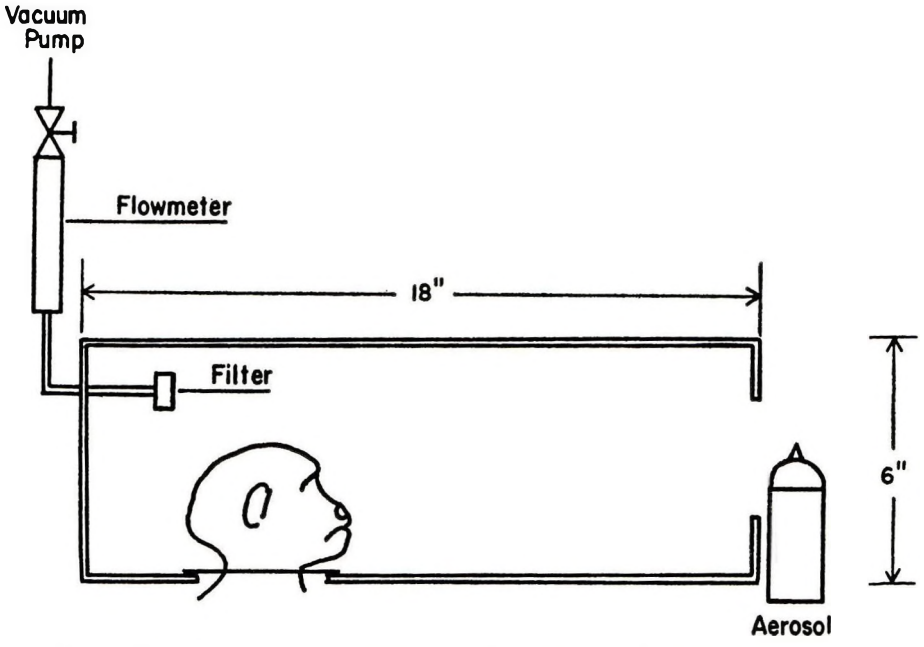

Figure 1. Exposure chamber and position of monkey head in relation to aerosol

In order to reduce the time between exposure and tissue removal, the two animals scheduled for immediate sacrifice were electrocuted. The other two were sacrificed by intravenous administration of pentobarbital. Tissues were removed as quickly as possible, taking care not to contaminate one sample with material from another.

For analysis of the radioactivity in the solid tissues, they were finely chopped and then homogenized in a blender. An aliquot of the homogenate was placed on a filter paper disc which was then placed in a Packard®* Sample Oxidizer for combustion and collection of the resulting labeled carbon dioxide. The latter was collected in ethanolamine to which was added methanol and a scintillator solution (0.55% Permablend III®* in toluene). This mixture was placed in counting vials and measured in a liquid scintillation counter.† All samples containing more than 200 dpm were counted to a standard error of 1%. Samples containing twice the background count but less than 200 dpm (as determined by a 1-min count) were counted to a 10% standard error.

For analysis of liquids, 200 μl. of blood or urine were placed on filter paper discs and processed as for solid tissues.

*Packard Instrument Co., Downers Grove, Ill.
†Mark I, Nuclear-Chicago, Des Plaines, Ill.

Room air at 6 l./min was drawn through the face mask of the two surviving monkeys and this, plus the exhaled breath, was bubbled through two gas traps containing ethanolamine/methanol (9/4) for collection. A flowmeter attached to the inlet of the mask monitored flowrate and respiration. The trapping solutions were assayed for $^{14}CO_2$ and other non-CO_2-radioactivity (presumed to be unmetabolized IPM).

Results

The tissue distribution of radioactivity in the two monkeys sacrificed immediately after exposure is shown in Table I. For purposes of calculation, these results were averaged. In these animals it may be assumed that metabolism was negligible during the 30 breaths taken. Thus, the distribution of label corresponds to the distribution of the total product. Of particular interest was the distribution of activity within the lung. Therefore, we separately measured each lobe. All lobes were very similar, indicating no noticeable variations in the pattern of deposition.

Table I

Distribution of Radioactivity following Inhalation Exposure
(Immediately after Exposure)

	Monkey A ($\mu c \times 10^4$)	Monkey B ($\mu c \times 10^4$)
Skin or skin substitute (per in.^{2})	860.00	1360.00
Nasal septum	110.00	324.00
Trachea	9.88	29.70
Bifurcation	6.92	5.95
Lung (total)	109.41	67.13
Stomach	1.28	108.48
Esophagus	3.19	16.66
Bile	0	0

The tissue distribution 24 hours after exposure is given in Table II. It will be noted that the total exhaled radioactivity is comparatively high.

No radioactivity was found in the blood and urine samples in monkeys A and B. In animals C and D, urine samples were collected periodically and blood was taken after 5 min and again after 24 hours. The levels here were very low. This is shown in Tables III and IV.

The airborne concentration of radioactivity in the exposure chamber during the exposure was obtained by assay of the exit port filter. These results are shown in Table V, along with the concentration of spray formulation to which they correspond. These values were very reproducible.

Table II

Distribution of Radioactivity following Inhalation Exposure
(Twenty-four Hours after Exposure)

	Monkey C (μc x 10^4)	Monkey D (μc x 10^4)
Skin or skin substitute (per in.^{2})	1070.00	3750.00
Nasal septum	12.74	3.52
Trachea	1.69	3.72
Bifurcation	1.19	N.D.
Lung (total)	19.20	11.48
Liver	36.41	20.55
Kidney	3.89	5.02
Stomach	13.57	14.34
Esophagus	1.21	1.94
Bile	0.74	0.56
Feces	0.012	N.D.
Exhaled radioactivity in 24 hours as $^{14}CO_2$ or ^{14}C-IPM	678.60	1740.90

Table III

Urine Levels of Radioactivity

Sampling Time (Hours)	Monkey C (Total μc x 10^4)	Monkey D (Total μc x 10^4)
0.38	0.832	...
0.50	...	9.67
0.93	1.904	...
1.55	0.028	...
4.27	2.02	...
5.88	2.04	...
10.20	...	3.92
18.13	4.95	...
20.72	3.32	...

Table IV

Blood[a] Levels of Radioactiivity

Time of Sampling	Monkey C (Total μc x 10^4)	Monkey D (Total μc x 10^4)
5 min post exposure	0.0	0.0
24 hrs post exposure	0.55	0.0

[a]Assuming the blood volume to be 54.1 (44.3–66.6) ml/kg of body weight (1).

Table V

"Airborne" Concentration of Formulation in the Chamber

	μc Radioactivity/Liter Air	μg Formulation/Liter Air
Monkey A	0.057	0.498
Monkey B	0.055	0.479
Monkey C	0.065	0.567
Monkey D	0.045	0.394

Discussion

Based on these values, calculations have been made of the amount of the product absorbed, the amount reaching the lower respiratory tract, and the percentage of radioactivity excreted in 24 hours.

Estimation of the portion of the released dose reaching the lower respiratory tract was made in the following manner:

$$\text{Formula I: } \% = \frac{\text{radioactivity}^{\bullet} \text{ in trachea + bifurcation + lung}}{\text{total radioactivity released in chamber}} \times 100$$

This was calculated to be 0.02%.

The per cent of radioactivity remaining in any organ after 24 hours was calculated in the following manner:

$$\text{Formula II: } \% = \frac{\text{radioactivity in an organ at 24 hours}^{\dagger}}{\text{radioactivity in an organ immediately after exposure}^{\ddagger}} \times 100$$

This was calculated to be 17.4% for the lung, 13.85% for the trachea, and 17.9% for the bifurcation. The average for the entire lower respiratory tract (so defined in Formula I) was 16.8%.

It was not possible to calculate directly the total dose absorbed initially. Although very little activity could be found in tissues outside the respiratory tract, the amount in the nasopharyngeal portion of the tract could not be readily collected for quantitation. The amount could, however, be estimated in three independent ways which were in reasonably good agreement.

First, the airborne concentration in the chamber was measured using an air filter in the exhaust system to take out all the radioactivity. Using an average figure of 50 ml for the tidal volume and 30 breaths, this gives 833×10^{-4} μc inhaled from the data in Table V. This figure is probably a little low since it does not include any material impinging directly from the spray in the mouth or nasal openings.

•Mean of monkeys A and B.
†Mean from monkeys C and D.
‡Mean from monkeys A and B.

Second, an estimate was made of the amount striking the forehead skin directly. In a square inch this was 1760×10^{-4} μc as a mean. This figure is probably a little high since the nasal openings and mouth are probably somewhat less than one square inch, depending on how wide open the mouth was during exposure.

Third, the amount absorbed may be estimated from the amount excreted in 24 hours. Very little was excreted in the urine, bile, or feces, but substantial quantities were excreted in the breath. The mean for monkeys C and D was 1210×10^{-4} μc. In each of the tissues where direct comparison could be made of the amount absorbed in monkeys A and B and the amount remaining in monkeys C and D, it was found that a 75–85% decline had occurred. Thus, it would be estimated that about 1500×10^{-4} μc was initially absorbed. Averaging these three estimates gives a mean of 1364×10^{-4} μc. Formula III gives 0.25% as the total absorbed portion of the spray.

$$\text{Formula III: } \% = \frac{\text{total radioactivity absorbed (mean)}}{\text{total radioactivity released in chamber}} \times 100$$

Comparing this to the amounts reaching the lower respiratory tract calculated from Formula I, it is evident that only about 10% of the absorbed total dose has reached the lower respiratory tract.

The distribution of radioactivity in the lower respiratory system shown in Table I was quite uniform. The specific activity (counts per mg of tissue) in the trachea and bifurcation was a little higher than in the lungs. As previously mentioned, it did not seem to accumulate in any portion of the lungs. The amounts of radioactivity reaching the other nonrespiratory tissues was very small immediately after exposure. A little was found in the stomach but none in the blood or bile.

The data 24 hours post-exposure in Table II show that only trace amounts were found in the blood and urine. Of the other organs, a small amount was found in the liver and stomach and smaller amounts in the kidneys and esophagus. Thus, very little activity left the respiratory tract.

The radioactively labeled IPM was of high specific activity (376 μc/mg). Thus, the levels of activity in this table correspond to very small quantities of the tagged compound (ranging from 0.22 to 0.46 μg in these nonrespiratory tissues).

The principal route of excretion was as carbon dioxide in the exhaled breath. The time course of this excretion for monkeys C and D is shown in Fig. 2.

As indicated above, about 85% of the dose initially found in the tissues had been excreted in 24 hours. The rate of excretion at the end of the 24-hour time period was still appreciable compared to the earlier rates. From this observation and from the very small amounts found in other tissues, it appears that most of the metabolism occurred in the respiratory tract.

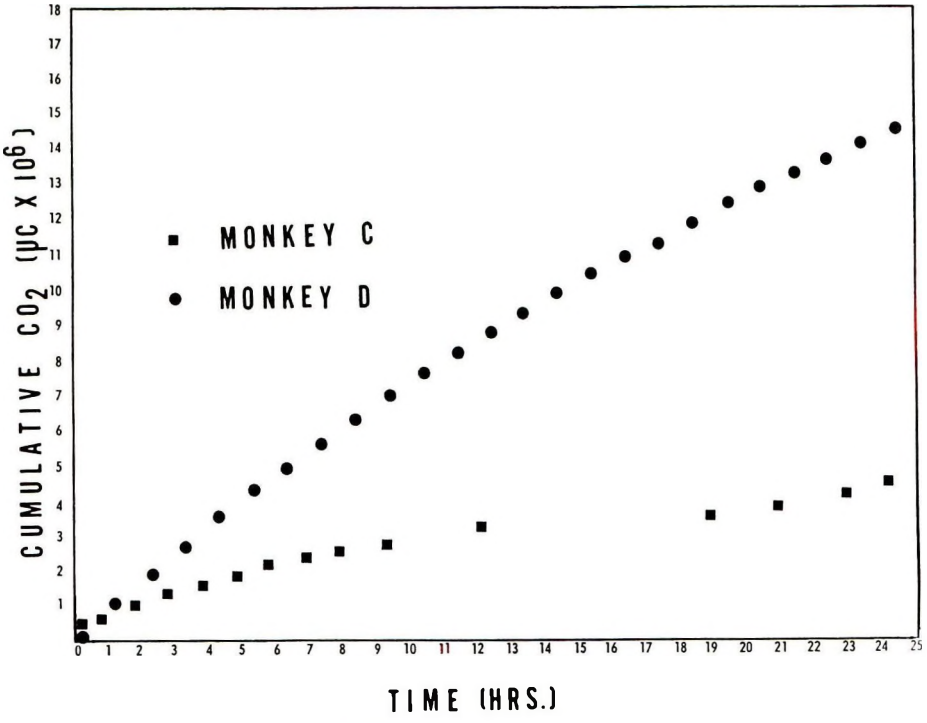

Figure 2. Exhalation of $^{14}CO_2$

Assays of the exhaled breath were also made for radioactivity other than CO_2 (presumably unmodified IPM). A significant amount of this was found as shown in Fig. 3.

Although IPM is not considered to be volatile, small amounts can evaporate. Because of its high specific activity in this test, its presence in the breath is not too surprising. An assay of the radioactivity on the nasal septum tissue, in fact, showed a decline of over 95% in 24 hours, which could be mainly *via* evaporation of IPM into the face mask used to collect the exhaled breath.

In monkey D, in order to check on the possibility of absorption through the skin of the face and head, a mask was placed over the head, leaving holes only for the nose and mouth. Comparing these results with monkey C, no appreciable difference in relative tissue distribution patterns was noted. Thus, it appears that absorption through the skin was not an important route in these experiments.

The total product absorbed in the 5 sec of exposure amounts to only 1 mg of the formulation concentrate. The toxicity of each of the ingredients contained therein is very low. The active ingredient, aluminum chlorhydrate, is incorporated into the product as a solid impalpable powder. In 1957, Cambell *et al.* (2) published an exhaustive review entitled "Aluminum in the En-

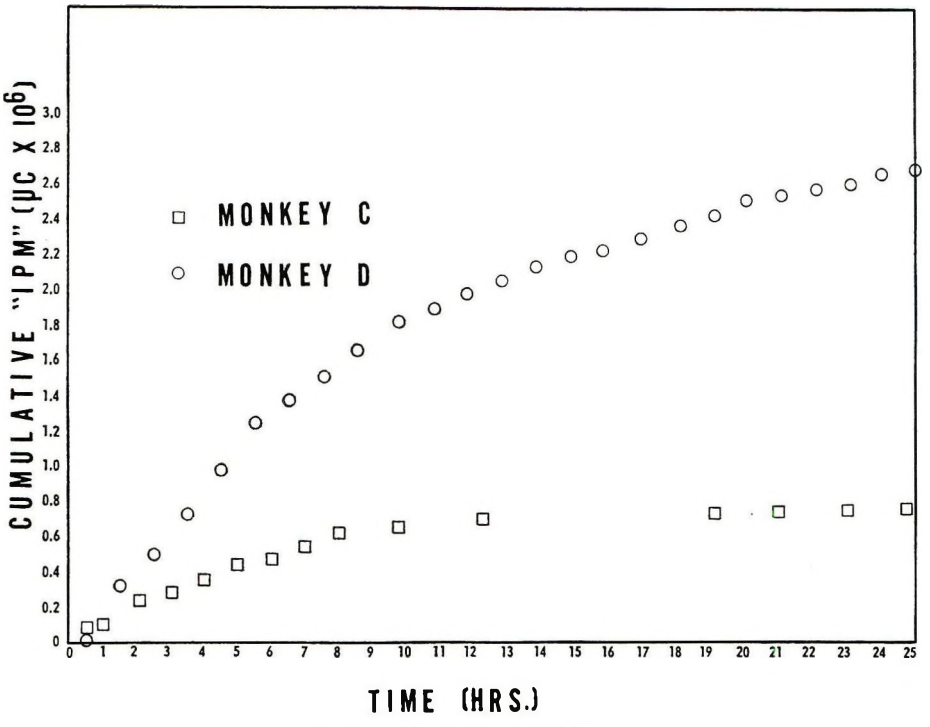

Figure 3. Exhalation of IPM

vironment of Man" in which numerous books, reports, and articles were assembled and abstracted. These authors conclude that after consideration of the wide distribution of aluminum in the normal environment, e.g., soil, atmosphere, vegetation, and water, as well as in food, food processing, food containers, and medicinal agents, there are "no problems associated with aluminum in the environment of man and that none appeared on the horizon." Estimates of the quantity of aluminum in the diet of the ordinary adult, including amounts derived from aluminum utensils, range from 10 to 100 mg per day. Recalling that aluminum is the third most abundant element on the earth's surface and widely distributed as soft, low density materials, these estimates appear reasonable. The two most likely routes by which aluminum enters the body are oral ingestion and inhalation. No evidence for topical absorption has been reported (3).

The major component of the vehicle is a commercial grade of isopropyl myrisate, a colorless and practically odorless liquid. It contains 95.0% isopropyl myristate. The remainder is mainly isopropyl palmitate (up to 4%), isopropyl laurate (up to 1.5%), and traces of isopropyl tridecanoate and isopropyl pentadecanoate. It is widely used in cosmetic formulations and drugs.

A summary of its toxicity evaluation indicates it is nontoxic and neither a primary irritant nor a sensitizer (4).

The other component of the formulation is the anticaking ingredient, Bentone-34. This is a proprietary composition which is a reaction product of a bentonite clay and dimethyl distearyl ammounium chloride. A toxicological examination (5) by the supplier indicates no evidence of local or systemic reactions resulting from chronic topical exposure. It is nontoxic and approved for use as a food additive.

Summary

It has been shown that direct exposure of the face to this aerosol spray antiperspirant from a distance of about 12 in. leads to the uptake of only 0.25% of the spray formulation concentrate. About 10% of this (0.02%) reaches the lower respiratory tract. About 85% of the absorbed IPM is excreted in 24 hours, mainly as carbon dioxide in the breath. Very little reaches any of the tissues other than the lungs. Since only 1 mg of the formulation concentrate is absorbed and the toxicity of the components is reported to be low, it is unlikely that a hazard exists.

Acknowledgment

The authors gratefully acknowledge the able technical assistance of Mr. Charles Ulrich of Huntingdon Research Center, Baltimore, Md.

(Received May 24, 1974)

(1) Altman, P. L., and Dittmer, D. S., *Biology Data Book*, FASEB, Washington, D.C., 1964.
(2) Campbell, I. R., Cass, J. S., Clolak, J., and Kehoe, R. A., Aluminum in the environment of man, *Ind. Health*, **15**, 359–448 (1957).
(3) Blank, I. H., Jones, J. L., and Gould, E., A study of the penetration of aluminum salts into excised human skin, *Proc. Sci. Sec. Toilet Goods Ass.*, 29, 32–5 (June 1958).
(4) Deltyl Extra Bulletin, Givaudan Corp., 125 Delawanna Avenue, Clifton, N.J. 07014.
(5) Toxicological Examination of Bentone-34, N. L. Industries, P.O. Box 420, Hightstown, N.J.

J. Soc. Cosmet. Chem., **25**, 655–666 (December 1974)

Fluorometric Determination of Formaldehyde-releasing Cosmetic Preservatives

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Presented October 9, 1973, Joint Symposium of the Association of Official Analytical Chemists and the Society of Cosmetic Chemists, Washington, D.C.

Synopsis—The PRESERVATIVES, 2-nitro-2-bromo-1,3-propanediol, 1-hydroxymethyl-5,5-dimethylhydantoin, and methane bis[*N,N'*-(5-ureido-2,4-diketotetrahydroimidazole)-*N,N'*dimethylol] contain HYDROXYMETHYLENE FUNCTIONAL GROUPS which oxidize to FORMALDEHYDE under mild conditions of temperature and pH. Formaldehyde released was reacted with 2,4-pentanedione and ammonia to produce 3,5-diacetyl-1,4-dihydrolutidine which was measured by FLUOROMETRY. Using this technique, the three preservatives were determined in cosmetics with average recoveries ranging from 96 to 106%.

Formaldehyde was released quantitatively from 1-hydroxymethyl-5,5-dimethylhydantoin. About 50% of the theoretical yield was obtained from methane bis[*N,N'*-(5-ureido-2,4-diketotetrahydroimidazole)-*N,N'*-dimethylol]. Formaldehyde derived from 2-nitro-2-bromo-1,3-propanediol was highly dependent on temperature and at 60°C an average value of 28% of theoretical was obtained.

Introduction

The compounds, 2-nitro-2-bromo-1,3-propanediol (Bronopol®),† methane bis[*N,N'*(5-ureido-2,4-diketotetrahydroimidazole)*N,N'*-dimethylol] (Germall 115®),‡ and 1-hydroxymethyl-5,5-dimethylhydantoin (hydroxymethyldimethylhydantoin)§ (Fig. 1) belong to a class of compounds which Parker (1) has called the "new generation" of cosmetic preservatives. They are incorporated into a wide variety of cosmetic formulations. They contain methylol

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†Bronopol is manufactured by the Boots Company in England and is distributed in the United States by Goldschmidt Chemical Co.

‡Germall 115 is manufactured by Sutton Laboratories, Roselle, N.J.

§Analabs Inc., North Haven, Conn.

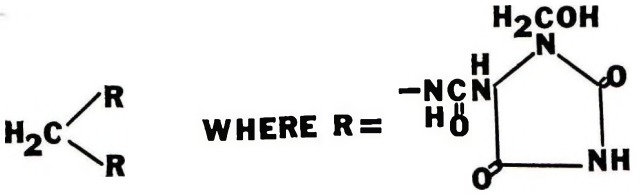

Figure 1. Structures of methylol-containing preservatives (HMDMH refers to hydroxymethyldimethylhydantoin)

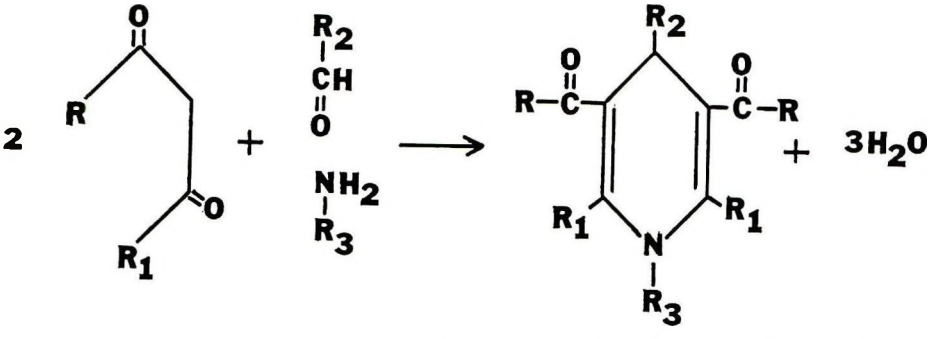

Figure 2. Hantzsch reaction producing a fluorescing derivative from a β-diketone, an aldehyde, and an amine

functional groups and are water-soluble. They do not absorb in the ultraviolet (UV) region of the electromagnetic spectrum and decompose at elevated temperatures. The two latter properties preclude determination of these cosmetic preservatives by UV spectrophotometry or by gas chromatography. However, the hydroxymethylene groups of these compounds, which theoretically can be oxidized to formaldehyde, and their solubility in aqueous media suggest the possibility of determining them by the fluorometric method for formaldehyde devised by Belman (2). Belman's procedure is based on the earlier work of Nash (3) who, utilizing the Hantzsch reaction, estimated

formaldehyde by reacting it with 2,4-pentanedione and ammonia to form 3,5-diacetyl-1,4-dihydrolutidine (DDL) which he measured spectrophotometrically. The equation for this reaction is shown in Fig. 2. The Hantzsch reaction has been applied to the determination of formaldehyde in cosmetics (4).

In the present study the necessary conditions were developed for oxidation of the hydroxymethylene groups of these preservatives. The formaldehyde produced became a reactant in the Hantzsch reaction. The DDL formed was measured fluorometrically because fluorometry is considerably more sensitive than spectrophotometry. Sensitivity becomes critical for certain of these compounds because of the low concentrations used in many cosmetic products.

Experimental

Apparatus

A fluorescence spectrophotometer,* xenon lamp, xenon power supply 150, were used. Optimal excitation was 410 nm and emission 510 nm. Slit widths were set at 10 nm.

Reagents

The preservatives were Bronopol (mp 128–132°C), hydroxymethyldimethylhydantoin (mp 97–100°C) and Germall 115 (decomposed above 160°C). Stock solutions containing 0.05–2.0 mg of preservative per ml in 10% methanol were prepared as required. Solvents were ACS or equivalent grade.

A 2*M* aqueous ammonium acetate buffer solution was prepared daily, the pH was adjusted to 6.00 with glacial acetic acid, and the buffer was then made 0.02*M* in acetylacetone (2,4-pentanedione,† purified by distillation, and the fraction boiling at 134–137°C collected; product should be clear, colorless, and nonfluorescing before use). To prepare 100 ml of the buffer solution, the required amounts are 15.4 g of ammonium acetate, 0.30 ml of acetic acid, and 0.20 ml of acetylacetone. Formaldehyde standard solutions were prepared daily from 36.8% certified ACS formaldehyde‡ in 10% methanol (0.1 to 0.8 μg of formaldehyde per ml).

Preparation of Sample

Approximately 100 mg of clear sample containing from 0.02 to 1.0 mg of preservative was accurately weighed, transferred to a volumetric flask with 10% methanol, and diluted to volume with 10% methanol. Further dilutions

*Perkin-Elmer Corp., Norwalk, Conn., Model MPF-3.
†Analabs Inc., North Haven, Conn.
‡Fisher Scientific Co., Pittsburgh, Pa.

were made, if necessary, to bring the expected formaldehyde concentration within the range of the formaldehyde standards.

Approximately 1 g of opaque sample containing from 0.05 to 10.0 mg of preservative was accurately weighed, transferred with a minimum of water to a separatory funnel, acidified with a few drops of concentrated HCl, and extracted with two 30-ml portions of $CHCl_3$. (The volume of water used varied with the amount of preservative present in the sample.) The $CHCl_3$ extract was discarded. The aqueous phase was made 10% in methanol, transferred to a volumetric flask, and diluted to volume with 10% methanol. Further dilution was made, if necessary, so that the expected formaldehyde concentration approximated that of the standards.

The samples were scanned for fluorescence at 510 nm (see below). If none was detected, reaction mixtures were prepared, and fluorescence was determined as described below.

Formation of DDL from Standards and Samples

To freshly prepared acetylacetone reagent was added an equal volume of sample or standard solution. A total volume of 4 ml was found convenient. The reaction mixture was maintained at 60°C for 1 hour, then cooled, and the fluorescence was determined.

Determination of Fluorescence

Fluorescence spectra were recorded from 420 nm to approximately 700 nm. A sample sensitivity setting was selected which kept intensities on scale and, in the case of the standard solutions, covered the range of the scale. The intensity of the unknowns was determined at the same sample sensitivity setting. If readings for the unknowns did not fall well within the range of the standards, the reactions with unknowns and standards were repeated to conform to this requirement.

Calculations

Fluorescence intensities of formaldehyde standards at 510 nm were plotted against concentration on linear graph paper. From this plot, the amount per ml of formaldehyde in Germall 115 and hydroxymethylhydantoin unknowns was read. The concentration of these compounds was calculated by the following equation:

$$\text{g/ml}_{(x)} = \frac{\text{g/ml HCHO found} \times \text{MW}_{(x)}}{\text{MW HCHO}}$$

where x = Germall 115 or hydroxymethyldimethylhydantoin. Fluorescence spectra of standard reaction mixtures of Bronopol were obtained, the intensity

at 510 nm *vs.* concentration was plotted, and the concentrations of Bronopol unknowns were determined directly from this plot.

Results and Discussion

In preliminary experiments, varying amounts of Bronopol were mixed with a shampoo base and diluted with 10% methanol; 2 ml of each solution was added to an equal volume of the acetylacetone-ammonium acetate reagent. The reaction mixtures, including formaldehyde standards, were heated at 37°C for 1 hour. They were cooled and their fluorescences were measured. Representative data are presented in Table I. Formaldehyde derived from Bronopol was determined from the calibration curve of the known formaldehyde reaction mixtures. The concentration of preservative added to the reaction mixture and the per cent determined given in this and subsequent tables were calculated assuming molar stoichiometry, although two of the compounds (Bronopol and Germall 115) have two methylol functional groups. Examination of the data given in Table I shows that the amount of formaldehyde derived from Bronopol at 37°C is relatively low and variable. The

Table I
The Dependence of the Concentration of 3,5-Diacetyl-1,4-dihydrolutidine Formed from Two Methylol-containing Compounds on Reaction Temperature and pH of Cosmetic

Preservative	Reaction Temperature (C°)	Preservative Added to Cosmetic[a] (mg)	Cosmetic (1 g sample)	Preservative Determined (%)
Bronopol	37	9.54	Shampoo	70
Bronopol	37	9.54	Shampoo	47
Bronopol	37	0.954	Shampoo	84
Bronopol	60	9.54	0	114
Bronopol	60	9.54	Shampoo	109
Bronopol	60	0.954	Shampoo	114
Bronopol	60	9.54	Basic shampoo	115[b]
Bronopol	60	9.54	Basic bath oil	120[c]
Hydroxymethyl-dimethylhydantoin	37	10.0	Vanishing cream	94
Hydroxymethyl-dimethylhydantoin	37	1.00	Vanishing cream	102
Hydroxymethyl-dimethylhydantoin	37	0.100	Vanishing cream	100

[a] These solutions were diluted before performing the reaction so that the magnitude of their fluorescence peaks would be similar to those of the formaldehyde standards.

[b] A shampoo containing Bronopol was made basic, allowed to stand for one hour; pH was then adjusted to approximately 7.

[c] A bath oil containing Bronopol was made basic and allowed to stand overnight; pH was then adjusted to approximately 7.

Hantzsch reaction with Bronopol was repeated with different reaction temperatures and pH's of the cosmetic. Reference to Table I shows that at 60°C the yield of formaldehyde from Bronopol is greater and less variable than at 37°C. The pH of the cosmetic had little effect on the amount determined. The pH of the reaction was not varied because the pH chosen is optimal for the determination of formaldehyde.

Included in Table I are data which show that hydroxymethyldimethylhydantoin can be determined reliably by the fluorometric method for formaldehyde if a reaction temperature of 37°C is used. However, since it was necessary to perform the reaction at a higher temperature to obtain better results with Bronopol, subsequent reactions with all three compounds were performed at 60°C. Some of the results of these determinations are shown in Table II. It is evident that Germall 115 and hydroxymethyldimethylhydantoin can be estimated in this manner. The results for Bronopol are different from those obtained earlier at 60°C (Table I). To overcome this daily variability, in the next series of experiments known solutions of Bronopol were included in the determinations and the amount of Bronopol found was based on a graph of standard solutions of Bronopol rather than on that of formaldehyde.

The final series of experiments, the results of which are reported in Tables III and IV, were blind studies, that is, solutions of these compounds were prepared by a colleague and their concentrations were unknown to the present authors.

Table II
3,5-Diacetyl-1,4-dihydrolutidine Derived from Three Methylol-containing Compounds Held at Reaction Temperature 60°C, pH 6, for 1 Hour

Preservative	Cosmetic (1 g sample)	Preservative Added to Cosmetic[a] (mg)	Preservative Added to Reaction (μg/ml) (HCHO equivalent)	Found (μg/ml) (HCHO equivalent)	Preservative Determined (%)
Germall 115	Bath oil	0.634	0.186	0.20	108
Germall 115	Bath oil	0.634	0.186	0.20	108
Germall 115	Shampoo	0.634	0.186	0.20	108
Hydroxymethyl-dimethylhydantoin	Bath oil	0.602	0.427	0.400	94
Hydroxymethyl-dimethylhydantoin	Bath oil	0.602	0.427	0.420	98
Hydroxymethyl-dimethylhydantoin	Shampoo	0.602	0.427	0.400	94
Bronopol	Bath oil	0.584	0.320	0.20	63
Bronopol	Bath oil	0.584	0.320	0.250	78
Bronopol	Shampoo	0.584	0.320	0.220	70

[a] These solutions were diluted before performing the reaction so that the magnitude of the fluorescence peaks would be similar to those of the HCHO standards.

Table III
Fluorometric Determination of 3 Methylol-containing Compounds in Shampoo Utilizing the Hantzsch Reaction at 60°C, pH 6, for 1 Hour

Preservative	Known Concentration (mg/ml)	Concentration Determined (mg/ml)	% Found[a]	% of Theoretical (Average)[b]
Germall 115	1.0	1.0	100	
Germall 115	0.50	0.52	104	
Germall 115	0.10	0.10	100[e]	51
Hydroxymethyl-dimethylhydantoin	0.15	0.14	93	
Hydroxymethyl-dimethylhydantoin	0.020	0.020	100[d]	96.5
Bronopol	0.15	0.12, 0.17	97[e]	
Bronopol	0.080	0.070	99	
Bronopol	0.020	0.020	100	28

[a] Calculations based on 1:1 molar stoichiometry (1 mole methylol-containing compound yields 1 mole formaldehyde).
[b] Values are averages of those given in the previous column adjusted for the stoichiometry observed.
[c] Interference extracted.
[d] Interference diluted.
[e] Average of two determinations.

During the course of the study, reported in Table III, a number of observations were made which are pertinent to the fluorometric determination of these preservatives in cosmetics. The unknowns were prepared for assay by adding three 1-ml portions of the solution of the unknown to 100 mg of a shampoo base and diluting to 5, 10, or 100 ml with 10% methanol. The reaction mixtures were made from these dilutions. It was found that Raman scattering interfered with the emission intensity of the most concentrated solution by shifting its baseline. The other dilutions gave acceptable baselines which were corrected for relatively minor shifts before determination of peak heights. This initial step gave a rough estimate of the amount of preservative in the unknowns so that it was possible to prepare a solution giving a fluorescence intensity which fell well within the limits of the formaldehyde calibration curve. This was necessary because if the peak happened to occur near the origin of the calibration curve, imprecise results were obtained. Similarly, on occasion, the determination was inadequate if the intensity maximum appeared on the upper portion of the standard curve. These discrepancies can be understood by examining Fig. 3, which shows the daily variation of the fluorescence intensity of DDL as a function of the concentration of formaldehyde in the reaction mixture. The data presented in this figure are typical of many such standard curves and were obtained using an acetylacetone-ammonium acetate reagent ranging in age from 0 to 7 days. They do not differ es-

Table IV
Fluorometric Determination of 3 Methylol-containing Compounds in Shampoo and Skin Cream Utilizing the Hantzsch Reaction at 60°C, pH 6, for 1 Hour

Preservative	Cosmetic	Known Concentration (mg/ml)	Concentration Determined (mg/ml)	Per Cent Determined
Germall 115	Shampoo	1.0	1.1	110
Germall 115	Shampoo	0.10	0.11	110
Germall 115	Shampoo	0.050	0.052	104
Germall 115	Skin cream	1.0	1.1	110
Germall 115	Skin cream	0.10	0.11	110
Germall 115	Skin cream	0.050	0.052	104
Hydroxymethyl-dimethylhydantoin	Shampoo	1.0	1.0	100
Hydroxymethyl-dimethylhydantoin	Shampoo	0.10	0.090	90
Hydroxymethyl-dimethylhydantoin	Shampoo	0.052	0.050	96
Hydroxymethyl-dimethylhydantoin	Skin cream	1.0	0.93	93
Hydroxymethyl-dimethylhydantoin	Skin cream	0.10	0.094	92
Hydroxymethyl-dimethylhydantoin	Skin cream	0.052	0.050	96
Bronopol	Shampoo	1.1	1.2, 0.92	100
Bronopol	Shampoo	0.11	0.11, 0.11	100
Bronopol	Shampoo	0.053	0.063, 0.051 0.044	102
Bronopol	Skin cream	1.1	0.90	82
Bronopol	Skin cream	0.11	0.091	83
Bronopol	Skin cream	0.053	0.055	104

sentially from those reported by Belman (2). It is to be noted, however, that a variable background fluorescence is contributed from the reagent itself, and occasionally a downward deviation from linearity is observed at 0.4 mg/ml formaldehyde. Thus, dilutions of the sample were made which gave an intensity reading on the linear portion of the standard curve if the initial concentration of the unknown permitted such a manipulation. If the initial concentration was sufficiently low so that it was necessary to determine its fluorescence intensity near the origin, the problem could be solved by extraction from the shampoo of the ingredients causing the Raman scattering and by use of freshly prepared reagent, which gave a consistent and lower background fluorescence (Fig. 4). In this study, the per cent of the true value determined ranged from 93 to 104 for the three compounds (Column 4, Table III). In the last column of Table III, the average per cent of the theoretical yield of formaldehyde derived from these compounds is given. One of the two hydroxy-

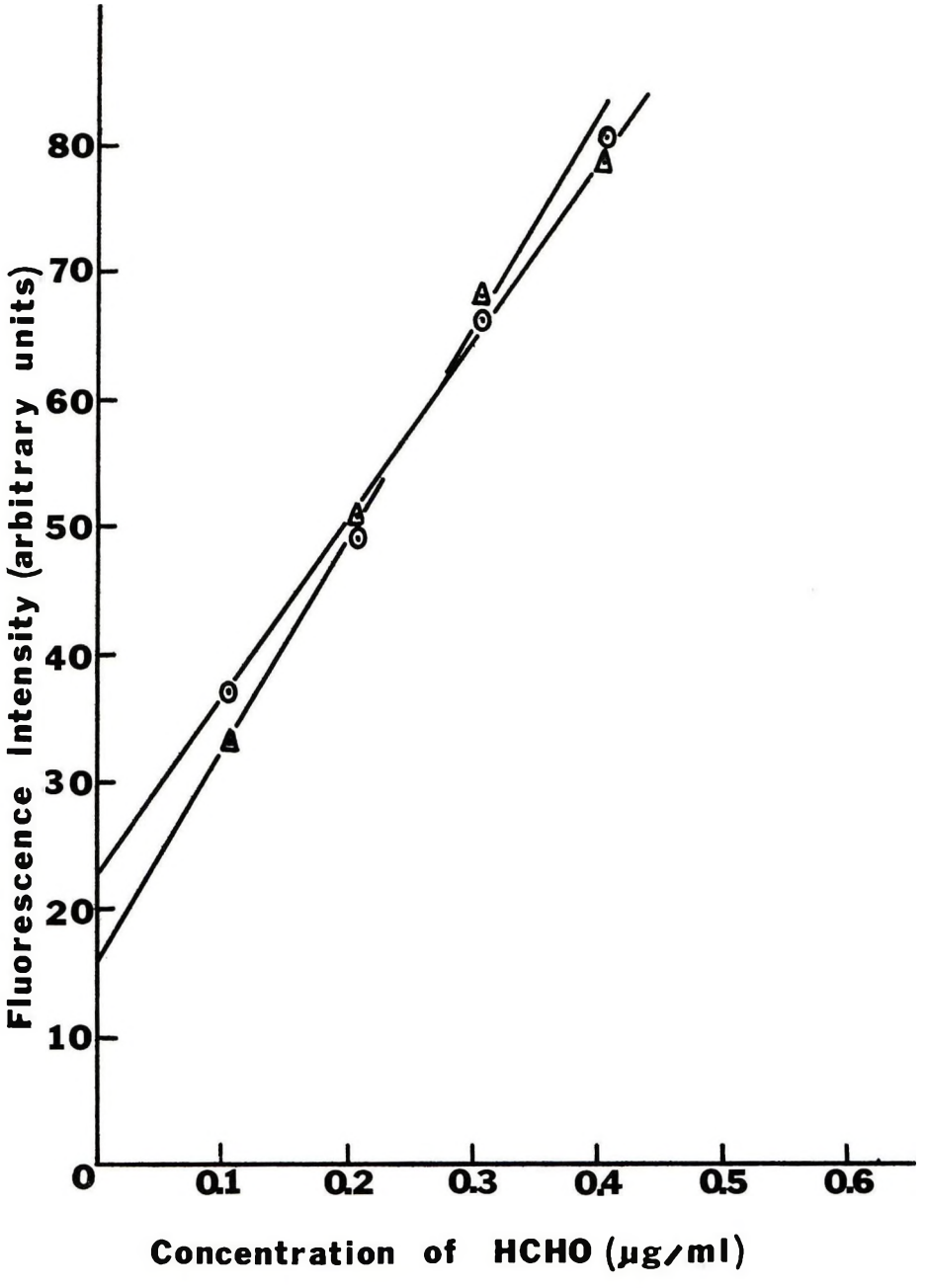

Figure 3. Day-to-day variation of fluorescence intensity of DDL as a function of formaldehyde concentration
Δ = day x; $\bullet$ = day y

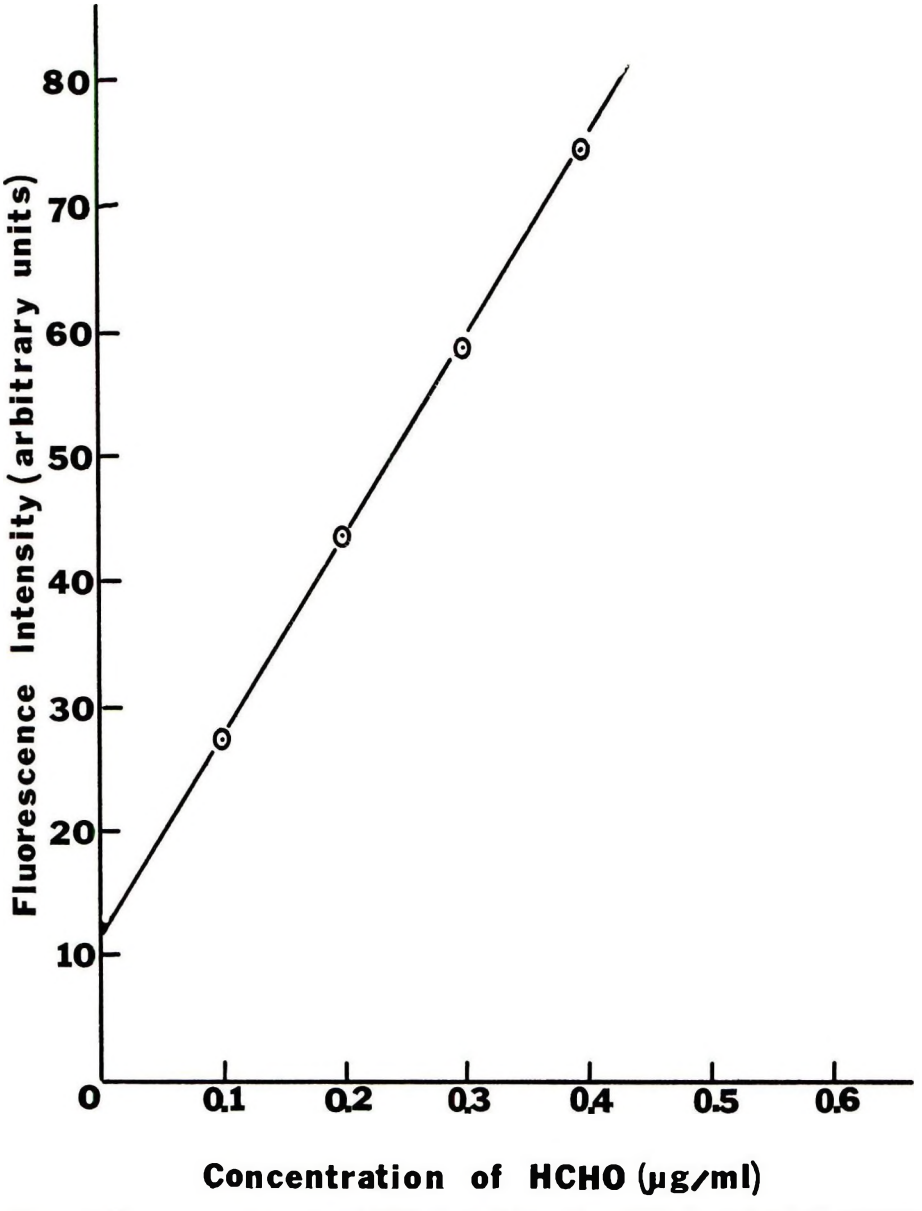

Figure 4. Fluorescence intensity of DDL derived from formaldehyde, using fresh reagent

methylene groups of Germall was oxidized to formaldehyde, the one methylol group of hydroxymethyldimethylhydantoin was converted to formaldehyde, and at 60°C, Bronopol yielded slightly more than a quarter of a mole of its potential formaldehyde.

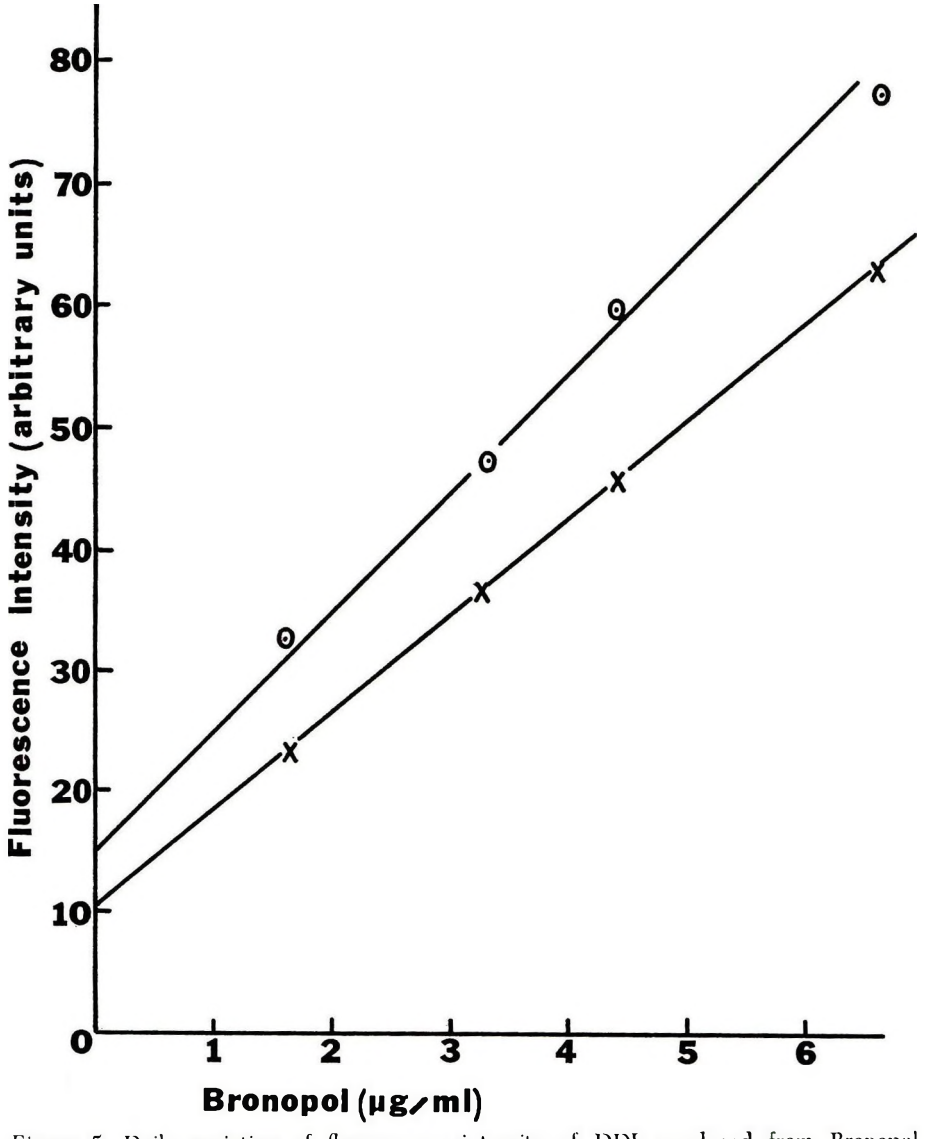

Figure 5. Daily variation of fluorescence intensity of DDL produced from Bronopol

In the final blind study, reported in Table IV, a protocol similar to that given above was followed. In this experiment, however, the unknowns were mixed with a skin cream base in addition to a shampoo base. The cream, with added preservative, was extracted with $CHCl_3$ from an acid aqueous dispersion to remove ingredients that would otherwise have led to turbidity in the reaction mixtures. The results were essentially the same as those found previously at a reaction temperature of 60°C. With regard to the data for Brono-

Table V

Statistical Analysis of Data Obtained from the Fluorometric Determination of Bronopol, Germall 115, and Hydroxymethyldimethylhydantoin in Cosmetics

Compound	Mean Per Cent Determined	Average Relative Error	Mean ± Standard Deviation[a] (mg/ml)
Bronopol	96.2[b]	+3.9[b]	1.10 ± 0.18
Bronopol			0.11 ± 0.011
Bronopol			0.052 ± 0.0095
Germall 115	106.0[c]	−6.4[c]	1.0 ± 0.044
Germall 115			0.10 ± 0.0044
Germall 115			0.161 ± 0.0160
Germall 115			0.050 ± 0.0024
Hydroxymethyl-dimethylhydantoin	96.5[d]	+4.0[d]	1.0 ± 0.048
Hydroxymethyl-dimethylhydantoin			0.15 ± 0.0092
Hydroxymethyl-dimethylhydantoin			0.10 ± 0.005

[a] Standard deviations of the means were calculated from 3 replicate determinations.
[b] Average of 14 determinations ranging in concentration from 1.10 to 0.0200 mg/ml.
[c] Average of 12 determinations ranging in concentration from 1.00 to 0.0500 mg/ml.
[d] Average of 14 determinations ranging in concentration from 1.00 to 0.0200 mg/ml.

pol, it must be pointed out that it was frequently necessary to replicate the determination in order to obtain accurate results (Tables III and IV). This may be due to the marked dependence of the release of formaldehyde from Bronopol on the temperature of the reaction. Figure 5 shows two Bronopol calibration curves determined on separate days. They are clearly different and it is conceivable that the variability resulted from less than ideal thermal control. Table V presents a statistical analysis of the results of the fluorometric determination of these hydroxymethylene-containing preservatives. It can be concluded from an examination of these analyses that Germall 115 and hydroxymethyldimethylhydantoin in cosmetics can be determined by the fluorometric method for formaldehyde at a reaction temperature of 60°C. Bronopol can be determined reliably in this fashion if the samples are replicated.

(Received June 28, 1974)

References

(1) Parker, M. S., Some aspects of the use of preservatives in combination, *Soap Perfum. Cosmet.*, **46**, 223–4 (1973).
(2) Belman, S., The fluorometric determination of formaldehyde, *Anal. Chim. Acta*, **29**, 120–6 (1963).
(3) Nash, T., Estimation of formaldehyde, *Biochem. J.*, **55**, 416–21 (1953).
(4) Wilson, C. H., Fluorometric determination of formaldehyde in cosmetic products, *J. Soc. Cosmet. Chem.*, **25**, 67–71 (1974).

J. Soc. Cosmet. Chem., **25**, 667–680 (December 1974)

Photostabilität und Hautaffinität - zwei Kriterien für kosmetische Lichtschutzsubstanzen am Beispiel der Naphthalin-1,5-bis-harnstoffe

UDO HOPPE*

Nach einem Vortrag vor der Société Française de Cosmétologie, gehalten in Paris am 20. 6. 1973

Synopsis—Photostability and skin affinity — two criteria for cosmetic light protective substances, e.g. naphthalene-1,5-bisureas. — The assessment of ULTRAVIOLET LIGHT ABSORBERS for SUNSCREENING PRODUCTS includes not only practical utility and absence of toxicity, both of which play an important role, but the equally important aspects of PHOTOSTABILITY and SKIN AFFINITY. With the aid of a simple illuminator it is shown that — with or without the addition of DIHYDROXYACETONE AS A PHOTOSENSITIZER — some light protective substances in hydroalcoholic solution show varying photostability. NEW NAPHTHALENE-1,5-BISUREAS are described which are stable and, depending on their substitution, can be used as UV-B OR UV-A ABSORBERS. Rinse tests have shown that these compounds adhere well to PIGSKIN. Furthermore, they exhibit the remarkable and unusual PROPERTY OF FORMING GELS in hydrophobic solvents.

Bei der Beurteilung von Ultraviolett-(UV-)absorbern für Lichtschutzmittel spielen neben Atoxizität, (UV-)Absorptionsspektrum und technologischer Anwendungsmöglichkeit Photostabilität und Hautaffinität der Verbindungen eine bedeutende Rolle. Um Photoreaktionen an Lichtschutzsubstanzen untersuchen zu können, ist die Wahl einer möglichst sonnenähnlichen Strahlenquelle Voraussetzung. Aus angegebenen Einzelwerten von P. Bener (1) wurde der Verlauf des Photonenstroms errechnet. Er ist in *Abb. 1* dargestellt. Der Ort Biel ist für eine vergleichende Betrachtung sehr günstig, weil es wahrscheinlich ist, im Flachland und im Mittelgebirge ähnliche UV-Intensitäten anzutreffen. Von R. E. Barker wurde der Photonenstrom, der unterhalb von 290 nm auf die Erde einfällt, mit 10^{16} Photonen/cm^2 · Monat ermittelt (2). Aus diesen Gründen wurde ein Laboratoriums-Hg-Hochdruckstrahler für die im folgen-

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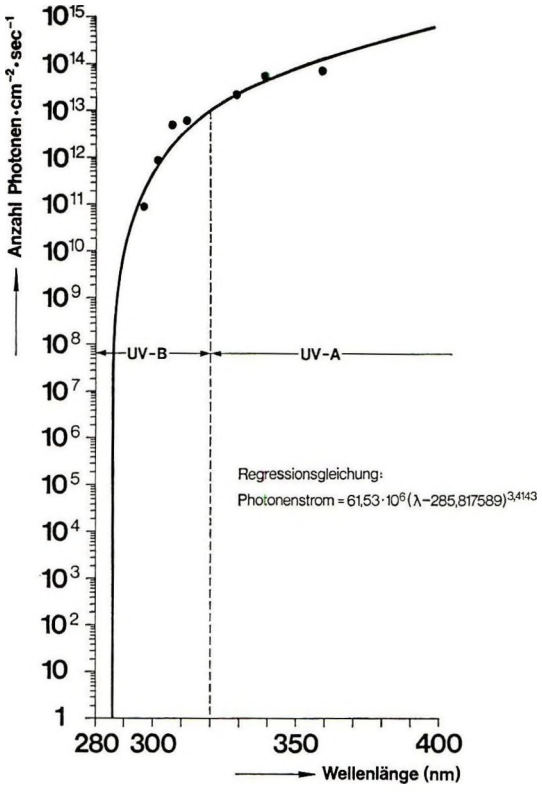


Abbildung 1

Verteilung der Sonnenlichtintensität. Photonenstrom, gemessen in Biel/Schweiz (47°10′ n. B., 7°15′ ö. L.) 316 m über NN, 62—63° Sonnenhöhe, Luftmasse 1,08 (Juli 1967)

den beschriebenen Belichtungsversuche eingesetzt. Die Energieverteilung dieser Tauchlampe zeigt *Abb. 2*. Man erkennt, daß durch den ca. 1 mm starken Mantel aus Borosilikatglas keine meßbare UV-Strahlung unterhalb von 292 nm in die Lösung eintritt. Die Apparatur muß dauernd mit Wasser gekühlt werden.

Belichtungsversuche

Bei der gewählten Versuchsanordnung *(Abb. 3, Tabelle 1)* stellte sich in dem zu 90% gefüllten 2-l-Kolben eine Reaktionstemperatur von 35° C ein, die sehr gut der menschlichen Hauttemperatur entspricht. Mit Hilfe eines Magnetrührers wurde dauernd konstant gerührt. Reaktionsmedium und Tauchrohr wurden mit Stickstoff gespült.

Nach Beobachtungen von A. Kornhauser et al. (4) sensibilisiert Dihydroxyaceton (DHA) die Photodimerisierung von Thymin. Daher wurde vor

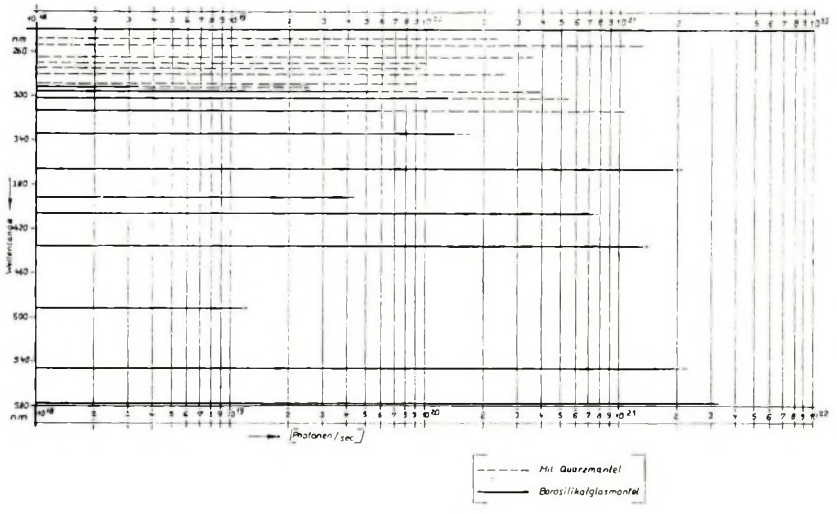


Abbildung 2

Energieverteilung eines Laboratoriums-Hg-Hochdruckstrahlers, nach Herstellerangaben berechnet (3)

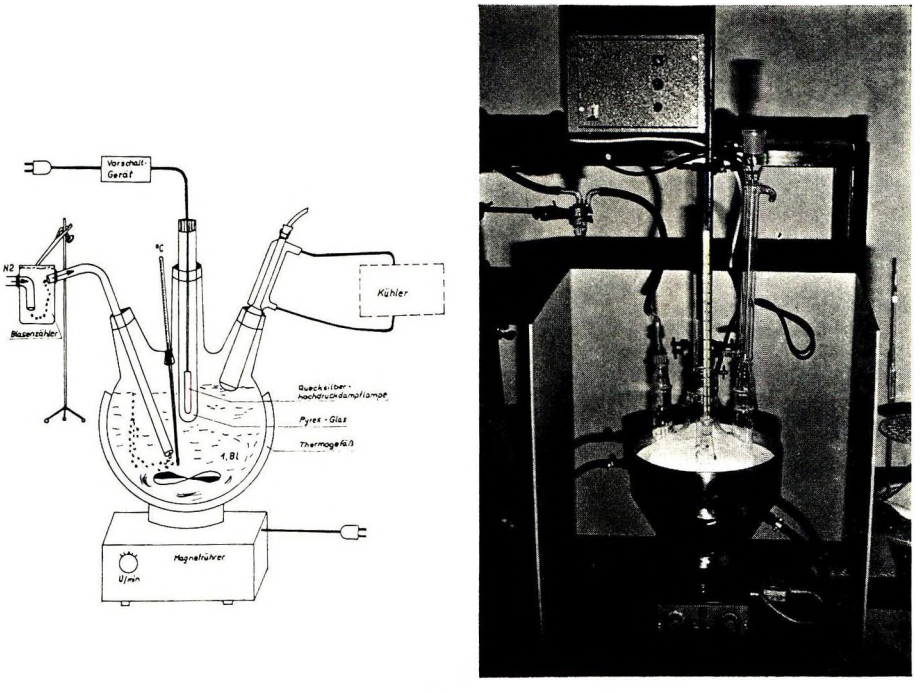


Abbildung 3

Laboratoriumsapparatur zur Messung der Photostabilität organischer Substanzen

Wellenlänge nm	Extinktion E	Durchlässigkeit D (%)
280	2,00	1,00
285	1,48	3,31
290	1,04	9,12
295	0,72	19,05
300	0,50	31,62
305	0,35	44,67
310	0,25	56,23
315	0,17	67,61
320	0,12	75,86
325	0,08	83,18
330	0,06	87,10
335	0,045	90,16
340	0,035	92,26

Tabelle 1

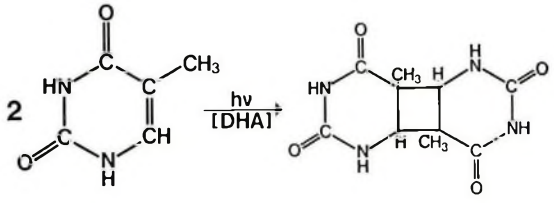
Extinktion E und Durchlässigkeit D von 1 mm dickem Borosilikatglas im UV-Bereich

Belichtung in einer zweiten Versuchsreihe DHA zu der Lichtschutzsubstanz in äquimolekularen Mengen gegeben.

DHA ist oft Bestandteil hautbräunender Kosmetika (auch in Kombination mit Lichtschutzsubstanzen); physiologisch tritt es als ein Glykoseprodukt nach dem Embden-Meyerhof-Abbau auf. Im Absorptionsmaximum (274 nm in Äthanol) ergibt sich der molare Extinktionskoeffizient zu 15 ($n \rightarrow \pi^*$-Übergang). Die Halbwertsbreite der Absorptionsbande beträgt $\Delta\upsilon\,\frac{1}{2} = 6555$ [cm^{-1}]. Aus dieser sehr geringen Übergangswahrscheinlichkeit läßt sich eine Oszillatorstärke von $f = 4{,}2 \cdot 10^{-4}$ errechnen; bei den hier untersuchten Lichtschutzsubstanzen liegt der entsprechende Wert bei $f \sim 5 \cdot 10^{-1}$. Da die Absorptionsintensität ein Maß für die Zahl der Elementarprozesse pro Zeit ist, muß der Anregungszustand des DHA um den Faktor 10^3 länger dauern als der der Lichtschutzsubstanzen. Belichtet man nach dem beschriebenen Verfahren eine $2 \cdot 10^{-3}$ molare Lösung von Thymin in Wasser über 24 Stdn. bei 35° C, so zeigt sich praktisch keine Veränderung am UV-Spektrum; die Spektren wurden jeweils in einer Verdünnung von $5 \cdot 10^{-5}$ Mol vermessen.

Ein Zusatz von $2 \cdot 10^{-3}$ Mol DHA bewirkt jedoch bei gleichen Bedingungen einen Abfall der Absorption von 100 auf 19,5 %, was durch Dimerisierung des Thymins zwanglos erklärt werden kann. A. Kornhauser und M. A. Pathak nehmen für diesen Reaktionstyp einen Energieübertragungsmechanismus nach

G. O. Schenck an; die Triplettenergie des Thymins liegt bei 70, die des DHA bei 76 Kcal · mol^{-1} (4). Thymindimere, die 1960 von R. Beukers und W. Berends entdeckt wurden (5), beobachtete man vor kurzer Zeit auch in vivo in der Desoxyribonucleinsäure von Meerschweinchenhaut bei Belichtung mit 290 bis 320 nm (6).



In wäßriger Lösung wurde gleichfalls das System Urocaninsäure/DHA untersucht *(Abb. 4)*. Die 1953 von A. Zeníšek und J. A. Král im menschlichen Schweiß als natürliche Lichtschutzsubstanz entdeckte Säure (7) weist in der *cis*- und in der *trans*-Form sehr ähnliche Extinktionskoeffizienten auf (8) (9). Bei der Belichtung mit und ohne Zusatz von DHA ergab sich ein Abfall der Extinktion von 100 auf ca. 74 %. Es sei diskutiert, daß auch hier eine Dimerenbildung, wie sie J. H. Anglin et al. beschrieben haben, einsetzt (10) (11). Die Lage der *trans-cis*-Umlagerung läßt sich durch die hypsochrome Verschiebung des Absorptionsmaximums zwanglos deuten (man beobachtet eine Verschiebung von 283 auf 280 nm in Methanol). Als wasserlösliche Lichtschutzsubstanzen haben die Salze der p-Methoxyzimtsäure zunehmend Bedeutung erlangt.

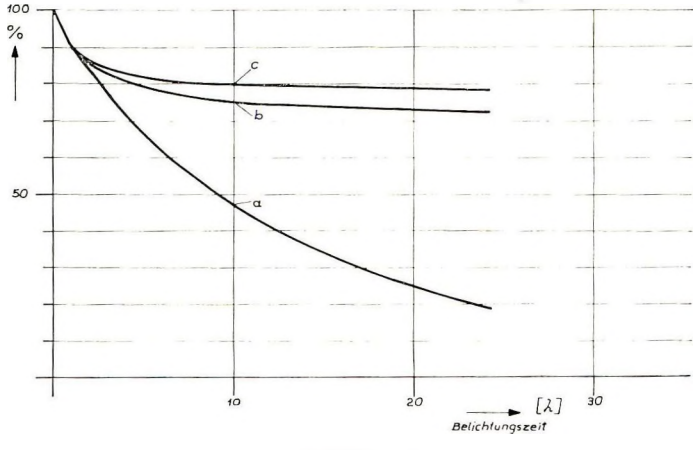


Abbildung 4

Photostabilität in wäßriger Lösung.
a . . . Thymin, b . . . Urocaninsäure, c . . . Methoxyzimtsäure

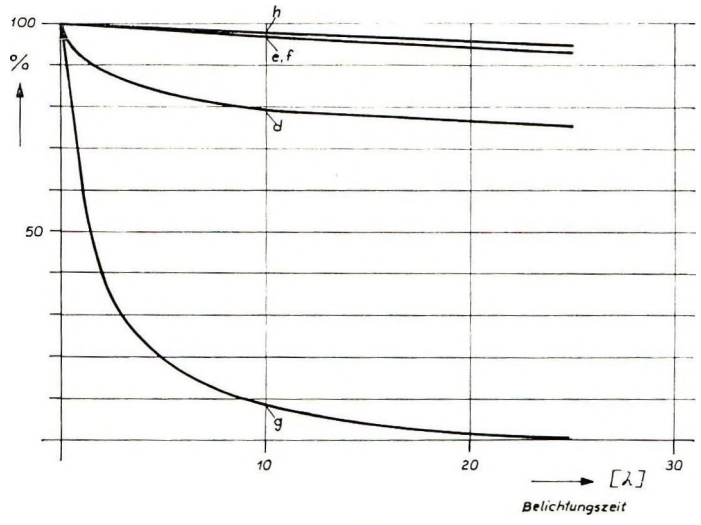


Abbildung 5

Photostabilität in wäßrig-äthanolischer Lösung
d ... p-Methoxyzimtsäureäthylester, e ... Benzylidencampher, f ... p-Methylbenzylidencampher, g ... 5-(3,3-Dimethyl-2-norbornyliden)-3-penten-2-on h ... N,N'-1,5-Naphthylen-N", N"'-p,p'-bis-(phenylencarbo-2-octyldodecyl-1-oxy-harnstoff)

Die Photodimerisierung der Zimtsäuren zu den Truxill- und zu den Truxinsäuren ist seit langer Zeit bekannt (12 (13). Diese Reaktion gelang nach A. Mustafa auch mit Sonnenlicht (14). Bei der Belichtung in wäßriger Lösung wurde mit und ohne Zusatz von DHA lediglich ein Extinktionsabfall von 100 auf 79% beobachtet. Ähnlich verhält sich auch der Äthylester der p-Methoxyzimtsäure, der als Modellsubstanz für die verschiedenen, im Handel befindliche p-Methoxyzimtsäureester untersucht wurde *(Abb. 5)*. Diese Verbindung wurde durch Claisen-Kondensation aus Anisaldehyd und Essigsäureäthylester synthetisiert und anschließend dreimal durch Tieftemperaturumkristallisation gereinigt; es ergab sich gas-chromatographisch eine Reinheit von über 99,6%. Als Lösungsmittel bei der Belichtung diente ein Gemisch aus Wasser-Äthanol (4:3). Auch hier ist kein signifikanter Einfluß des DHA auf den Extinktionsverlust von je 23% zu registrieren *(Abb. 5)* gewesen. Als photochemisch sehr stabil erweisen sich im gleichen Lösungsmittelgemisch die bicyclischen Lichtschutzsubstanzen Benzylidencampher und p-Methyl-benzylidencampher.

Ganz anders verhält sich bei der Belichtung das 5-(3,3-Dimethyl-2-norbornyliden)-3-penten-2-on in einem Gemisch aus Wasser:Äthanol (1:1 Volumteile). Mit und ohne DHA-Zusatz ist nach 24stündiger Belichtung kein Ausgangsprodukt mehr vorhanden; gas-chromatographisch konnten hauptsächlich vier Photoprodukte nachgewiesen werden.

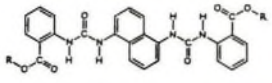
 o,o	ber. Länge (Å)	Fp (°C)	Analyse	
			theor.	gef.
R-				
2-Äthyl-n-hexyl-	35,7	280	%C: 71,16 %H: 7,39 %N: 7,90	71,38 7,28 7,99
2-n-Butyl-n-octyl-	40,5	290	%C: 73,14 %H: 8,35 %N: 6,32	73,06 8,59 6,99
2-n-Pentyl-n-nonyl-	43,0	240	%C: 73,94 %H: 8,73 %N: 6,39	74,47 8,70 6,38
2-n-Hexyl-n-decyl-	45,2	270 (Z)	%C: 74,64 %H: 9,07 %N: 6,00	74,61 9,20 5,96
2-n-Heptyl-n-undecyl-	48,0	198	%C: 75,26 %H: 9,38 %N: 5,66	75,16 9,38 5,90
2-n-Octyl-n-dodecyl-	50,0	192	%C: 75,83 %H: 9,64 %N: 5,36	75,14 9,85 5,50
2-n-Decyl-n-tetradecyl-	55,0	180	%C: 76,77 %H: 10,10 %N: 4,84	76,54 10,26 5,04
2-n-Dodecyl-n-hexadecyl-	60,0	180	%C: 77,55 %H: 10,48 %N: 4,41	77,62 10,48 4,51

Tabelle 2
o,o'-Phenylen-1,5-naphthylen-bis-harnstoffe

Da vor kurzem Naphthyl- (15) und andere Arylharnstoffe (16) als photostabile und gelbildende Lichtschutzsubstanzen beschrieben werden konnten, wurde versucht, durch Verlängerung des Moleküls diese Eigenschaften weiter zu untersuchen. In *Tabelle 2* sind die N,N'-1,5-Naphthylen-N", N"'-o,o'-bis-(phenylencarbalkoxy-harnstoffe) aufgeführt, die aus den o-Aminobenzoesäureestern in Chlorbenzol mit 1,5-Naphthalindiisocyanat gewonnen wurden. Ab einer bestimmten Kettenlänge bilden diese Harnstoffe in Mineralölen und anderen organischen Lösungsmitteln feste, isotope (transparente) Gele *(Tabelle 3)*. Die Metaderivate verhalten sich analog. In den Tabellen 2, 3 und 4 sind auch die aus Stereomodellen berechneten Längen der Moleküle angegeben. Während die Naphthylharnstoffe eine Gestalt ähnlich einfachen Klammern haben (15), handelt es sich bei den Naphthylen-bis-harnstoffen um eine Art Doppelklammern *(Tabelle 4)*.

Von den p-bis-Harnstoffen liegen bereits toxikologische Daten vor: $LD_{50} > 5000$ (mg/kg, per os); Draize- und Patch-Test sind negativ, keine Unverträglichkeitsreaktionen.

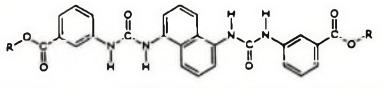
 m,m	ber. Länge [Å]	Fp [°C]	Analyse theor.	Analyse gef.
R-				
2-Äthyl-n-hexyl-	40,3	265 (Z)	%C: 71,16 %H: 7,39 %N: 7,90	71,38 7,44 7,71
2-n-Butyl-n-octyl-	45,0	275 (Z)	%C: 73,14 %H: 8,35 %N: 6,82	73,27 8,21 6,91
2-n-Pentyl-n-nonyl-	47,4	285 (Z)	%C: 73,94 %H: 8,73 %N: 6,39	73,54 9,11 6,54
2-n-Hexyl-n-decyl-	49,6	270 (Z)	%C: 74,64 %H: 9,07 %N: 6,00	74,36 8,96 6,09
2-n-Heptyl-n-undecyl-	52,1	260	%C: 75,26 %H: 9,38 %N: 5,66	75,41 9,43 5,66
2-n-Octyl-n-dodecyl-	54,5	270	%C: 75,83 %H: 9,64 %N: 5,36	75,72 9,70 5,46
2-n-Decyl-n-tetradecyl-	59,3	265	%C: 76,77 %H: 10,10 %N: 4,84	76,82 10,20 4,88
2-n-Dodecyl-n-hexadecyl-	64,0	270	%C: 77,55 %H: 10,48 %N: 4,41	77,91 10,30 4,45

Tabelle 3
m,m′-Phenylen-1,5-naphthylen-bis-harnstoffe

Die UV-Spektren dieser drei Substanzklassen sind aus der *Abb. 6* ersichtlich. Das UV-B und großenteils das UV-A werden überdeckt. Die p-Phenylen-naphthylen-bis-harnstoffe weisen die höchsten Extinktionskoeffizienten auf; sie sind daher am besten geeignet, Sonnenbrand und Sonnenbräunung zu verlangsamen. Die Photostabilität des N,N′-1,5-Naphthylen-N″,N‴-p,p′-bis-(phenylen-carbo-2-octyldodecyl-1-oxy-harnstoffs) ist in *Abb. 5* wiedergegeben. Belichtet wurde in Äthanol mit und ohne DHA-Zusatz; keine Veränderungen am UV-Spektrum.

Hautaffinität

Zur Prüfung auf hautaffines Verhalten wurde eine früher beschriebene Spülapparatur benutzt (15). Als Substrat wurden lebendfrische Schweineohren verwendet, weil deren Präparation einfacher ist. Um die Menge der aufgetragenen Kosmetika festzulegen, wurde deren gewohnheitsmäßige Verteilung auf menschlicher Haut ermittelt. Die Häufigkeitsverteilung von Lichtschutzsalben ergab sich aus Einzelwerten von A. Wiskemann (17) zu 404 ± 60 mg/100 cm².

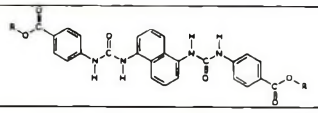
 p,p	ber. Länge (Å)	Fp (°C)	Analyse	
			theor.	gef.
R-				
2-Äthyl-n-hexyl-	40,6	290 (Z)	%C: 71,16 %H: 7,39 %N: 7,90	71,62 7,45 8,14
2-n-Butyl-n-octyl-	45,6	280 (Z)	%C: 73,14 %H: 8,35 %N: 6,82	73,56 8,26 6,81
2-n-Pentyl-n-nonyl-	48,0	285 (Z)	%C: 73,94 %H: 8,73 %N: 6,39	73,37 8,65 6,54
2-n-Hexyl-n-decyl-	50,1	260 (Z)	%C: 74,64 %H: 9,07 %N: 6,00	74,96 9,51 6,04
2-n-Heptyl-n-undecyl-	52,8	265 (Z)	%C: 75,26 %H: 9,38 %N: 5,66	75,69 9,38 5,95
2-n-Octyl-n-dodecyl-	55,1	280 (Z)	%C: 75,83 %H: 9,64 %N: 5,36	75,83 9,46 5,39
2-n-Decyl-n-tetradecyl-	60,0	245 (Z)	%C: 76,77 %H: 10,10 %N: 4,84	77,25 10,18 4,84
2-n-Dodecyl-n-hexadecyl-	64,8	235 (Z)	%C: 77,55 %H: 10,48 %N: 4,41	77,90 10,73 4,30

Tabelle 4
p,p′-Phenylen-1,5-naphthylen-bis-harnstoffe

In bedeutend geringeren Mengen werden Lichtschutzöle mit 75 ± 6 mg/100 cm² und flüssige Lichtschutzemulsionen mit 211 ± 14 mg/100 cm² aufgetragen, wie aus unveröffentlichten Einzelwerten (18) und nach eigenen Versuchen berechnet werden konnte.

Je nach Darreichungsform wurden auf die ca. 75 cm² großen Streifen aus Schweineohren 50 bis 300 mg Lichtschutzmittel aufgetragen und mit dem Finger verteilt. Nach einer Stunde Einwirkung wurden 2 Hautstreifen — zusammen mit einer gleichgroßen unbehandelten Haut — mit 180 L/h Wasser (25° C) gespült. Nach einer Abtropfzeit von 15 min wurden die Hautstreifen bei Raumtemperatur mit jeweils 250 ml Äthanol extrahiert. Nach 12 Stdn. Schütteln wurde durch Extinktionsmessungen gegen entsprechende Blindversuche die auf der Haut verbliebene Menge bestimmt.

In der *Abb. 8* ist die Affinität verschiedener Lichtschutzsubstanzen zu Schweinehaut dargestellt. Nach 6 Stdn. Spülzeit fanden sich bei einer O/W-Emulsion mit 3 Gew.-% N-1-Naphthyl-N′-p-phenylencarbo-2-octyldodecyloxy-harnstoff noch 70% und bei einer O/W-Emulsion mit 1 Gew.-% 1,5-

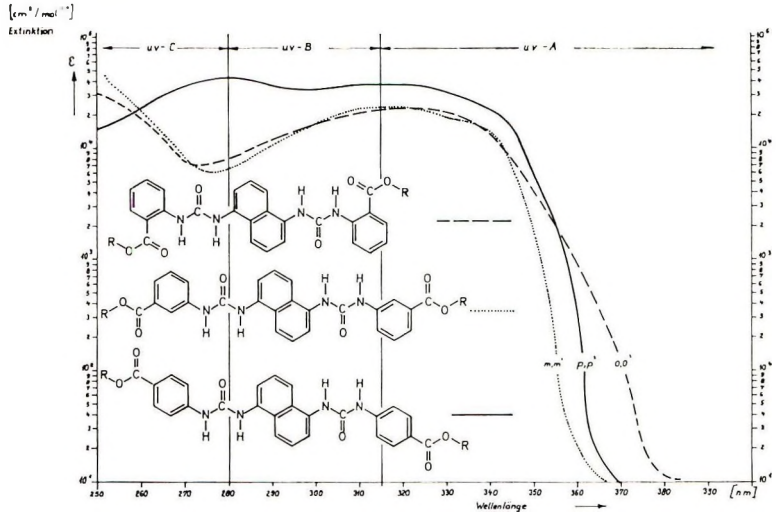


Abbildung 6

Absorptionsspektren der o,o'-, m,m'- und p,p'-Phenylen-1,5-naphthylen-bis-harnstoffe

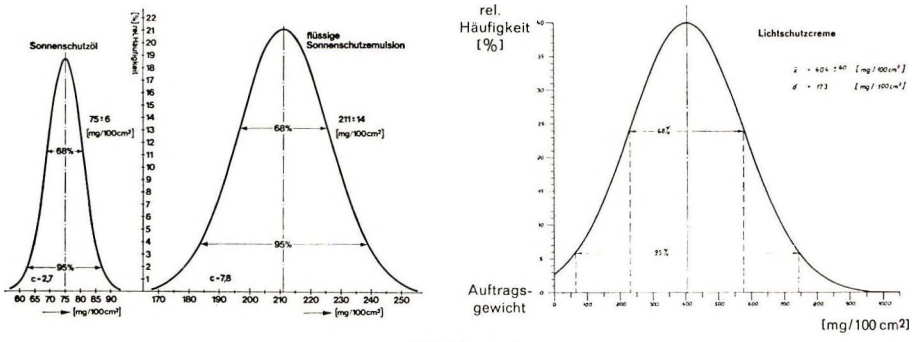


Abbildung 7

Häufigkeitsverteilung der Auftragsmenge eines Lichtschutzöles, einer flüssigen Lichtschutzemulsion („Milch") und einer Lichtschutzcreme, dargestellt mit unterschiedlichen Klassenbreiten — berechnet nach unveröffentlichten Einzelwerten von Wiskemann (18) und nach eigenen Versuchen.

Naphthylen-bis(N-p-phenylencarbo-2-octyldodecyloxy-harnstoff) noch 48% auf der Schweinehaut, während eine Lotion (Äthanol:Wasser:Glycerin, 50:30:20 Volumteile) mit 5 Gew.-% p-Aminobenzoesäure nach 5,6 min bis auf 4% abgespült war. Zur Herstellung vgl. (19).

Zur Prüfung des etwaigen Zusammenhangs der Hautaffinität der Mono- und der bis-Harnstoffe mit der Gelfestigkeit wurde die Gelpenetration bei 20° C in Paraffinöl gemessen *(Abb. 9)*.

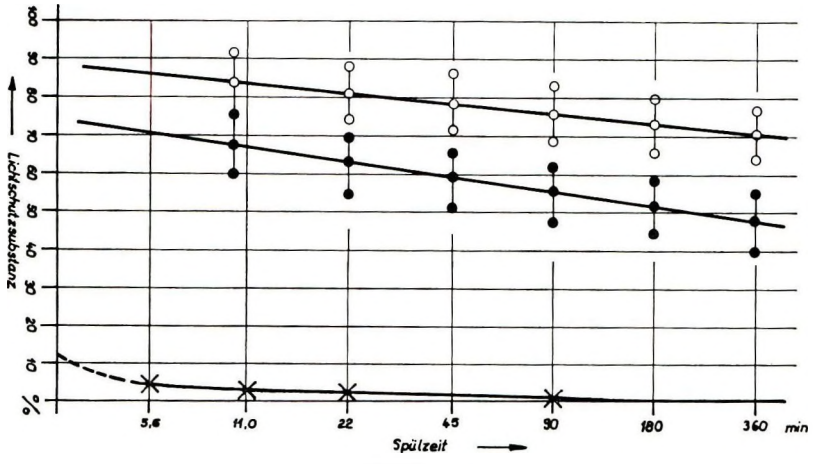


Abbildung 8

Affinität (Abklingkurven von Lichtschutzpräparaten) verschiedener Lichtschutzpräparate zu Schweinehaut

O/W-Emulsion mit 3 Gew.-% N-1-Naphthyl-N'-p-phenylencarbo-2-octyldodecyloxy-harnstoff

O/W-Emulsion mit 1 Gew.-% 1,5-Naphthylen-bis [N-p-phenylencarbo-2-octyldodecyloxy-harnstoff]

Lotion mit 5 Gew.-% p-Aminobenzoesäure in einer Lösung aus 50 Vol.-% Äthanol, 30 Vol.-% Wasser, 20 Vol.-% Glycerin

Die Gele wurden 24 Stdn. vor der Messung angesetzt. Es zeigte sich, daß der 35 g schwere Kegel des Penetrometers in das bis-Harnstoffgel tiefer eindringt als in das Mono-Harnstoffgel. Das heißt, daß die letztgenannten Gele eine größere Festigkeit aufweisen. Interessanterweise ergibt sich für den gemessenen Bereich eine lineare Abhängigkeit des Penetrometergrades vom Logarithmus der molaren Konzentration der Harnstoffe.

Das hautaffine Verhalten von Lichtschutzgelen bei den Spülbedingungen 180 L/h Wasser (25° C) scheint mit den Gelfestigkeiten parallel zu laufen. Von einem Paraffinölgel mit 3 Gew.-% N-1-Naphthyl-N'-p-phenylencarbo-2-octyldodecyloxy-harnstoff waren nach 6 Stdn. noch 55 % und von einem Paraffinöl-Gel mit 2 Gew.-% 1,5-Naphthyl-bis-(N-p-phenylencarbo-2-octyldodecyloxy-harnstoff) noch 37 % auf der Haut vorhanden *(Abb. 10)*. Die Untersuchungen über weitere dieser Harnstoff-Derivate sind noch nicht abgeschlossen.

Zusammenfassung

Bei der Beurteilung von Ultraviolettabsorbern für Lichtschutzmittel spielen neben Atoxizität und technologischer Anwendungsmöglichkeit Photostabilität und Hautaffinität der Substanzen eine bedeutende Rolle. Mit Hilfe einer ein-

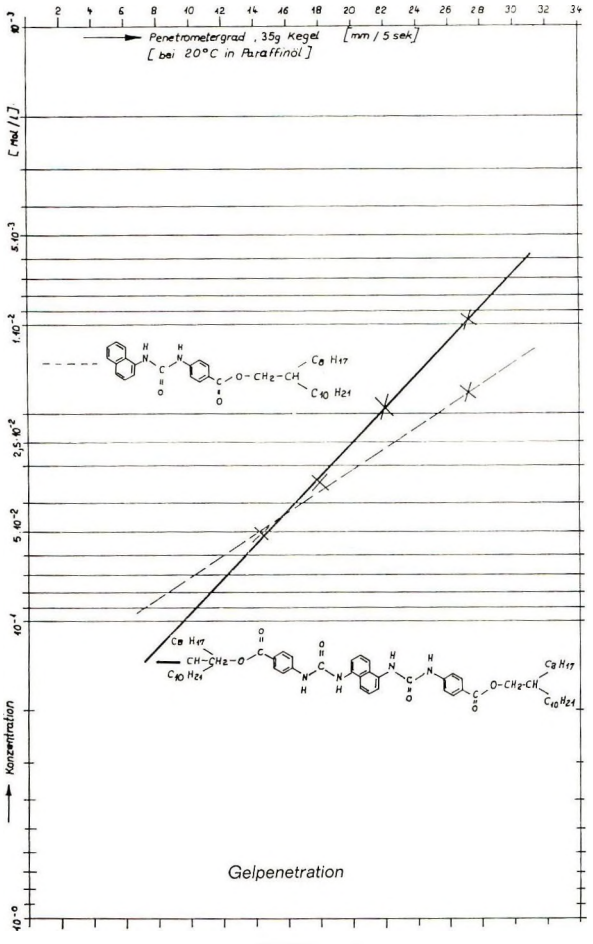


Abbildung 9
Festigkeit von Lichtschutzgelen · Gelpenetration

fachen Belichtungsapparatur wird gezeigt, daß — mit und ohne Zusatz von Dihydroxyaceton als Photosensibilisator — einige Lichtschutzsubstanzen in wäßrig-alkoholischer Lösung unterschiedliche Photostabilität aufweisen. Es werden neue Naphthalin-1,5-bis-harnstoffe beschrieben, die stabil sind und je nach Substitution als UV-B oder UV-A-Absorber eingesetzt werden. Diese Verbindungen haften gut auf Schweinehaut, wie an Abspülversuchen gezeigt wird. Sie zeichnen sich ferner durch ihre ausgeprägten gelbildenden Eigenschaften in hydrophoben Lösungsmitteln aus.

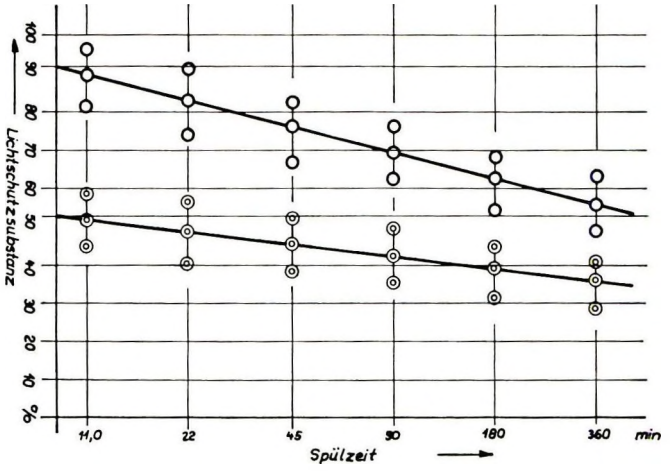


Abbildung 10

Affinität (Abklingkurven von Lichtschutzgelen) von Lichtschutzgelen zu Schweinehaut

3 Gew.-% N-1-Naphthyl-N'-p-phenylencarbo-2-octyldodecyloxy-harnstoff in Paraffinöl

2 Gew.-% 1,5-Naphthyl-bis- [N-p-phenylencarbo-2-octyldodecyloxy-harnstoff] in Paraffinöl

Literatur

(1) Bener, P., Measured and theoretical values of the spectral intensity of ultraviolet zenith radiation and direct solar radiation at 316, 1580 and 2818 m a.s.l. 1. 1. 1967—31. 12. 1969, *Edit. Phys.-Meteor. Observatorium Davos, Final Scientific Report — July 1970*

(2) Barker, Jr., R. E., *Photochem. Photobiol.* **7**, 275 (1968)

(3) Original Hanau Quarzlampen GmbH, *Firmenschrift Tauchlampen für die chemische Industrie*, D-645 Hanau

(4) Kornhauser, A., and Pathak, M. A., *Z. Naturforsch.* **27 b**, 550 (1972)

(5) Beukers, R., and Berends, W., *Biochim. biophysica Acta* **41**, 550 (1960)

(6) Pathak, M. A., Krämer, D. M., and Güngerich, U., *Photochem. Photobiol.* **15**, 177 (1972). — Zur DNA-Reparatur beim Menschen vgl. Berndt, J., *Angew. Chem.* **85**, 289 (1973)

(7) Ženíšek, A., and Král, J. A., *Biochim. biophysica Acta* **12**, 479 (1953); vgl. auch Vandenbelt, J. M., Childs, C. E., Lundquist, D., and Saladonis, J., *Science* **119**, 514 (1953)

(8) Kurogochi, J., Fukui, I., Nakagawa, T., and Jamamoto, I., *Jap. J. Pharmacol.* **6**, 147 (1957)

(9) Ženíšek, A., and Krs, V., *J. Soc. Cosmet. Chemists* **21**, 817 (1970)

(10) Anglin, Jr., J. H., and Everett, M. A., *Biochim. biophysica Acta* **88**, 492 (1964)

(11) Anglin, Jr., J. H., and Batten, W. H., *Photochem. Photobiol.* **11**, 271 (1970)

(12) Stobbe, H., and Bremer, K., *J. prakt. Chem. [N. F.]* **123**, 1 (1929)

(13) Schmidt, J. M. J., *J. chem. Soc.* 1964, 2014; vgl. auch Criegee, R., und Höver, H., *Chem. Ber.* 93, 2521 (1960)

(14) Mustafa, A., *Chem. Rev.* 51, 1 (1952)

(15) Hoppe, U., *J. Soc. Cosmet. Chemists* 24, 317 (1973); Gesellschaft Deutscher Kosmetik-Chemiker e. V. (Herausgeber), *Berichtsband VII. IFSCC-Kongreß Hamburg, 12.—15. 9. 1972*, Hamburg 1973, p. 387

(16) Hoppe, U., *DOS* 2 143 671 vom 8. 3. 1973

(17) Wiskemann, A., *Fette, Seifen, Anstrichmittel* 70, 361 (1968)

(18) Wiskemann, *Persönliche Mitteilung*, 1973

(19) Willis, I., and Kligman, A. M., *Arch. Dermatology* 102, 405 (1970); zur Frage der Auftragsmengen vgl. Langner, A., and Kligman, A. M., *Arch. Dermatology* 105, 851 (1972)

Book Reviews

REVIEW OF EMULSIONS AND EMULSION TECHNOLOGY (PART I), Edited by Kenneth J. Lissant. Marcel Dekker, Inc., New York, 1974. 440 pages. Price $39.50.

Reviewing Part I of a two-part volume on emulsions and emulsion technology where the information of especial interest to cosmetic chemists is in a yet unavailable Part II is somewhat like trying to evaluate a novel for which the ending has not been written. Nonetheless, the chapters dealing with basic theory, making and breaking emulsions, microemulsions, and medicinal emulsions are sufficiently universal in nature to be germane to the applications cosmetic chemists deal with.

Editor Lissant's two chapters—basic theory and making and breaking emulsions—are good and treat the subjects quite well. The chapter on microemulsions by L. M. Prince is comprehensive and very well done, particularly that section dealing with practical applications. Although a better-than-average treatment of the subject, B. A. Mulley's chapter on medicinal emulsions is uneven in quality. The section on preservative systems is quite good in its treatment of the theoretical aspects of preservation but short on the practical aspects—e.g., key review articles on pharmaceutical and cosmetic preservatives are not listed. Because the author is British, the examples and nomenclature cited in the practical section almost invariably are drawn from British industrial and official sources, e.g. centrimide B. P. (British Pharmacopoeia), Dequalinium Chloride B.P., etc. Unfortunately, except for a British audience these references have limited value.

Generally speaking, this is a pretty fair reference for the beginner and, in some instances, the more experienced industrial chemist. However, considering the price of this volume, this reviewer is less than enthralled by the quality of the print (too small and varying in intensity of print) and the cover (too soft for a "hard" cover) and the caliber of the proofreading (inordinate number of typographical errors). Furthermore, Paul Becher's "Emulsions: Theory and Practice" is a better book overall, even though last revised in 1965, and considerably less expensive (almost half the price).—ROBERT MARCHISOTTO—Research Corporation, New York.

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2. Date of Filing September 25, 1974.
3. Frequency of Issue Seven times per year, Feb. Mar. May Aug. Sept. Nov. Dec.
4. Location of Known Office of Publication *(Street, city, county, state ZIP code) (Not printers)* 50 East 41st Street, New York, N.Y. 10017
5. Location of the Headquarters or General Business Offices of the Publishers *(Not printers)* 50 East 41st Street, New York, N.Y. 10017
6. Names and Addresses of Publisher, Editor, and Managing Editor.
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   Editor *(Name and address)* John J. Sciarra, St. John's University, Jamaica, N.Y. 11432.
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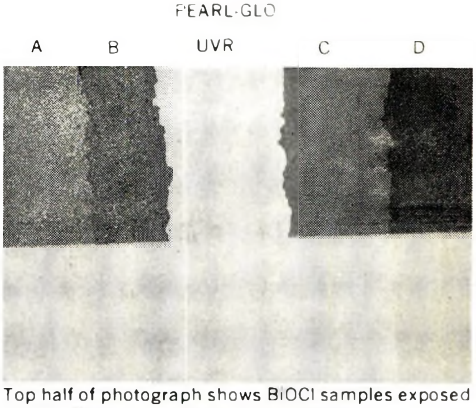

Top half of photograph shows BiOCl samples exposed to U.V. light. Lower half of photograph shows same samples unexposed.

uses: Eye shadows and blushers (in pressed powders, creams, lotions, wax sticks, crayons, pencils, pots and gels)

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