Vol 25 No 8 August 1974

Journal of the Society of Cosmetic Chemists

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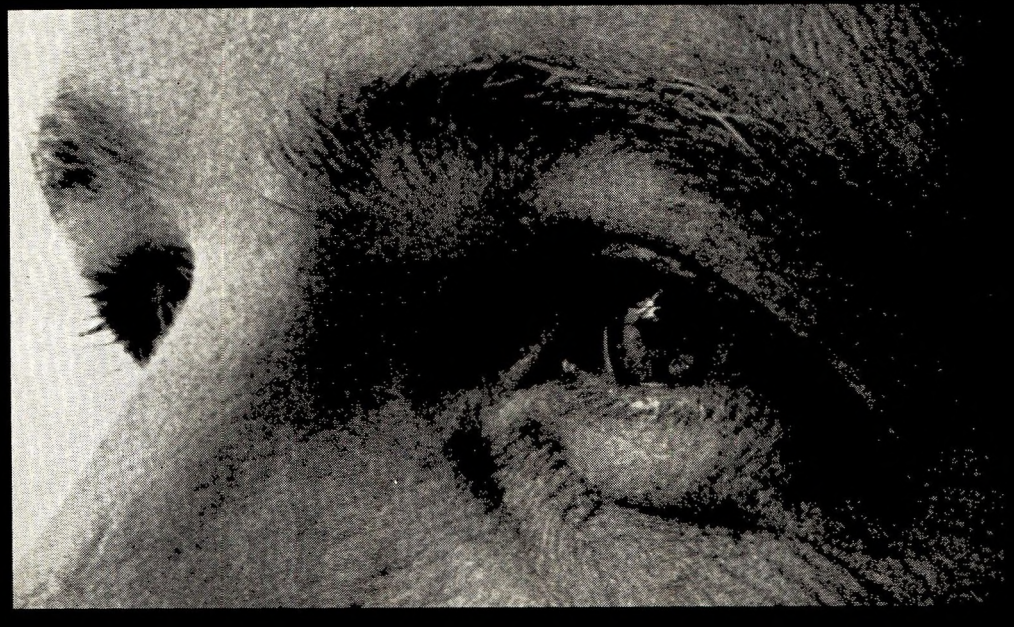

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Assay TiO_2	None	None	None	5%
Appearance	White, pearlescent, free flowing powder	Same	Same	Same
Particle size	Average 20:30 microns; 90% under 44 microns	Same	Average 20:40 microns; 90% under 44 microns	Average 30:30 microns; 85% under 44 microns
Lead	20 ppm max.	20 ppm max.	20 ppm max.	20 ppm max.
Arsenic	3 ppm max.	3 ppm max.	3 ppm max.	3 ppm max.
Microbial analysis	Total count: 100 colonies per gram maximum Pathogens: negative	Same	Same	Same

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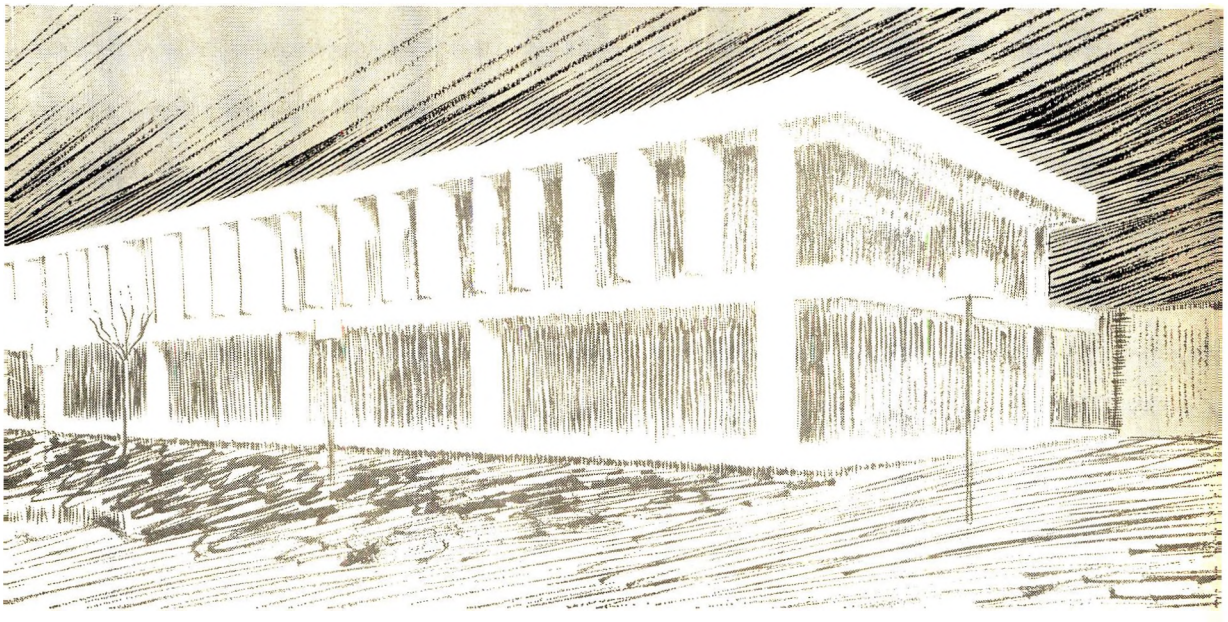

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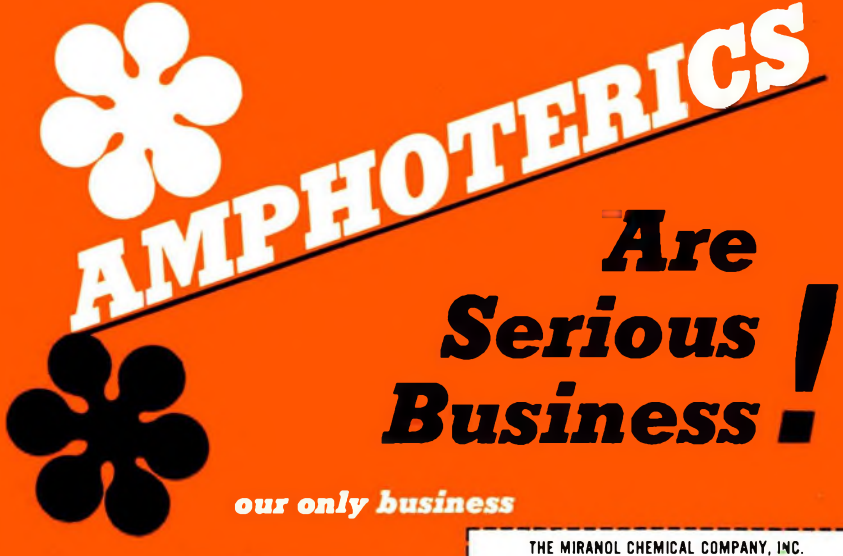

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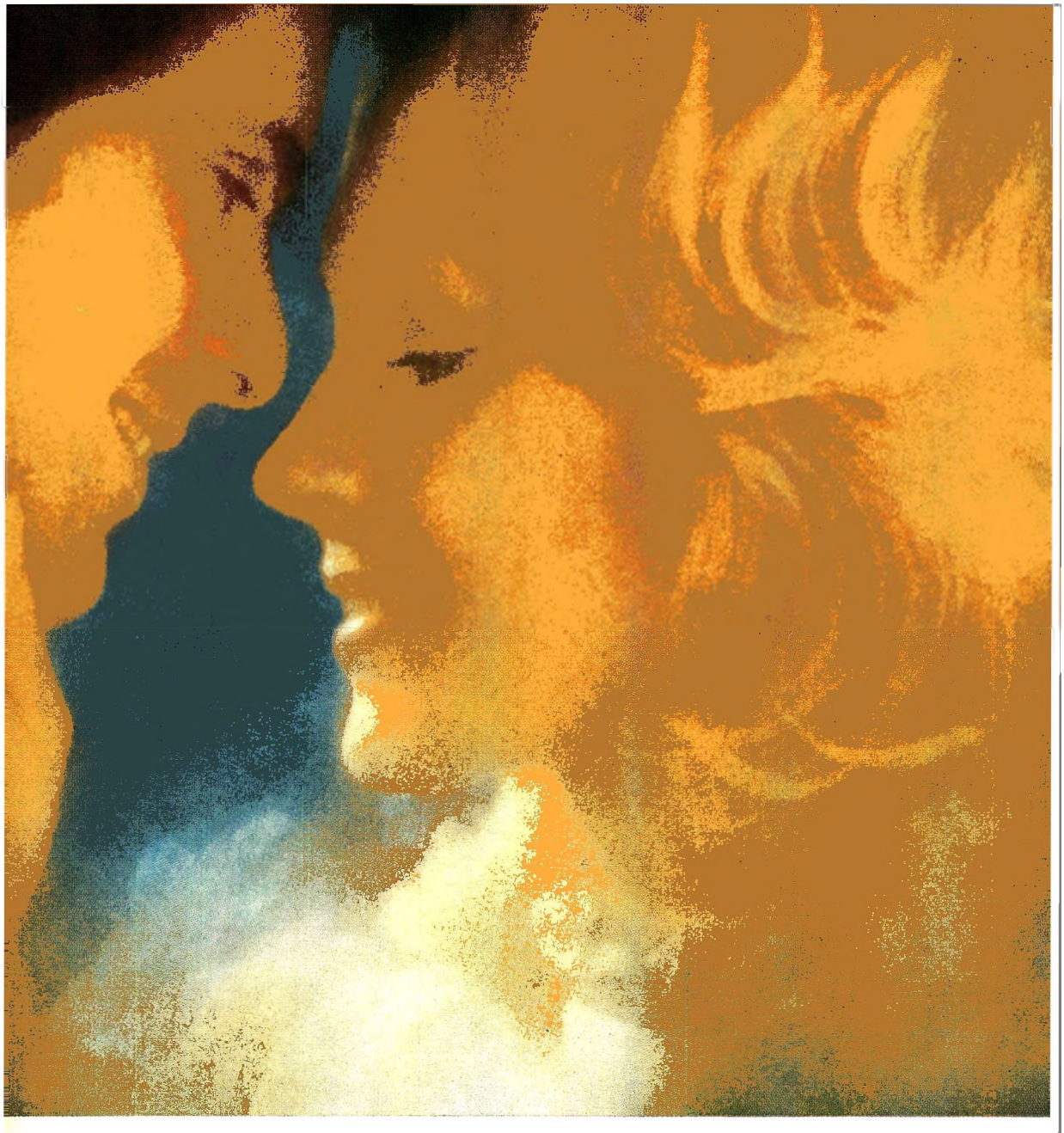

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SYNOPSES FOR CARD INDEXES

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.

Transepidermal moisture loss. II. The significance of the use thickness of topical substances: Gene R. Berube and Murray Berdick. *Journal of the Society of Cosmetic Chemists* **25,** 397 (August 1974)

Synopsis—The product development chemist would like to know or be able to predict how topical substances of interest to him affect the rate of water loss from the stratum corneum of the average consumer under conditions of actual use. Using basic diffusion theory, we have constructed mathematical models which enable data obtained under rigid experimental conditions to be extrapolated to actual field usage conditions. Under these conditions there is a thickness below which the product does not have a perceptible effect on the transepidermal moisture loss rate (TEML). We have defined this as the zero order thickness (L_z). Another useful reference point is the half occlusive thickness ($L_{0.5}$). A method is described for obtaining the use thickness (L_u) distribution. Knowing this distribution, the fractional reduction in TEML (γ) under use conditions can be calculated. L_z, $L_{0.5}$, L_u, and γ have been determined for a commercial petrolatum, 180 SUS mineral oil, 70 SUS mineral oil, a typical emollient cream, and a typical emollient lotion.

Polymerization into human hair: Clarence Robbins, Richard Crawford, D. W. McNeil, Julius Nachtigal, and Giuseppi Anzuino. *Journal of the Society of Cosmetic Chemists* **25,** 407 (August 1974)

Synopsis—Thioglycolic acid (TGA)–cumene hydroperoxide (CHP) and bisulfite–CHP systems are described for polymerizing methyl methacrylate (MMA) in human hair. An ethanol-water solvent system was employed. Diffusion rate control appears to predominate over a variety of reaction conditions. The influence of reagent concentrations and solvent effects on the reaction is also described. Polymerization is shown to occur more rapidly into either reduced-oxidized or bleached hair than into chemically unaltered hair. Partial hydrolysis of the hair fibers containing polymethyl methacrylate (PMMA) provides filament-like fragments, consisting primarily of PMMA, which were examined microscopically.

Effects of surface-active materials on the solubility, chemical stability, and availability of cutaneous applied agents: Bernhard C. Lippold. *Journal of the Society of Cosmetic Chemists* **25**, 423 (August 1974)

Synopsis—Surface-active materials in solution—especially above their cmc—influence cutaneously applied agents differently. The presence of micelles genrally improves solubility but can effect responses of intolerance. The rates of reactions of hydrolytic and oxidative processes are altered by micelle formers. In order to predict stabilization, exact knowledge of the decomposition reactions is required. With regard to availability of the agent, the presence of surface-active materials has far-reaching consequences. Reduction of availability, i.e., lowered activity, depends greatly on the physicochemical properties of the agents. The regularities pertaining to micellar solutions are definitely applicable to other systems.

Application of rheological studies to product formulation, stability, and processing problems: John B. Ward, James F. Kinney, and Hosny Y. Saad. *Journal of the Society of Cosmetic Chemists* **25**, 437 (August 1974)

Synopsis—The physical chemical principles involved in rheological measurements are briefly reviewed. Instrumentation including the Brookfield Viscometer, the Brookfield with Helipath, the Brookfield Plate and Cone Viscometer, and the Rotovisco Viscometer is discussed. Comparative data are presented for typical lotion, cream, and suspension products as measured with each of these instruments. The practical application of such data for formulation, stability, and processing studies is illustrated. The interpretive meaning of the mathematical equations governing this phenomenon and their application in achieving the desired effect are also discussed.

J. Soc. Cosmet. Chem., **25**, 397–406 (August 1974)

Transepidermal Moisture Loss. II. The Significance of the Use Thickness of Topical Substances

GENE R. BERUBE, B.S., and MURRAY BERDICK, Ph.D.*

Presented May 3, 1973, Seminar, Cincinnati, Ohio

Synopsis—The product development chemist would like to know or be able to predict how topical substances of interest to him affect the rate of water loss from the stratum corneum of the average consumer under conditions of actual use. Using basic diffusion theory, we have constructed mathematical models which enable data obtained under rigid experimental conditions to be extrapolated to actual field usage conditions. Under these conditions there is a thickness below which the product does not have a perceptible effect on the TRANSEPIDERMAL MOISTURE LOSS RATE (TEML). We have defined this as the zero order thickness (L_z). Another useful reference point is the half occlusive thickness ($L_{0.5}$). A method is described for obtaining the USE THICKNESS (L_u) distribution. Knowing this distribution, the fractional reduction in TEML (γ) under use conditions can be calculated. L_z, $L_{0.5}$, L_u, and γ have been determined for a commercial petrolatum, 180 SUS mineral oil, 70 SUS mineral oil, a typical emollient cream, and a typical emollient lotion.

Introduction

Blank (1–5) and Gaul (6, 7) have shown that a soft, smooth, and flexible skin can be achieved by plasticization of the stratum corneum with water. Flesch (8) has described three basic ways of achieving this hydration.

(a) Increasing the rate of diffusion of water from the lower epidermal layers to the stratum corneum
(b) Externally adding water directly to the stratum corneum
(c) Occluding the surface of the stratum corneum.

Hydration by Occlusion

The normal stratum corneum is a very efficient but not absolutely perfect barrier to water loss. Under normal conditions, water passes from the underlying tissues to the stratum corneum, dissolves in it, and diffuses through

*Chesebrough-Pond's Inc., Trumbull Industrial Park, Trumbull, Conn. 06611.

it to the exterior surface where it evaporates. This process is known as transepidermal moisture loss (TEML) or insensible perspiration, and is governed by the laws of diffusion, an excellent discussion of which can be found in Scheuplein (9, 10).

Hydration by occlusion is achieved by placing onto the surface of the skin a topical substance which has high diffusional resistance to water, thereby reducing the net water loss from the stratum corneum. One of the means used by cosmetic chemists to impart moisturization is by showing a reduction in TEML after the use of a topical substance.

Methods for Measuring TEML

There are nearly as many methods for measuring TEML *in vivo* as there are investigators in the field. A few of the more important ones are found in: Thiele and Schutter (11), van Gosselt and Vierhaut (12), Spruit and Malten (13), Baker and Kligman (14), Frost *et al.* (15), Goodman and Wolf (16), Johnson and Shuster (17), Lamke (18), and Berube *et al.* (19).

Evaluation of Topical Substances

Several papers have appeared in which the effect of cosmetic materials on transepidermal moisture loss have been evaluated: Powers and Fox (20), Baker (21), Berube *et al.* (19), Spruit (22), and Mezei and Ryan (23). While these papers provide inherent physical property data, they do not predict what will happen under consumer use conditions. It was the main purpose of this study to provide a means for predicting the effect of product usage under consumer use conditions.

Experimental

Instrumentation

The instrumentation used is a modified version of that described in Berube *et al.* (19). Cambridge Systems Model 880 Dew Point Hygrometers* were used in this study.

Skin temperatures are measured with a 10,000-ohm surface thermistor.† This thermistor is attached to the auxiliary channel in one of the hygrometers.

Control of Variables

Spruit and Malten (24) have divided the variables involved in these measurements into two groups: exogenous and endogenous. The exogenous variables are concerned with the environmental influences such as ambient temperature, relative humidity, and the psycho-environment. These variables were controlled with a Forma Scientific Environmental Room which can be controlled to ±0.1°C and ±3% relative humidity.

*EG&G, Environmental Equipment Div., Waltham, Mass.
†YSI Co., Inc., Yellow Springs, Ohio.

The endogenous variables are concerned with the stratum corneum's continuity, disease state, temperature, and hydration. All of these factors working in complex interrelationships produce variations in TEML—from one region of the body to another (13, 14), variation from one individual to another (25), and variation from day to day (13).

Determination of TEML Response of Untreated Subjects

The subject is placed into the environmental chamber at 20°C and 20% relative humidity. The sampling probe is centered on the volar forearm approximately 3 cm from the elbow. The thermistor is centered 0.5 cm below the probe. The subject is allowed to come to equilibrium (about 0.5 to 0.75 hour). After equilibrium is obtained, the environmental temperature is gradually increased to give a slightly increasing skin temperature (about 1°C per hour) and the skin temperature and TEML are recorded. This is continued until sufficient data are collected to describe the subject's TEML-skin temperature response.

Determination of Topical Substance Response

At the end of the above experiment, the probe is removed, the test substance is applied, and the thickeness is determined as described in Berube *et al.* (19). The thermal-TEML response is again recorded. Several different thicknesses are applied to several different subjects.

Test Materials

Vaseline®° brand Petroleum Jelly, 180 SUS Mineral Oil, and 70 SUS Mineral Oil samples were obtained. A typical emollient lotion (Lotion 78) and a typical emollient cream (Cream 88) from Balsam and Sagarin (26) were prepared. The formulas are reproduced in Table I.

Determination of Use Thickness (L_u)

A 20 cm by 5 cm square is marked on the volar forearm of a test panelist. The panelist is then given a preweighed sample of test material and asked to apply as much material as she likes to the area. The residual sample is reweighed and the thickness calculated as described (19).

Results and Discussion

Basic Diffusion Theory

As noted by Scheuplein (10), the stratum corneum is permeated by water through biologically passive diffusion. It can be described by:

$$J_s \, L_s = K_m \, D \, \Delta C \qquad (1)$$

where J_s = flux from subject
L_s = skin thickness

°Chesebrough-Ponds Inc., New York, N.Y.

K_m = solute-membrane distribution coefficient
ΔC = concentration gradient

It is evident that the diffusion coefficient is itself a function of concentration. It therefore becomes necessary to define a mean diffusion coefficient ($\overline{D}$) which is a function of C.

$$\overline{D} = K_m\, D\, f(c) \tag{2}$$

In our present experiments, the external concentration of water is essentially zero so that

$$\Delta C = C$$

where C is the concentration of water at the inner surface of the stratum corneum.

Combining these facts,

$$J_s\, L_s = \overline{D}\, C \tag{3}$$

Grice *et al.* (25) and Spruit and Herweyer (27) have shown J_s to be a temperature-dependent process. Diffusional processes follow Arrhenius behavior and

$$\overline{D} = \overline{D}_0\, \mathrm{Exp}\, [-E_D/(R\,T)] \tag{4}$$

where $\overline{D}_0$ is a frequency factor
and E_D = mean diffusion activation energy
R = gas constant
T = skin temperature in °K

Table I

Formulas for Typical Emollient Lotion and Typical Cream[a]

Ingredient	Lotion 78[b]	Cream 88[b]
Part A		
Cetyl alcohol	0.20	...
Stearic acid	1.00	15.00
Isopropyl palmitate	10.00	...
70 Mineral Oil	10.00	23.00
Tween 60	0.50	...
Arlacel 60	5.00	...
Beeswax	2.00	2.00
Lantrol	10.00	...
Propyl paraben	0.15	0.15
Atlas G-1441	...	6.00
Lanolin (anhydrous)	...	1.00
Part B		
Methyl paraben	0.15	0.15
Triethanolamine	0.40	...
Borax	0.10	...
Glycerol	5.00	...
Sorbitol (70%)	...	10.00
Water	55.20	42.40

[a] As described in Barnett (26).
[b] Perfume not used in the preparations. In cited formula, 0.30% perfume was used.

Substitution yields:

$$J_s L_s = C \overline{D}_o \text{ Exp } [-E_D/(R T_s)] \quad (5)$$

We can define:

$$k_1 = C D_o/LS \quad (6)$$

$$k_2 = -E_D/R \quad (7)$$

and:

$$J_s = k_1 \text{ Exp } (k_2/T) \quad (8)$$

A k_1 and k_2 can be used to describe the temperature-TEML response.

Normal TEML Responses

An idealized TEML-skin temperature response is shown in Fig. 1. The k_1 and k_2 for each of 16 subjects were calculated by least squares linear regression analysis utilizing a computer. Results are shown in Table II.

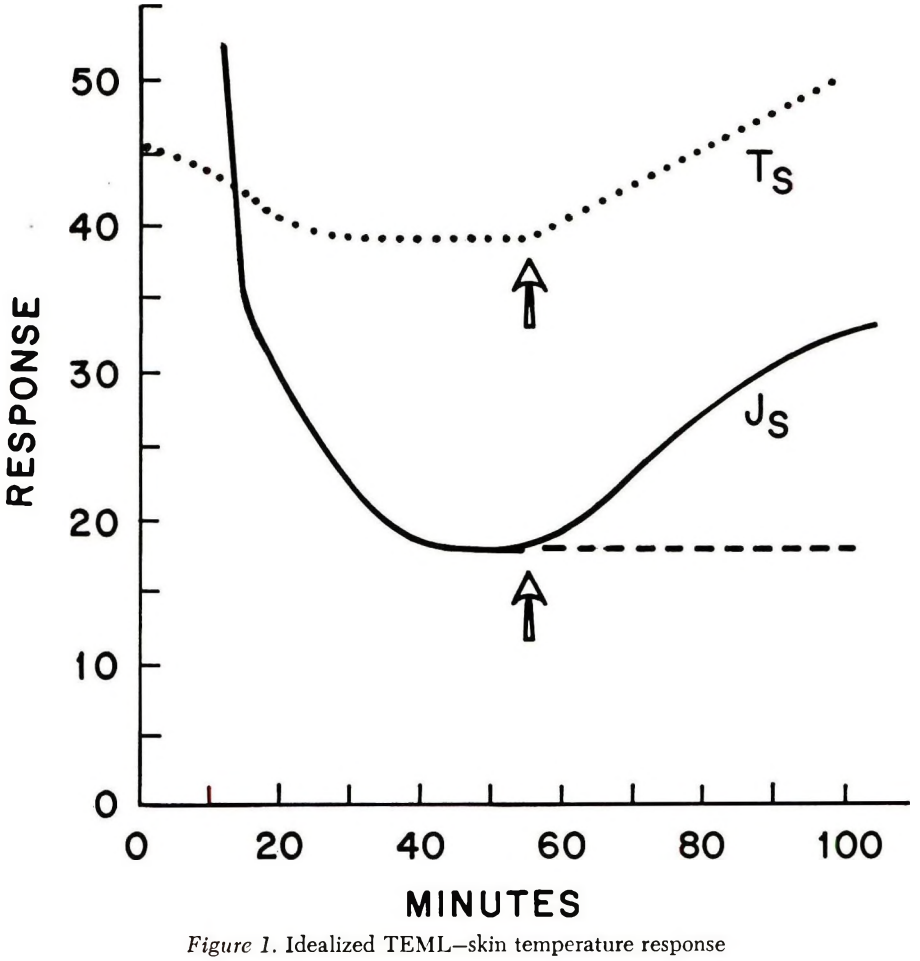

Figure 1. Idealized TEML–skin temperature response

Table II

Results of Least Squares Linear Regression Analysis of TEML–Skin Temperature Data

Subject	Age (years)	Height (inches)	Weight (pounds)	k_1	k_2	Index of Determination
1	18	67.0	100	3.56×10^{-10}	0.064	−0.992
2	21	64.0	105	2.35×10^{-30}	0.219	−0.991
3	28	63.8	122	1.25×10^{-24}	0.176	−0.991
4	28	65.5	160	1.63×10^{-31}	0.075	−0.992
5	29	60.0	110	2.82×10^{-05}	0.029	−0.990
6	29	62.0	140	1.14×10^{-03}	0.016	−0.989
7	30	66.0	157	1.84×10^{-15}	0.104	−0.992
8	31	58.5	125	8.91×10^{-04}	1.980	−0.985
9	32	66.5	125	1.27×10^{-12}	0.012	−0.993
10	35	65.0	128	8.34×10^{-04}	0.015	−0.983
11	46	63.5	124	8.38×10^{-13}	0.083	−0.990
12	50	64.0	121	1.42×10^{-11}	0.075	−0.990
13	55	63.0	159	6.30×10^{-22}	0.153	−0.991
14	57	64.0	200	2.49×10^{-23}	0.164	−0.991
15	58	65.0	150	6.12×10^{-17}	0.116	−0.991
16	58	64.0	151	6.01×10^{-15}	0.115	−0.992

Test Materials

Similarly, a k_3 and k_4 can be defined for each thickness test of a material. These will describe the TEML-skin temperature response for the combination of material and stratum corneum.

Diffusion and Topical Substance Thickness

The residual fraction of J_s (α) after application of a product can be calculated from the experimental data:

$$\alpha = \text{treated/untreated} = (J_s + p)/Js \tag{9}$$

$$\alpha = (k_3/k_1)\ \text{Exp}\ [(k_4 - k_2)/Ts] \tag{10}$$

Since Lp is much thicker than Ls and Ls does not change by orders of magnitude, α is proportional to Lp. A least squares linear regression analysis shows

$$L = k_5\ (1/\alpha) \uparrow k_6 \tag{11}$$

to be a reasonable fit for the range of thicknesses normally observed.

Zero Order Thickness

When $k_6 = O$, $(1/\alpha) = 1$ and $L = k_5$. We define this thickness of the product as the zero order thickness (L_z). This is the thickness of a test material below which the material has no effect on TEML.

Half Occlusive Thickness

Knowing k_5 and k_6 one can easily calculate the thickness necessary to produce any level of occlusion. The half occlusive thickness ($L_{0.5}$) is·

$$L_{0.5} = k_5\ (2) \uparrow k_6 \tag{12}$$

This figure is a more realistic property of the material than the occlusive thickness which we have reported earlier (19).

Fraction Reduced

The fractional reduction (γ) in TEML produced by a product can be calculated from residual fraction (α).

$$\gamma = 1 - \alpha \tag{13}$$

Use Thickness

While L_z and $L_{0.5}$ are properties of the product, they do not predict the effect of the material under use conditions. To do so, we must know the distribution of use thickness (L_u). Use thickness distributions were determined at the 95% confidence levels for the test materials and are recorded in Table III.

Table III

Use Thickness Mean and 95% Confidence Limits for Several Test Substances

Test Substances	Use Thickness (mm)
Vaseline brand petroleum jelly	0.029 ± 0.011
180 SUS Mineral Oil	0.010 ± 0.009
70 SUS Mineral Oil	0.015 ± 0.002
Cream 88	0.030 ± 0.010
Lotion 78	0.025 ± 0.008

Calculation of the Fractional Reduction of TEML by the Test Material at Use Thickness and Any Skin Temperature

A computer program has been written and is schematically represented in Fig. 2. The raw data are fed into the computer and the constants and indexes for their determination are calculated and output. The L_z, $L_{0.5}$, and γ at the mean use thickness and low and high range are calculated from 30 to 35°C.* These data are displayed in Table IV.

While the L_z and $L_{0.5}$ show 180 SUS mineral oil to be highly effective, the use experiment shows it not to be as good as the emollient cream and lotion. This is mainly because the subject will not use an adequate thickness of these materials because of their feel characteristics.

Conclusions

While numerous methods for evaluating the skin and products used thereon are available to obtain the transepidermal moisture loss properties of these materials, the computer has enabled us to develop a method for predicting

*Malin (28) has shown this temperature range to represent volar forearm skin temperature.

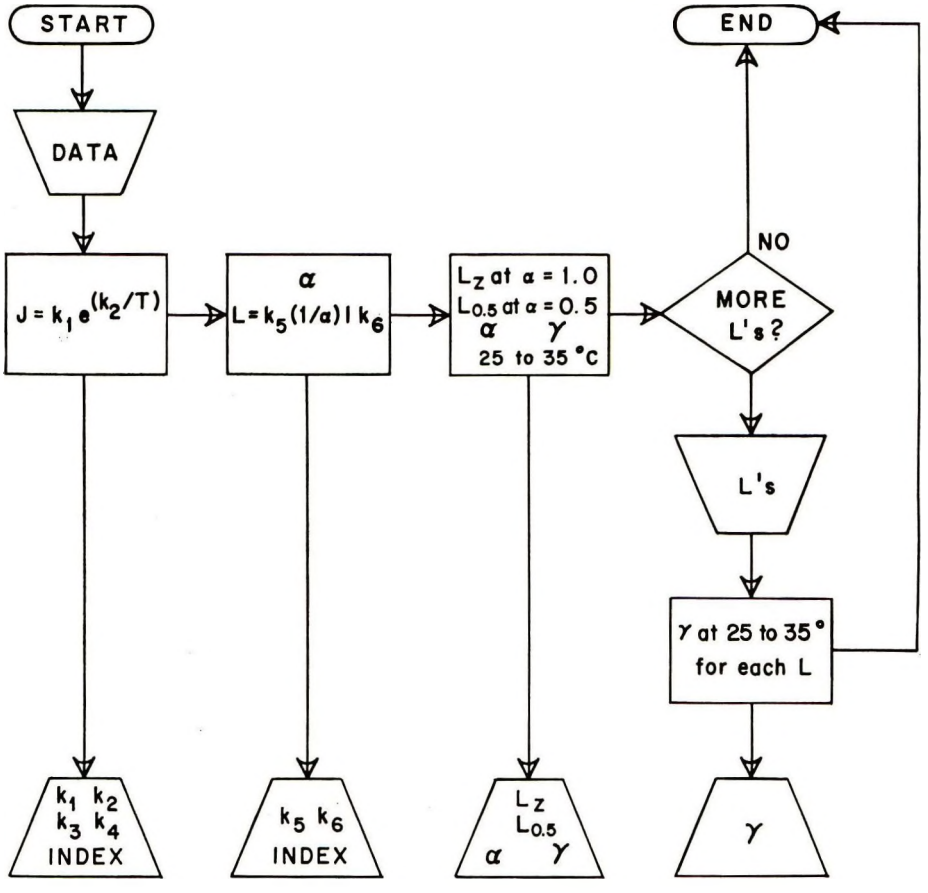

Figure 2. Flow diagram for computer program for manipulation of experimental data

Table IV

Results of Computer Program for Calculation of Various Constants and Indexes

Test Substance	L_z (mm)	$L_{0.5}$ (mm)	γ at L_U $-s$	x	$+s$
70 SUS Mineral Oil	0.014	0.021	0.00	0.10	0.28
180 SUS Mineral Oil	0.004	0.024	0.00	0.22	0.36
Cream 88	0.017	0.046	0.11–0.09	0.32	0.45
Lotion 78	0.009	0.021	0.46	0.62–0.55	0.71–0.63
Vaseline brand petroleum jelly	0.010	0.017	0.56	0.76	0.85–0.84

how these materials would perform under actual use conditions. Utilizing the thickness (use thickness) which a subject will use of a cosmetic material and the thickness-temperature variability matrix for transepidermal moisture loss rates, the fractional reduction in transepidermal moisture loss can be predicted under actual use conditions.

Experiments which we have carried out with Vaseline brand petrolatum, 180 SUS Mineral Oil, 70 SUS Mineral Oil, and a typical emollient cream and lotion have shown that the materials such as mineral oil with the highest occlusivity may not be used for psychorheological reasons at a thickness which will provide advantageous fractional reductions in transepidermal moisture loss. Conversely, emollient creams and lotions, while less occlusive in nature, have desirable psychorheological properties and will be used at use thicknesses which will provide a significant reduction in transepidermal moisture loss rate.

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Polymerization into Human Hair

CLARENCE ROBBINS, Ph.D.,* RICHARD CRAWFORD, Ph.D.,*
D. W. McNEIL, B.S.* JULIUS NACHTIGAL, Ph.D.,* and
GIUSEPPI ANZUINO, Ph.D.†

Synopsis—THIOGLYCOLIC ACID (TGA)–CUMENE HYDROPEROXIDE (CHP) and BISULFITE–CHP systems are described for polymerizing METHYL METHACRYLATE (MMA) in HUMAN HAIR. An ethanol-water solvent system was employed. Diffusion rate control appears to predominate over a variety of reaction conditions. The influence of reagent concentrations and solvent effects on the reaction is also described. POLYMERIZATION is shown to occur more rapidly into either reduced-oxidized or bleached hair than into chemically unaltered hair. Partial hydrolysis of the hair fibers containing polymethyl methacrylate (PMMA) provides filament-like fragments, consisting primarily of PMMA, which were examined microscopically.

Introduction

Two manuscripts (1, 2) from our laboratories describing chemical reactions of human hair containing synthetic polymer have already been published. This paper describes the polymerization reaction used in our earlier work and some characteristics of the synthetic polymer isolated by hydrolytic methods. Additional references and background to vinyl polymerizations in keratin fibers may be found in the first two articles of this series.

Experimental

Materials

Human Hair

The keratin fibers used in this investigation were brown human hair,‡ from European Caucasians, which were washed with 2% sodium lauryl sulfate and rinsed thoroughly with deionized water.

*Colgate-Palmolive Research Center, 909 River Road, Piscataway, N.J. 08854. This work was conducted at the Colgate-Palmolive Research Center where all correspondence should be addressed.
†Chatillon S.P. A., Largo Chatillon, Vercelli, Italy.
‡Purchased from De Meo Brothers, New York, N.Y.

Bleached Hair

Detergent-washed European brown hair (10 g) was weighed into a 1-l. beaker and treated with a solution containing 60 ml of 30% hydrogen peroxide and 240 ml of deionized water, and adjusted to pH 10.2 with concentrated ammonium hydroxide. After 30 min the solution was decanted and

Reduced-Oxidized Hair

the hair was thoroughly rinsed with deionized water.

Detergent-washed European brown hair was reduced for 30 min with 6% ammonium thioglycolate at pH 9.2 using a 33:1 solution-to-hair ratio followed by oxidation for 5 min with 1.4% sodium perborate using a 40:1 solution-to-hair ratio.

Methyl Methacrylate[*]

Monomer was washed with dilute alkali and distilled prior to use. All other chemicals were of reagent grade or of the highest purity available.

Procedures

Polymerization with TGA–Cumene Hydroperoxide

The hair was immersed in 6% ammonium thioglycolate at pH 9.2 for 10 min (unless otherwise specified) using a 20:1 solution-to-hair ratio at room temperature. The solution was then decanted and the fibers were rinsed for 2 min with deionized water and immersed at room temperature in water-alcohol (60:40) mixtures of MMA (10%) and CHP (3%) using a 20:1 solution-to-hair ratio (unless other concentrations are specified). After 30 min reaction time, the solution was decanted and the hair was rinsed with water and dried The amount of add-on was estimated by weight pickup measured at 55% RH before and after reaction.

Polymerization with Bisulfite–Cumene Hydroperoxide

The fibers were immersed in 5% sodium bisulfite dissolved in 45% ethanol for 10 min using a 20:1 solution-to-hair ratio at room temperature. The solution was then decanted and the fibers were rinsed for 2 min with deionized water and immersed in a solution of MMA and CHP as described in the above section.

Isolation of Polymer by Acid Hydrolysis

Polymer (PMAA)-containing hair was refluxed for 1½ hours in 5*N* hydrochloric acid using a 50:1 solution-to-hair ratio. The solution was decanted and the fibrous solid was washed with deionized water, filtered, and washed se-

[*]Borden Chemical Co., Philadelphia, Pa.

eral times again. The fibrous solid was then dried to a constant weight in a desiccator before microscopical examination.

Molecular Weight Determination

Flow times for 2% and lower concentrations of the polymer (PMMA) in benzene, as isolated above, were determined in a Ubbelohde-Cannon Dilution Viscometer Size 75° to provide an estimation of the viscosity average molecular weight (3).

Isolation of Fibrous Solid from Sodium Sulfide Reaction

Polymer-containing hair was shaken in 0.6*M* sodium sulfide in 1% sodium hydroxide solution for 18 hours using an 80:1 solution-to-hair ratio. The solution was decanted, the solid filtered, washed with water, and dried.

Results and Discussion

Add-On and its Relation to the Amount of Synthetic Polymer Formed in Hair

Previous publications (1, 4) describing reactions of human hair with vinyl monomers, under conditions conducive to polymerization, refer to add-on or polymer deposit as the amount of weight gain measured under conditions of constant temperature and relative humidity. Add-on is generally assumed to be synonomous with the amount of synthetic polymer deposited and/or grafted (incorporated) per unit weight of fibers. In order to test this assumption, we attempted to measure these two parameters in our reaction system. Figure 1 summarizes the results of this effort showing a linear relation between add-on and the per cent of polymer (PMMA) isolated up to 30% add-on. Over this range, the per cent polymer isolated generally corresponds to more than 80% of the total add-on. Therefore, we conclude that per cent add-on is a reasonable approximation to the amount of PMMA incorporated in the hair under these reaction conditions.

In the initial stages of this investigation, we decided to use moderate solution-to-hair ratios (25:1) where solution measurement could be made and where concentrations of the various reagents might be affected by depletion effects, permitting study of this important rate limiting factor.

The Reaction Scheme

Polymerization of a vinyl monomer into human hair *via* the reaction systems used in this study is a complicated multistep process summarized by the following nine-step reaction scheme:

1. Diffusion of reducing agent into the fibers
2. Chemical reaction with disulfide bonds in the fibers

°Cannon Instrument Company, State College, Pa.

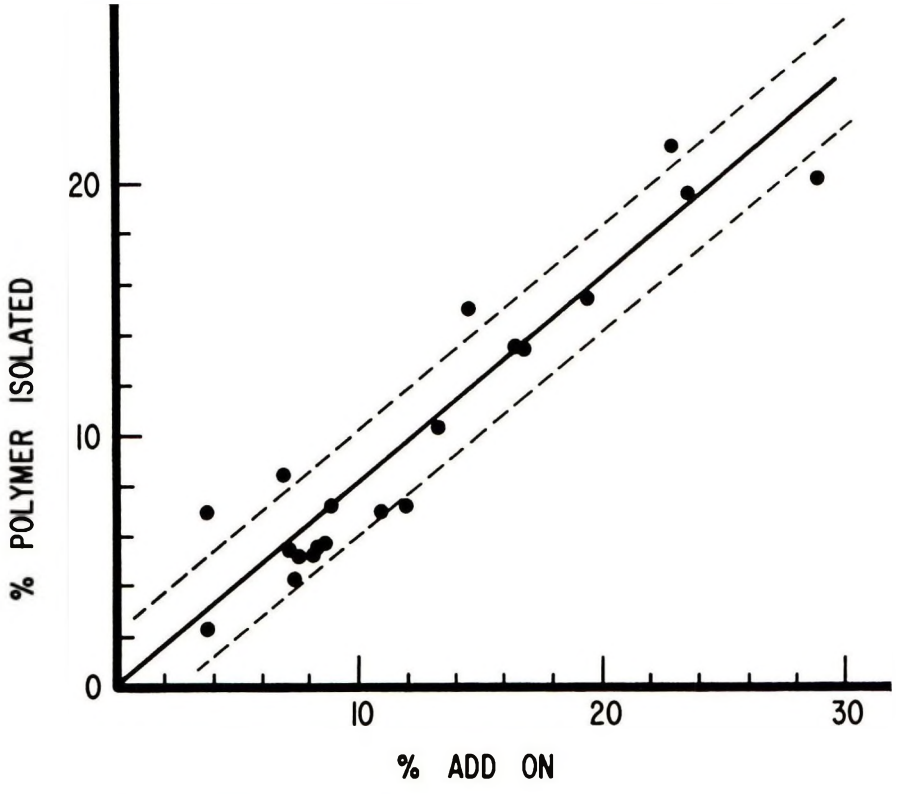

Figure 1. Add-on and its relation to the amount of PMMA isolated

3. Water rinse
4. Diffusion of oxidizing agent (CHP) into the fibers
5. Reaction between reduced hair and CHP
6. Diffusion of vinyl monomer (MMA) into the fibers
7. Chain-initiating reactions
8. Chain-propagation reactions
9. Termination of free radical chain

Influence of Steps 1, 2, and 3 on the Overall Reaction

Figure 2 depicts the results of experiments showing add-on *versus* reduction time using 6% TGA at pH 9.2 as the reducing system. Figure 2 also describes data where sodium bisulfite was used as the reducing agent. These results are similar to the data of Wolfram (4), who used a trihydroxymethyl phosphine–persulfate system, and show increasing add-on with increasing time of reduction.

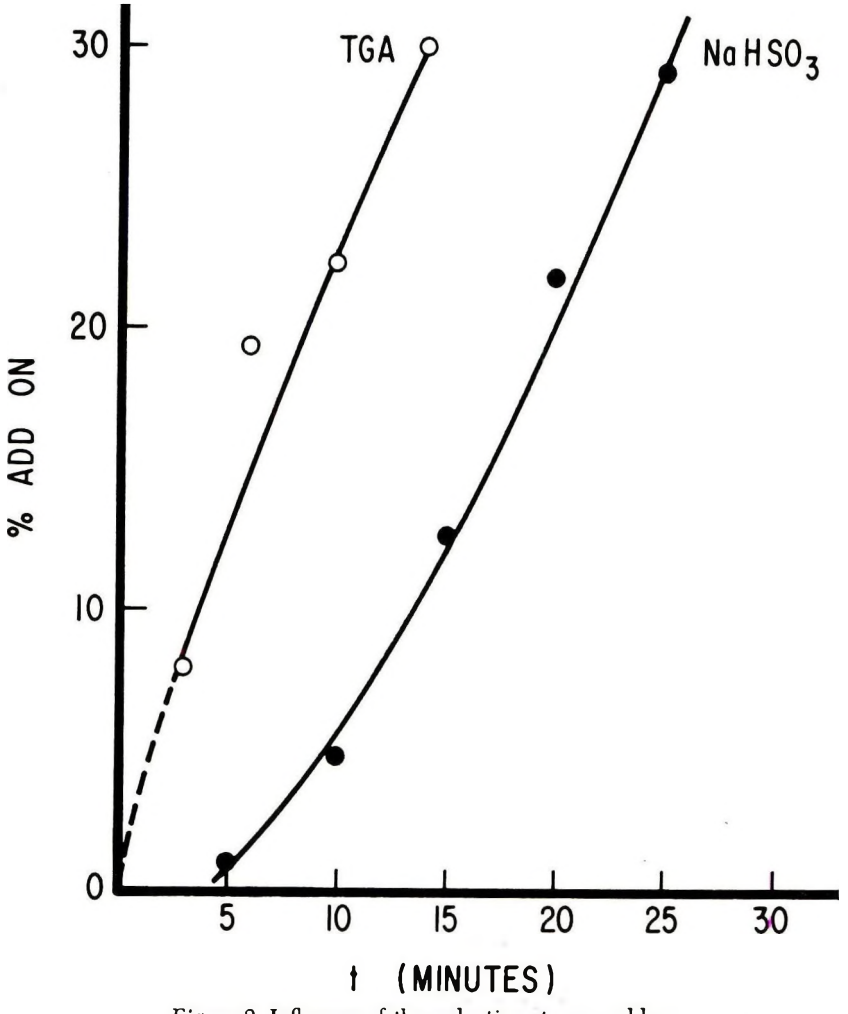

Figure 2. Influence of the reduction step on add-on

These data also show a faster initial rate of polymerization with the TGA system than with the bisulfite system, consistent with the faster rate of reduction of disulfide bonds in hair by TGA. The reaction of TGA with human hair has been shown to be diffusion-controlled (5). Therefore, these data show the importance of step 1, i.e., diffusion of the reducing agent into the fibers, to the overall polymerization reaction. Step 2, the chemical reaction of the disulfide bond with TGA is faster than diffusion and, therfore, of lesser importance to the kinetic scheme; however, the extent of this disulfide scission is the prime factor that controls the rate of penetration of monomer and initiator into the fibers, and controls the amount of polymer add-on as shown in Fig. 2 and in the scanning electron micrographs.

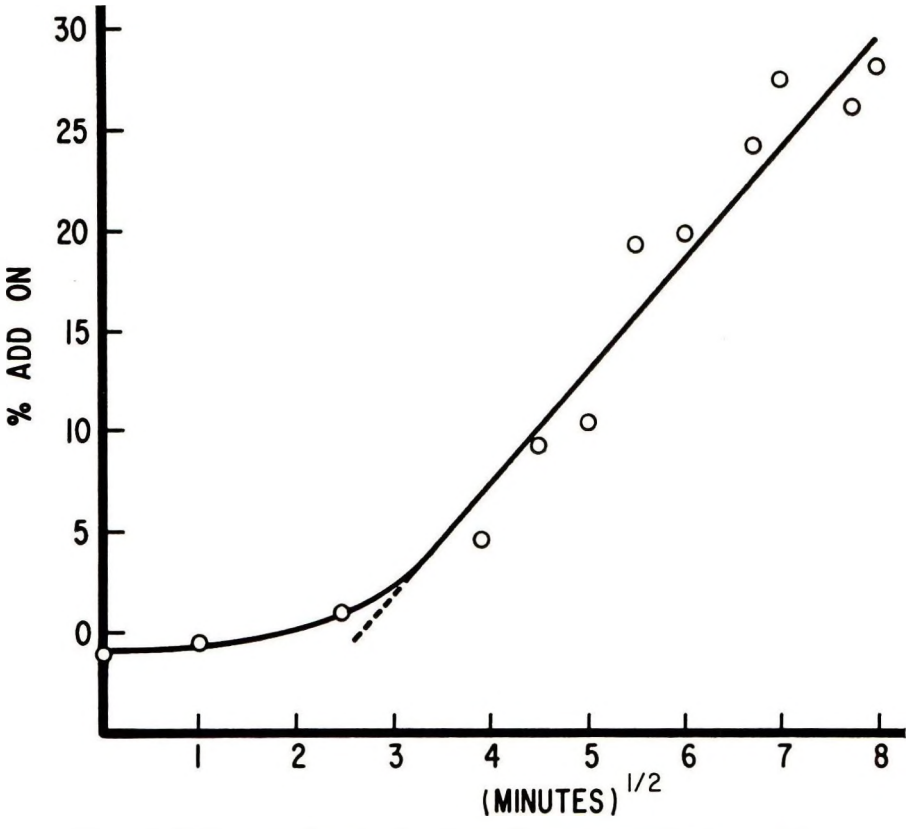

Figure 3. Add-on *vs.* polymerization time under constant reduction conditions

Lengthy rinses prior to the polymerization step were not required with either TGA or bisulfite as reducing agent. A short 2-min rinse under the tap was employed, providing reproducible results with a minimum of solution polymerization.

Steps 4–9, Additional Aspects of Diffusion Rate Control

Experiments were conducted measuring polymer add-on at different polymerization times. Results from these experiments are plotted in Fig. 3. The initial part of this curve shows a retardation effect, possibly an inhibition time, followed by a reaction linearly related to the square root of time, consistent with diffusion rate control into a cylinder of infinite length (6).

Considering the entire reaction sequence, only steps 1, 4, and 6 involve diffusion. The previous section describes how step 1 affects the rate of polymerization in the fibers. The roles of CHP and MMA concentrations on this reaction are illustrated graphically in Fig. 4 and 5. These plots show that the

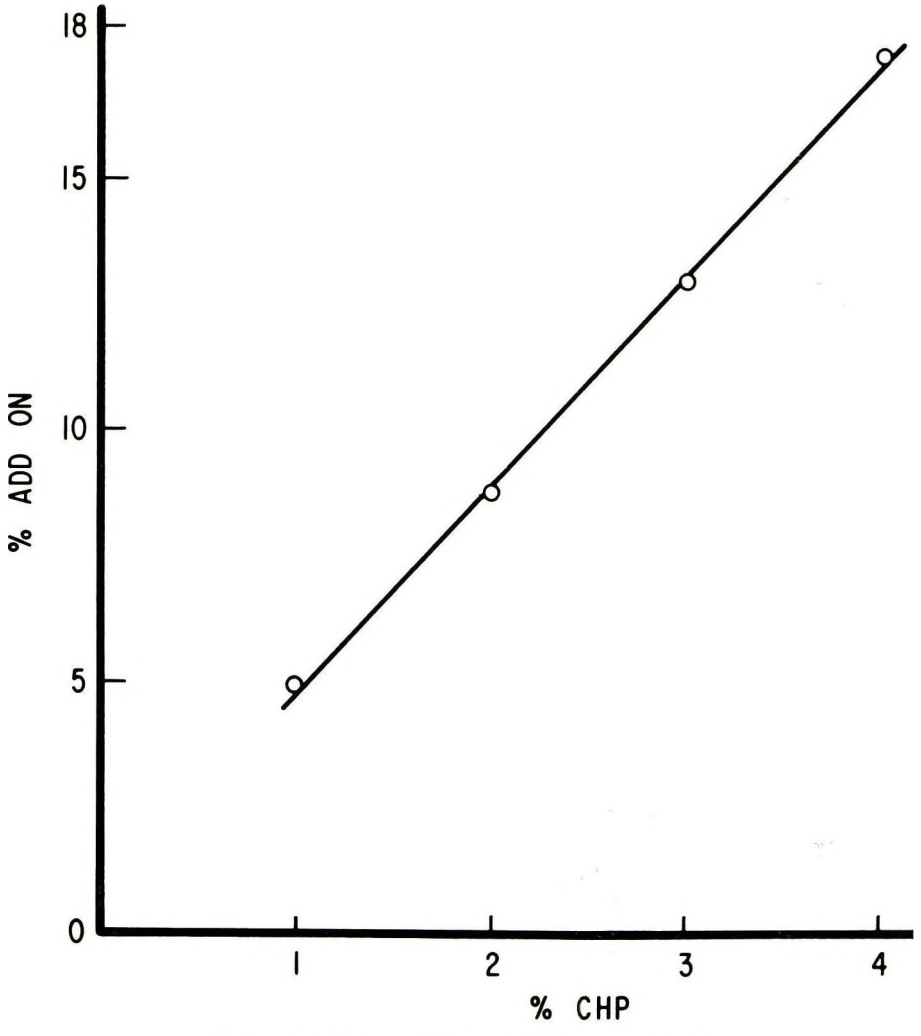

Figure 4. Add-on at different CHP concentrations

amount of add-on at 30 min is influenced by both oxidizing agent and vinyl monomer concentrations. These data in conjunction with diffusion rate control suggest that the diffusion of these species into the fibers (steps 4 and 6) is rate limiting, therefore step 1 can influence the rate of polymerization by controlling the density of crosslinks in the fibers and thereby controlling the rate of penetration of CHP and MMA into the fibers. Both steps 4 and 6 can be rate limiting but do not permit a further distinction. Assuming that both steps 4 and 6 are rate limiting permits the following conclusion. Anything that can accelerate diffusion of oxidizing agent and monomer into the fibers will increase the rate of add-on. The converse also holds; anything that retards dif-

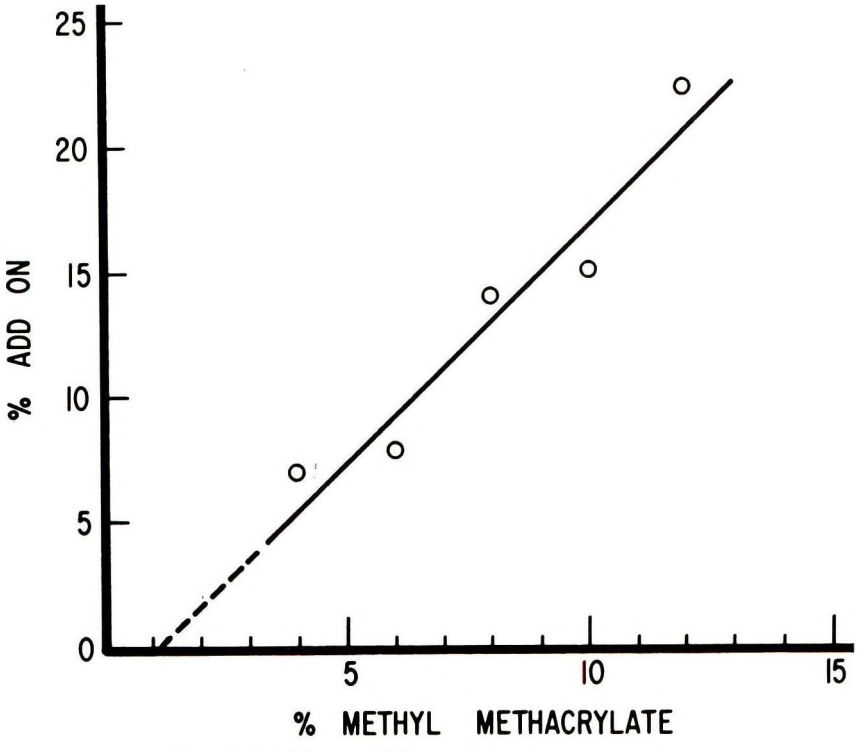

Figure 5. Add-on at different MMA concentrations

fusion of oxidizing agent and monomer into the fibers will decrease the rate of add-on.

The reactions described in Fig. 6 are proposed to account for step 5, generation of the free radical species which initiates polymerization. It is probable that sulfenic acid, a highly unstable species known to undergo complex disproportionation reactions (7), generates the free radical initiator. An alternative possibility is thioperoxide. Thioperoxides are known to initiate vinyl polymerizations under conditions of photolytic decomposition (8). Sulfenic acid or thioperoxide can be formed *via* nucleophilic displacement of mercaptide on hydroperoxide (Fig. 6). Steps 7, 8, and 9 (initiation, propagation, and termination) are described in Fig. 7. If the chain-initiating radicals are derived from the hair, then the polymer is grafted to the hair; however, if the chain-initiating radicals are formed from CHP or TGA, then the polymer is mechanically entrapped.

Influence of the Solvent System on Add-On

An ethanol-water solvent system was employed in this study to promote solubility of MMA and CHP, both essentially water-immiscible compounds.

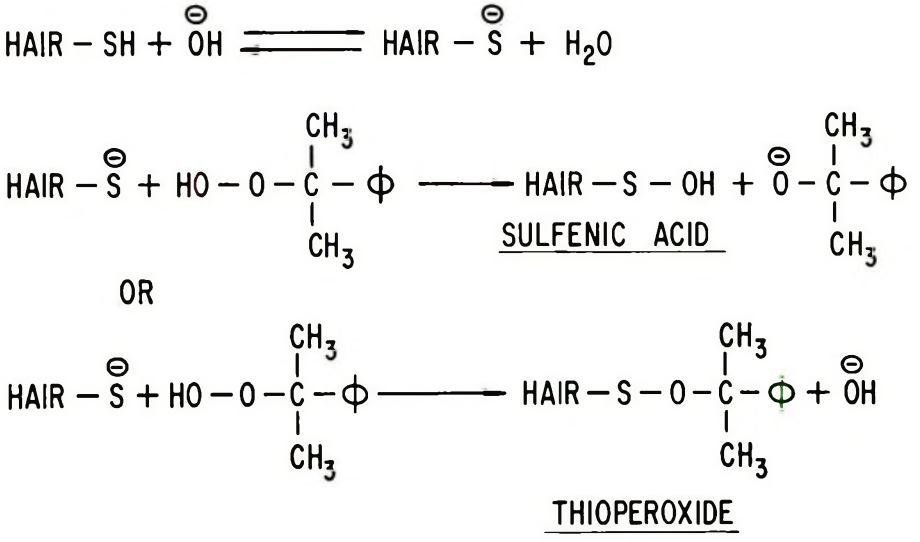

Figure 6. Proposed mechanism for step 5

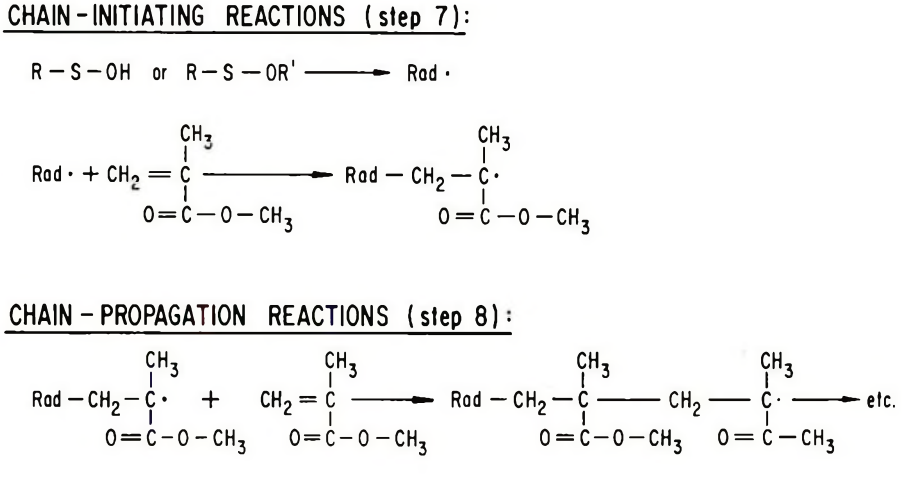

Figure 7. Initiation, propogation, and termination reactions

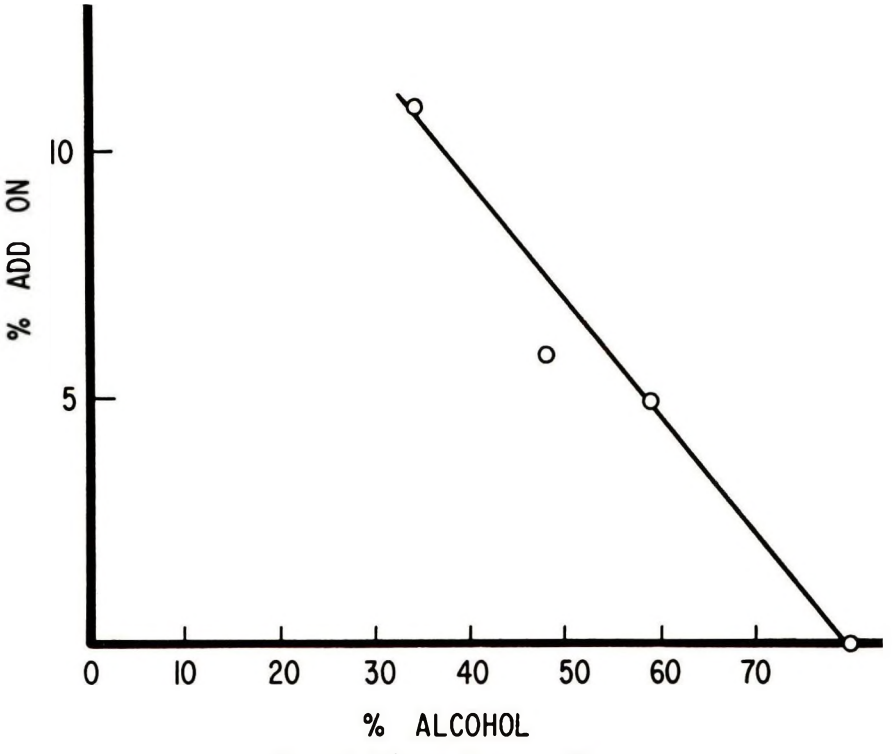

Figure 8. Solvent effects on add-on

Figure 8 shows the influence of the ethanol-water ratio on polymer add-on. This plot shows an increase in add-on with an increasing amount of water in the solvent system. The more water in the system, the greater the fiber swelling and the greater the driving force for deposition of water insolubles onto the fibers and, therefore, diffusion of these same species (CHP and MMA) into the hair. One might also postulate that the greater the amount of water in the solvent, the greater the tendency for emulsion polymerization, with polymer and/or hair serving as the internal phase. However, this suggestion is a moot point and we wish to stress the importance of diffusion to each of the steps which we feel provides a pragmatic explanation to the entire reaction scheme.

Polymerization into Reduced-Oxidized Hair

Extensive reduction followed by mild oxidation increases the penetrability of hair without producing an appreciable change in the disulfide content. Table I provides data showing polymer add-on under fixed conditions with the bisulfite polymerization system (reduction for 10 min followed by polymerization for 30 min) into reduced-oxidized hair. As predicted from our

Table I
Polymerization into Reduced-Oxidized Hair

No. Times Reduced-Oxidized	% Add-On
0[a]	15
1[a]	103
2	116

[a]There was no significant difference in the cystine content of these two hair samples as determined (9) by hydrolysis and analysis on a Beckman Spinco Amino Acid Analyzer, Model 120–C (Beckman Instruments Inc., Spinco Div., Palo Alto, Calif. 94303).

Table II
Polymerization into Bleached Hair

No. Bleaching Treatments	% of Original[a] Cystine Content in Hair	% Add On
0	100	12
1	88	18
2	85	21
3	80	25
5	. . .	38

[a]Determined in hair sample by Shinohara method (12) before polymerization.

previous conclusions, polymerization occurs more readily into reduced-oxidized hair than into unaltered hair. This suggests that polymerization will occur more readily into permanent waved hair than into cosmetically unaltered hair.

Polymerization into Oxidized (Bleached) Hair

In contrast to reduction followed by mild oxidation, vigorous oxidation as in bleaching increases the penetrability of hair and at the same time decreases the disulfide content (10, 11). Hair bleached 1, 2, 3, and 5 times with alkaline hydrogen peroxide (see experimental section) was treated with the bisulfite polymerization system. Data from these experiments are summarized in Table II.

These data show increasing add-on with decreasing cystine content in the fibers. From a strictly chemical point of view one might anticipate the reverse, i.e., increasing add-on with increasing cystine "concentration," the potential source of sulfhydryl, the reducing part of the redox system. The data suggest a diffusion-controlled process facilitated by decreasing the number of cross-links in the fibers, consistent with the previously stated conclusion; anything which accelerates diffusion of CHP and MMA into the fibers will increase the rate of add-on.

Table III
Effect of Previous Treatment of Hair on Molecular Weight

Previous Treatment of Hair Prior to Reductive Polymerization	Viscosity Ave. Mol. Wt.
Unaltered	7.5 to 10.2 x 10^4
Bleached	7.6 x 10^4
Reduced-oxidized	9.1 x 10^4

Polymer Identification and Molecular Weight

More extensively bleached hair (once as above with a 24-hour reaction time) provides an add-on of 119% PMMA, using the same conditions of polymerization. The synthetic polymer in this hair sample was isolated by acid hydrolysis, drying, and extraction with benzene. The residue from benzene extraction was identified as PMMA *via* infrared spectroscopy and refractive index. The viscosity average molecular weights (3) were estimated in polymer isolated in this manner from bleached, reduced-oxidized, and unaltered hair. These data (Table III) suggest that the previous history of the hair, i.e., prior to the reductive polymerization treatment, has little influence on the degree of polymerization of the polymer formed in hair under the conditions of reaction used in this study.

Microscopical Examination of Isolated Polymer

Figures 9 and 10 are copies of photographs taken with a scanning electron microscope (SEM). These photographs reveal the surface of human hair fibers containing a small amount (16%) and a large amount of PMMA (119%). The polymer coating on the fiber surface is thick in both cases, yet the fibers retain some of their surface identity, i.e., repeating irregularities perpendicular to the fiber axis, which correspond to scale edges covered by a thick layer of polymer.

Filament-like fragments were isolated from PMMA-containing hair after treatment with 5*N* hydrochloric acid. These fragments were up to several millimeters in length and roughly the same diameter as the polymer-containing fibers. Microscopical examination, solvent extraction, and infrared spectroscopy suggest that these fragments consist mainly of PMMA. Figures 11 and 12 are SEM photographs of the fibrous solid remaining after acid hydrolysis of hair containing 119% PMMA and 16% PMMA. Figure 12 is an end view and Figure 11 a cross section. The sample containing the larger amount of PMMA is a porous yet almost completely filled cylinder while only a thin-walled hollow cylinder remains from the sample with the lower add-on, consistent with a diffusion-controlled polymerization process. These results also suggest that the hydrolysis provides a rather selective removal of the hair from the polymer with only minor alterations to the gross structure of the PMMA.

Figure 9. Surface of hair fibers containing 119% PMMA

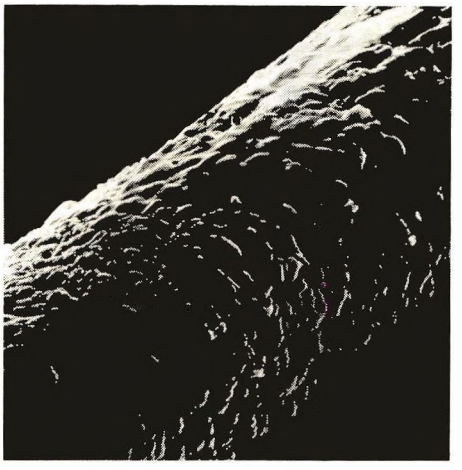

Figure 10. Surface of a hair fiber containing 16% PMMA

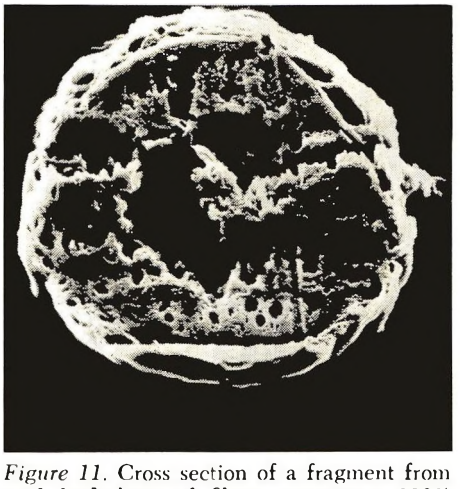

Figure 11. Cross section of a fragment from acid hydrolysis of fibers containing 119% PMMA

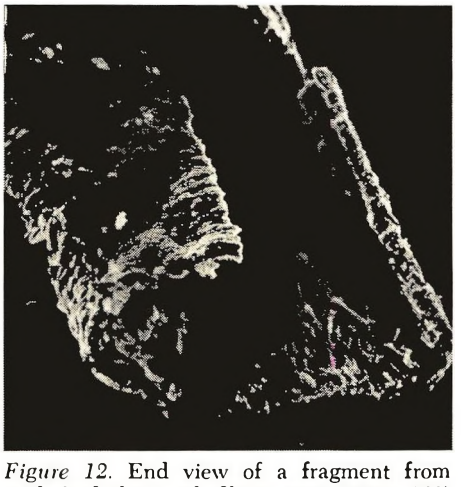

Figure 12. End view of a fragment from acid hydrolysis of fibers containing 16% PMMA

The fibrous solids are virtually inert to aqueous solvent systems; however, they are quickly disrupted by organic solvents such as benzene or ethylene dichloride, which dissolve the PMMA leaving behind pigment granules and a small amount of fibrous matter. The latter two components amount to approximately 10% by weight of the fibrous solid.

An interesting contrast to fibrous solid remaining after acid hydrolysis are similar structures which remain after treatment of PMMA-containing hair with sodium sulfide solution at room temperature for 18 hours (Fig. 13). Apparently the hair fiber structure is more inert to the sodium sulfide system,

Figure 13. End view of a fragment from sodium sulfide reaction with hair fibers containing 119% PMMA add-on

since treatment of fibrous solid remaining from this procedure with benzene or ethylene dichloride results in a relatively slow rate of dissolution leaving behind a much larger quantity of solid matter.

Summary

Thioglycolic acid–CHP and bisulfite–CHP are effective systems for polymerizing methyl methacrylate into human hair. The polymer forms initially at or near the fiber surface and grows inwardly. The rate of polymerization is governed by diffusion of CHP and/or MMA into the fibers. Polymerization occurs more rapidly into bleached or reduced-oxidized hair than into chemically unaltered hair, although degree of polymerization is not significantly affected by these same variables. Porous filament-like fragments consisting

primarily of PMMA were isolated by dissolving fiber from polymer through acid hydrolysis. Sodium sulfide solutions produced similar fragments, not as porous, containing more hair. The possibility for using related techniques for fiber structural studies exists.

Acknowledgment

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Society of Cosmetic Chemists Award Sponsored by International Flavors and Fragrances, Inc.

The 1973 Society of Cosmetic Chemists Award sponsored by International Flavors and Fragrances, Inc., has been presented to Mr. Sal DiBianca of the Mennen Company, for his paper entitled "Innovative Scanning Electron Microscopic Techniques for Evaluating Hair Care Products."

The award, consisting of a scroll and a $1000 honorarium, is presented annually to the author or authors of the most meritorious paper published in the JOURNAL OF THE SOCIETY OF COSMETIC CHEMISTS, U.S.A. Formal presentation was made by Mr. Mitchell Schlossman, Award Chairman, at the May 9, 1974, luncheon session during the Society's Seminar in Chicago, Illinois.

Left to right: Dr. Hyman Henkin, SCC President, Mr. Sal DiBianca, Award Recipient, and Mr. Mitchell L. Schlossman, Award Chairman

J. Soc. Cosmet. Chem., **25**, 423-435 (August 1974)

Auswirkungen grenzflächenaktiver Substanzen auf Löslichkeit, chemische Stabilität und Verfügbarkeit cutan applizierter Wirkstoffe

BERNHARD C. LIPPOLD *

Vortrag anläßlich der Vortrags- und Diskussionstagung der Gesellschaft Deutscher Kosmetik-Chemiker e.V., Baden-Baden, Bundesrepublik Deutschland, 14.—16. März 1974.

Synopsis—Effects of Surface-Active Materials on the Solubility, Chemical Stability, and Availability of Cutaneous Applied Agents.—SURFACE-ACTIVE MATERIALS in solution—especially above their CMC— influence cutaneously applied agents differently. The presence of MICELLES generally improves SOLUBILITY but can effect responses of INTOLERANCE. The rates of reactions of HYDROLYTIC and OXIDATIVE PROCESSES are altered by MICELLE FORMERS. In order to predict STABILIZATION, exact knowledge of the DECOMPOSITION REACTIONS is required. With regard to AVAILABILITY OF THE AGENT, the presence of surface-active materials has far-reaching consequences. Reduction of availability i.e. LOWERED ACTIVITY, depends greatly on the physicochemical properties of the agents. The regularities pertaining to micellar solutions are definitely applicable to other systems.

* Dr. Bernhard C. Lippold, Pharmazeutisch-technologische Abteilung am Institut für Pharmazie und Lebensmittelchemie der Universität München, D-8 München 2, Sophienstraße 10.

Grenzflächenaktive Substanzen finden als Hilfsstoffe bei der Herstellung cutan zu applizierender Zubereitungen vielfach Anwendung. In Lösungen und Sprays, Emulsionen und Suspensionen sowie Pudern und Reinigungsmitteln erfüllen sie so verschiedenartige Aufgaben wie Löslichkeitsverbesserung eingearbeiteter Wirkstoffe, Dispergierung von Öl in Wasser oder von Wasser in Öl und Benetzung suspendierter Partikel. Gleichzeitig können sie dabei durch spezifische Wechselwirkungen mit den verarbeiteten Substanzen deren chemische Stabilität und Verfügbarkeit beeinflussen und damit die Wirksamkeit der Zubereitung verändern. Gesetzmäßigkeiten hinsichtlich dieses Einflusses bestehen allerdings nur vereinzelt. Am übersichtlichsten sind die Verhältnisse bei Lösungen. An diesen relativ einfachen Systemen wird im folgenden auf charakteristische Auswirkungen, die Tensidzusatz bei cutan applizierten Wirkstoffen hervorrufen kann, eingegangen. Davon ausgehend können in gewissem Umfang Voraussagen auch für kompliziertere Systeme gemacht werden.

Grenzflächenaktive Substanzen (Tenside) mit entsprechend hydrophilen Eigenschaften assoziieren in wäßriger Lösung zu Micellen. Die Micellenbildung ist entscheidend für die Beeinflussung der Löslichkeit, der chemischen Stabilität und der Verfügbarkeit von Wirkstoffen, die in diesem System gleichzeitig enthalten sind. Die Betrachtungen lassen sich dadurch wesentlich vereinfachen, daß man eine micellare Lösung als kolloiddisperses Zweiphasensystem betrachtet (1) (2). Die Tensidaggregate stellen dabei die disperse Phase dar, Wasser ist das Dispersionsmittel.

Die Gegenwart dieser dispersen Phase, häufig auch als micellare Pseudophase bezeichnet, hat auf die Löslichkeit schlecht löslicher Substanzen praktisch immer einen positiven Einfluß. Die Solubilisation hat man sich als Aufnahme des schlecht löslichen Stoffes in die Micellen vorzustellen. Dabei ergeben sich drei prinzipielle Möglichkeiten der Einlagerung des Wirkstoffes in Tensidaggregate. Ein extrem lipophiler Stoff wird danach in das Innere der Micellen eingelagert, amphiphile Moleküle dagegen richten sich wie die Moleküle des Micellenbildners aus: Der hydrophile Moleküleanteil weist nach außen, der lipophile nach innen. Ist die amphiphile Substanz selbst ein Assoziationskolloid, entstehen Mischmicellen. Relativ hydrophile Verbindungen schließlich werden im allgemeinen nur an die äußeren Bereiche der Micellen gebunden. Diese Verhältnisse lassen sich z. B. über UV- und NMR-Spektren entsprechender Solubilisate belegen (1) (2) (3) (4).

Wo auch immer der lösungsvermittelte Stoff eingelagert wird, allgemein sollte zu erwarten sein, daß die Sättigungslöslichkeit mit zunehmender Tensidkonzentration annähernd linear ansteigt, wie aus folgender Ableitung zu ersehen ist:

$$VK_m = \frac{C_m}{C_w} = \frac{S_m/M}{S_w/W} = \frac{S_m \cdot W}{M \cdot S_w}$$

Dabei sind VK_m der Verteilungskoeffizient zwischen micellarer Pseudophase und Wasser, C_m bzw. C_w die Konzentrationen der Substanz S in der Micellenphase bzw. der wäßrigen Lösung außerhalb der Micellen. S_m bzw. S_w bedeuten die Substanzmengen in den Micellen bzw. in der wäßrigen Lösung, M und W sind die Volumina bzw. die Mengen an Micellenbildnern und Wasser. Setzt man für S_w die Sättigungsmenge der Substanz in Wasser (S_s) ein und für S_m die Differenz aus der insgesamt gelösten Menge (S_g) und der Sättigungsmenge in der wäßrigen Lösung (S_s), so folgt:

$$VK_m = \frac{(S_g - S_s) \cdot W}{M \cdot S_s} = k \cdot \frac{(S_g - S_s)}{M}$$

In der Formel ist der Quotient W/S_s zur Konstanten k zusammengefaßt. Bei Auftragung der Differenz $S_g - S_s$ gegen M resultiert bei Gültigkeit des Modells der micellaren Pseudophase und bei nicht zu niedrigen Wirkstoffkonzentrationen eine Gerade mit der Steigung VK_m/k.

Allerdings können sich auch gänzlich andere Verhältnisse ergeben, nämlich dann, wenn spezifische Wechselwirkungen zwischen den Assoziationskolloiden und den Wirkstoffen stattfinden.

Derartige spezifische Wechselwirkungen sind in *Abb. 1* besonders für cutan applizierte Wirkstoffe dargestellt.

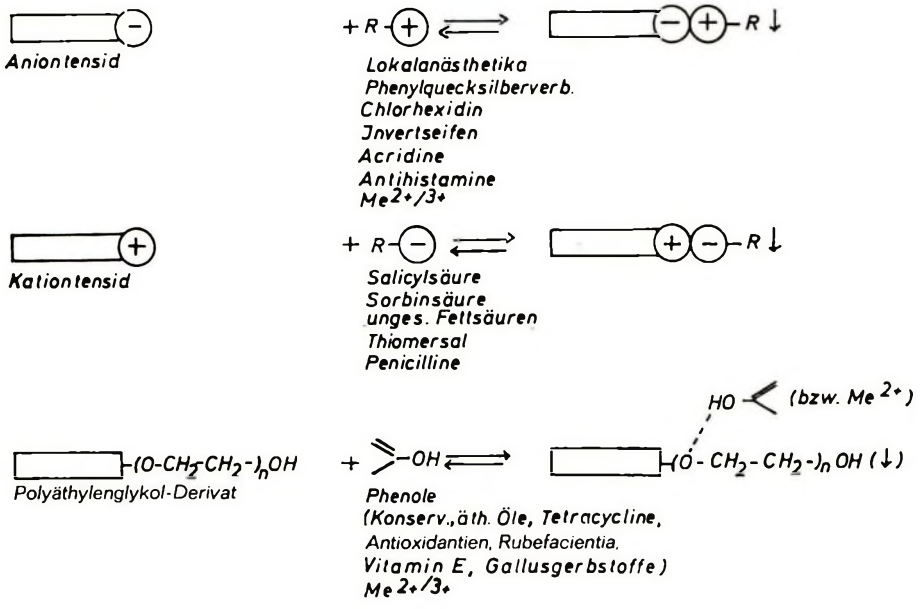

Abbildung 1

Reaktionsmöglichkeiten von Tensiden mit cutan applizierten Wirkstoffen

Danach reagieren anionische Tenside stöchiometrisch mit kationischen Substanzen, wobei schon bei niedrigen Konzentrationen Fällungen auftreten können. Diese gehen allerdings bei weiterer Tensidzugabe durch Solubilisation des Niederschlages in Lösung. Entsprechendes gilt für Wechselwirkungen zwischen kationischen Micellenbildnern und anionischen Wirkstoffen *(Abb. 1)*. Auch zwischen nichtionischen Tensiden vom Typ der Polyäthylenglykolderivate und Phenolen bzw. mehrwertigen anorganischen Kationen kann es zu Fällungsreaktionen kommen *(Abb. 1)*, die hier allerdings nicht stöchiometrisch verlaufen. Die Niederschläge sind ebenfalls solubilisierbar.

Kombinationen, die zu diesen Unverträglichkeitsreaktionen führen, stellen einerseits — technologisch gesehen — Kunstfehler dar, sie lassen sich aber andererseits zum qualitativen und quantitativen Nachweis der Reaktionspartner heranziehen (5) (6) (7). Die Beseitigung sichtbarer Unverträglichkeiten durch Lösungsvermittlung führt keineswegs generell zu einwandfreien Zubereitungen („larvierte Inkompatibilität") (8), vielmehr ist deren Wirksamkeit zu überprüfen.

Bei Vermittlung der Lösung von Farbstoffen wird durch die Einlagerung der Farbstoffmoleküle in Micellen der Farbcharakter häufig in typischer Weise verändert. Diese Befunde beruhen z. T. auf der Bildung salzartiger Verbindungen zwischen Farbstoff und Micellenbildner und deren Einlagerung in Tensid-Assoziate (5), z. T. aber auch auf dem direkten Einbau der Farbstoffmoleküle in die Micellen. Da die Farbänderung jeweils in dem Moment einsetzt, als Micellen in der Lösung sind, bei der kritischen Micellenbildungskonzentration, kann sie für deren Bestimmung herangezogen werden.

Die Assoziation der Tenside zu Micellen beeinflußt neben der Löslichkeit auch die chemische Stabilität inkorporierter Wirkstoffe. Die erste grundlegende Arbeit auf diesem Gebiet erschien 1960 von S. RIEGELMANN (9). Sie behandelt den Effekt des Einschließens von Benzocain in Micellen auf dessen Stabilität. Die zahlreichen weiteren Untersuchungen zu diesem Fragenkomplex [z. B. (10)—(20)] lassen nur eine zusammenfassende Darstellung zu, wobei zwischen der Beeinflussung hydrolytischer und oxidativer Reaktionen unterschieden werden soll.

Cutan applizierte Ester, die hydrolytischer Zersetzung unterliegen können, kommen aus der Reihe der baktericiden p-Hydroxybenzoesäureester, der Lokalanästhetika vom Typ der p-Aminobenzoesäureester sowie der Steroid- und Fettsäureester. Ebenfalls zu den hydrolytischen Reaktionen ist die Abspaltung von Chlor z. B. aus dem Konservierungsmittel Trichlorbutanol zu rechnen. Bei all diesen Substanzen hat sich gezeigt, daß die Hydrolyse durch Aufnahme in Micellen verlangsamt werden kann, daß die Stabilität in Gegenwart von Micellenbildnern häufig verbessert ist. Das trifft allerdings keineswegs immer zu. Bei kationischen Tensiden etwa in alkalischer Lösung ist häufig Hydrolysebeschleunigung festzustellen. Durch die positive Ladung der Tensid-Assoziate werden Hydroxid-Ionen angezogen, die trotz Aufnahme der Ester in Micellen vermehrte hydrolytische Spaltung bewirken können. Entsprechend kann bei Aniontensiden die mit Säure katalysierte Hydrolyse verstärkt werden. Nur im Fall nichtionischer Micellenbildner ist grundsätzlich mit Stabilisierung zu rechnen, gleichgültig ob Wasser, Protonen oder Hydroxid-Ionen die Esterspaltung hervorrufen.

Neben der Ladung der Tensidmicellen ist die Verteilung der Ester zwischen micellarer Pseudophase und Wasser entscheidend für den Stabilisierungseffekt, denn nur der gebundene Esteranteil kann stabilisiert werden. So zeigt sich z. B., daß der stabilisierende Effekt homologer Polyäthylenglykol-Fettalkoholäther auf die Hydrolyse von Nicotinsäureestern durch Alkali mit

ihrem Bindungsvermögen korreliert werden kann (20) *(Abb. 2)*. Der Stabilisierungsgrad Q, der angibt, um wieviel die Halbwertzeit der Hydrolyse der Nicotinsäureester durch Alkali durch Micellenbildner vergrößert wird, d. h. um wieviel stabiler die Ester sind, nimmt mit steigender Bindung zu. Allerdings ergibt sich aus *Abb. 3*, daß bei Tensiden mit konstantem Kohlenwasserstoffanteil und variierter Polyäthylenglykolkette bei gleicher Bindung sich Unterschiede in der Stabilisierung durch die Micellenbildner feststellen lassen. Dabei ist die Verhinderung der Hydrolyse um so wirksamer, je länger die Polyäthylenglykolkette ist. So erhöht sich z. B. bei einer Bindung von ca. 95 % die Stabilität um das 8—22fache *(Abb. 3)*. Diese Befunde lassen sich folgendermaßen deuten: Da die Estergruppe im hydratisierten äußeren Bereich der Micellen fixiert sind (4), bewirken längere Polyäthylenglykolketten einen besseren Schutz vor hydrolytischer Zersetzung als kürzere. Es zeigt sich also, daß nicht nur das Ausmaß der Solubilisation die Stabilisierung beeinflußt, sondern auch die Art der Einlagerung in die Micellen. Damit kommt auch der gezielten Auswahl nichtionischer Lösungsvermittler bei Stabilitätsproblemen besondere Bedeutung zu.

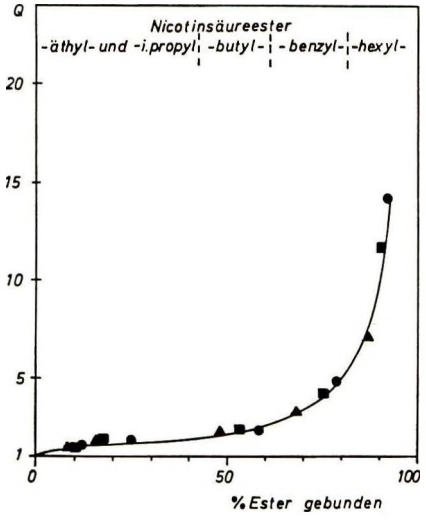

Abbildung 2

Stabilisierungsgrad (Q) der Nicotinsäureester in Abhängigkeit vom Bindungsvermögen der Tenside (Boratpuffer pH 10,0; Ionenstärke 0,08; 20° C); Polyäthylenglykol-1000-Lauryläther, Polyäthylenglykol-1000-Myristyläther, Polyäthylenglykol-1000-Palmityläther

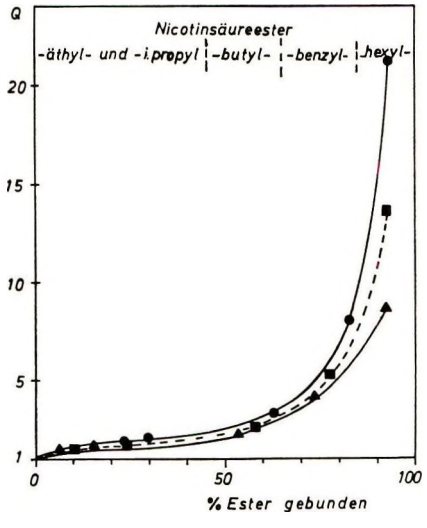

Abbildung 3

Stabilisierungsgrad (Q) der Nicotinsäureester in Abhängigkeit vom Bindungsvermögen der Tenside (Boratpuffer pH 10,0; Ionenstärke 0,08; 20° C); Polyäthylenglykol-900-Stearyläther, Polyäthylenglykol-1400-Stearyläther, Polyäthylenglykol-2000-Stearyläther

Die Auswirkung von Micellenbildnern oberhalb der kritischen Micellenbildungskonzentration auf Oxidationsreaktionen sind komplexer (10) (17) (18) (19). Bei der Beurteilung entsprechender experimenteller Befunde sind die Vorgänge der Autoxidation von besonderem Interesse. Bei einfachen Oxidationsreaktionen *(Abb. 4)* reagiert das Ausgangsprodukt nach Aktivierung direkt mit Sauerstoff zum Oxidationsprodukt. Dabei können Licht, Wärme oder Schwermetalle die Reaktion katalysieren. Außerdem ist die Reaktionsgeschwindigkeit vielfach von der Wasserstoffionenkonzentration abhängig. Derartige Reaktionen sind z. B. typisch für die Autoxidation der Phenole und ihrer Derivate. Experimentelle Ergebnisse zeigen, daß diese Reaktionen in micellarer Lösung im allgemeinen langsamer ablaufen. Dabei kann angenommen werden, daß die Micellen den Zutritt von Sauerstoff zu den solubilisierten Substanzen erschweren. Darüber hinaus dürfte ein Schutz etwa gegenüber katalytisch wirkenden Metallionen gegeben sein.

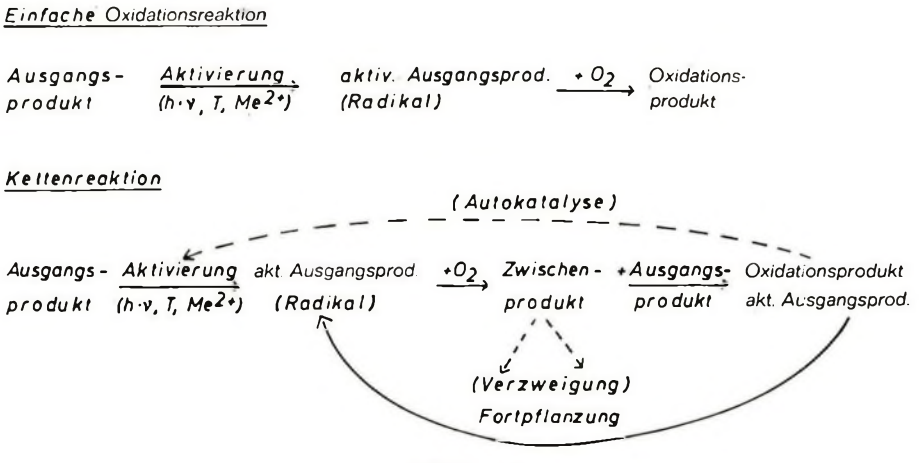

Abbildung 4

Schematische Darstellung von einfachen und Kettenreaktionen bei oxidativen Prozessen

Bei Kettenreaktionen *(Abb. 4)* ergibt sich ein anderes Bild. Hierzu gehören z. B. die Autoxidation ungesättigter Fettsäuren und ihrer Ester, von Aldehyden etwa aus ätherischen Ölen und von Vitamin A. Diese Reaktionen werden nach einmaliger Aktivierung wegen des Mechanismus der Kettenfortpflanzung um so schneller, je höher die „lokale" Konzentration des Ausgangsproduktes ist. Nur bei entsprechend hohen Konzentrationen ist ohne erneute Aktivierung weiterer Ablauf der Reaktion möglich, können autokatalytische Prozesse und Kettenverzweigungen wirksam werden. Setzt man voraus, daß der geschwindigkeitsbestimmende Schritt bei oxidativen Kettenreaktionen

nicht die Reaktion mit Sauerstoff ist *(Abb. 4)*, ergibt sich folgendes *(Abb. 5)*: Die wäßrige Lösung der Substanz besitzt relativ hohe Stabilität, da der Wirkstoff molekulardispers vorliegt ($c < c_s$)*. Nach Überschreiten der kritischen Micellenbildungskonzentration wird die Substanz von Micellen aufgenommen. Die Oxidationsgeschwindigkeit beschleunigt sich sprunghaft wegen der relativ hohen lokalen Konzentration in den Micellen. Weiterer Tensidzusatz bewirkt, daß die Substanzkonzentration pro Micelle abnimmt, die Stabilität sich erhöht. Geht man allerdings von einer Dispersion der instabilen Substanz aus (gestrichelte Linie in *Abb. 4*, $c > c_s$), so ist mit Tensidzusatz eine ständige Abnahme der Oxidationsgeschwindigkeit zu erwarten, da die zunächst großen dispersen Teilchen durch die zugefügten grenzflächenaktiven Stoffe besser zerteilt bzw. emulgiert und dann solubilisiert werden. Durch die damit erfolgende Abnahme der lokalen Konzentration nimmt die Stabilität zu. Bei solchen Kettenreaktionen dagegen, für die der geschwindigkeitsbestimmende Schritt der Sauerstoffzutritt ist, kann Einschluß durch Micellen und damit Behinderung der Umsetzung mit Sauerstoff in jedem Fall stabilisierend wirken. Die dargestellten Gesetzmäßigkeiten sind allerdings nicht immer so klar zu erkennen, da z. B. zusammen mit den Hilfsstoffen Peroxide oder Schwermetallspuren als Verunreinigungen in das System eingeschleppt werden können.

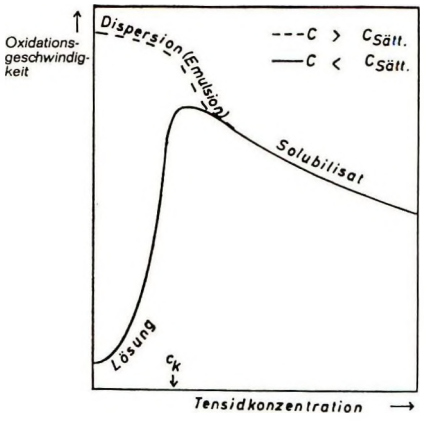

Abbildung 5

Oxidationsgeschwindigkeit von Wirkstoffen nach dem Mechanismus der Kettenreaktion als Funktion der Tensidkonzentration

* c = vorhandene Wirkstoffkonzentration
c_s = Sättigungskonzentration des Wirkstoffes

Der dritte wesentliche Gesichtspunkt für die Beurteilung cutan zu applizierender Lösungen ist die Verfügbarkeit der Wirkstoffe, ein entscheidendes Kriterium für die Wirksamkeit eines Präparates. Unter der biologischen oder Bioverfügbarkeit einer Wirksubstanz aus einer Zubereitung ist dabei die relative Menge zu verstehen, die durch Resorption den Blutkreislauf erreicht (21). Vereinfacht ausgedrückt bedeutet das: Bioverfügbarkeit = resorbierte Menge Wirkstoffe in %. Bei cutaner Applikation spielt allerdings die Bioverfügbarkeit nur in den wenigen Fällen tatsächlich erwünschter Resorption eine Rolle, z. B. bei der cutanen Gabe von Testosteron. Viel häufiger dagegen wird eine direkte lokale Wirkung angestrebt, d. h. eine oberflächliche oder nach Penetration in die Epidermis bzw. Permeation in das Corium, ohne daß dabei allerdings Resorption ausgeschlossen werden kann. Substanzen, die in diesem Zusammenhang zu nennen sind, gehören zu den Lokalanästhetika, den Antihistaminen, den Antimykotika, Corticoiden, Antiperspirantien, Vitaminen, Rubefazientien und vielen anderen. Bei diesen ist also nur eine „lokale" Bioverfügbarkeit notwendig, d. h. es ist die Frage nach der Freisetzung der Wirkstoffe aus der Zubereitung zu stellen. Gleiches gilt für Konservierungsmittel, die in cutan zu applizierenden Zubereitungen häufig enthalten sind. Gerade diese können in Zubereitungen starker Aktivitätsminderung unterworfen sein (8). Besonders Tenside spielen bei der Beeinflussung der Freisetzung von Wirkstoffen und damit bei der Veränderung der Wirksamkeit von Zubereitungen eine große Rolle.

Aus Untersuchungen von E. Ullmann et al. (11) geht z. B. hervor, daß Antibiotika in Tensidlösungen entscheidenden Aktivitätsänderungen unterliegen. Das zeigt *Abb. 6*. Die relative biologische Aktivität, ermittelt durch die Größe des Hemmhofes im Agardiffusionstest, nimmt bei niedrigen Tensidkonzentrationen zunächst zu, sinkt dann allerdings ab. Die anfängliche Wirkungssteigerung könnte dabei auf geringe bakteriostatische Eigenschaften des Tensids selbst und auf Erhöhung der Membrandurchlässigkeit der Bakterien zurückzuführen sein. Bei hohen Tensidkonzentrationen werden diese Effekte dann allerdings von dem wirkungsmindernden Einschluß der Antibiotika durch die Micellen übertroffen. Dabei ist in *Abb. 6* bei der freien Säure Phenoxymethylpenicillin mit stärkerem Einschluß in Micellen zu rechnen als beim hydrophilen Kaliumsalz; der Wirkungsverlust ist dementsprechend ausgeprägter. Ähnliche Ergebnisse sind für Chloramphenicol, Tetracyclin und Bacitracin nachweisbar (11). Diese Befunde in vitro sind allerdings nicht ohne weiteres auf Verhältnisse in vivo übertragbar. Hierbei sind die Verhältnisse wesentlich komplexer. Micellarer Einschluß könnte zwar einer-

seits die Verfügbarkeit verringern, andererseits gelten grenzflächenaktive Substanzen aber als Gleitschienen und Penetrationsbeschleuniger (21).

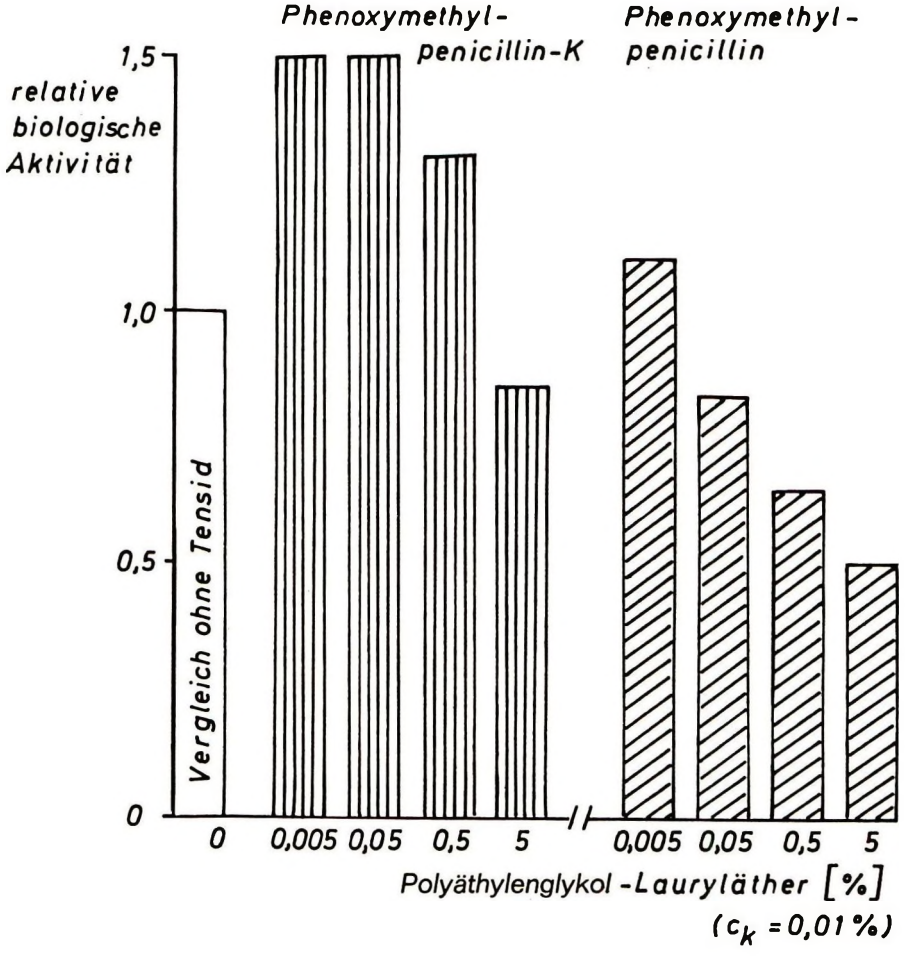

Abbildung 6

Relative biologische Aktivität von Penicillinen in Tensidlösungen unterschiedlicher Konzentrationen

Untersuchungen zur Aktivitätsbeeinflussung von phenolischen Konservierungsmitteln in micellarer Lösung von Polyäthylenglykolderivaten zeigen, daß Phenolderivate eine entscheidende Wertminderung erfahren können (6) (7). Der Mechanismus dieser Wertminderung ist folgendermaßen zu erklären: Zwischen Phenolderivat und Polyäthylenglykol-Fettsäureester bildet sich un-

terhalb der kritischen Micellenbildungskonzentration ein Addukt durch Wasserstoffbrückenbildung *(Abb. 1)*. Dieses Addukt wirkt noch bakteriostatisch und baktericid. Bei entsprechend hoher Phenolkonzentration kommt es zur Fällung. Beim Überschreiten der kritischen Micellenbildungskonzentration wird das lipophile Addukt von den Micellen solubilisiert, es verliert damit seine antibakteriellen Eigenschaften. Die Inaktivierung der Phenole ist aber keineswegs gleichartig, vielmehr zeigt sich, daß sie um so größer ist, je lipophiler die Phenole bzw. ihre Fällungsprodukte sind. Eine entsprechende Beziehung ist in *Abb. 7* zu sehen. Mit zunehmenden Verteilungskoeffizienten VK der Phenole für das System Ölsäuredecylester/Wasser vermindert sich sein Wert. Ganz ähnliche Verhältnisse ergeben sich, wenn die Verteilung zwischen micellarer Pseudophase und Wasser zugrunde gelegt wird (VK_m): Je mehr vom eingesetzten Phenol von der micellaren Pseudophase aufgenommen wird, desto mehr nimmt die Inaktivierung zu. Bei Hexachlorophen beträgt sie in 5%iger Polyäthylenglykol-2200-Stearatlösung bereits 1000, d. h. es muß die 1000fache Menge eingesetzt werden, damit die gleiche antibakterielle Wirkung zustande kommt wie in einer wäßrigen Lösung. Die Kenntnis der Bindung von Konservierungsmitteln an Micellen erlaubt es, aufgrund der genannten Zusammenhänge Voraussagen über derartige Inaktivierungen zu treffen.

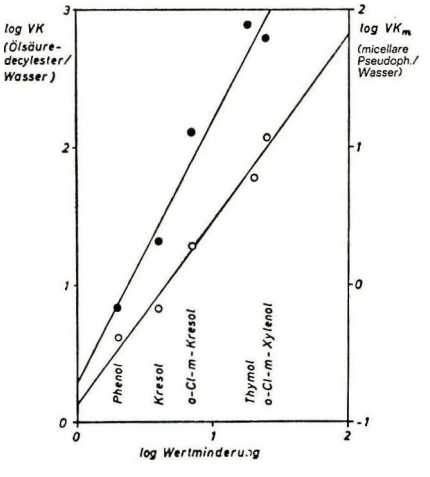

Abbildung 7

Beziehungen zwischen dem Logarithmus der Wertminderung von Phenolen in 5%iger Polyäthylenglykol-2200-Stearatlösung und dem Logarithmus ihrer Verteilungskoeffizienten (VK)

Ein ganz anderes Problem der Freisetzung bzw. Verfügbarkeit ergibt sich bei der Solubilisation von Duftstoffen, etwa ätherischer Öle. Derartige Solubilisate, häufig aus Kostengründen alkoholischen Lösungen vorgezogen, können unerwartete Begleiterscheinungen zeigen. Durch den bevorzugten Einschluß einer Komponente der Mischung kann erhebliche Geruchsverschiebung eintreten oder auch der Gesamtgeruch stark abgeschwächt werden.

Die für micellare Lösungen geltenden Gesetzmäßigkeiten lassen in gewissem Ausmaß auch Voraussagen auf kompliziertere Systeme zu, insbesonders dann, wenn sie ähnliche oder zumindest vergleichbare physikalisch-chemische Eigenschaften besitzen (16). Aus *Abb. 8* wird deutlich, daß z. B. im Falle des Systems Öl-Wasser-Tensid zwischen der molekulardispersen Lösung des Tensids, der micellaren Lösung und dem Solubilisat einerseits und der Emulsion bzw. dem Gel vom Typ der kristallinen Lösungen andererseits nur quantitative Unterschiede bestehen, die sich aus den Mengenverhältnissen der einzelnen Partner ergeben (23). Die wechselseitig ineinander überführbaren Systeme lassen sich auch auf entsprechende ölige Zubereitungen ausdehnen *(Abb. 8)*, für die analoge Gesetzmäßigkeiten abgeleitet werden können.

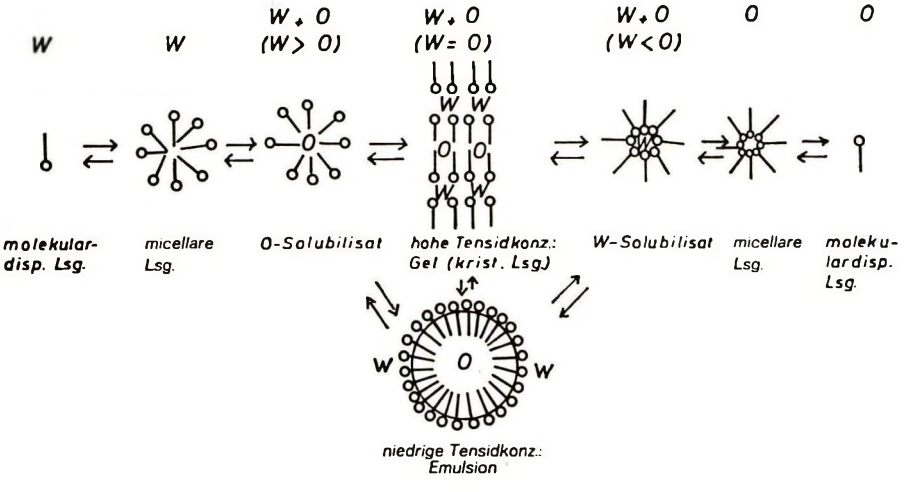

Abbildung 8

Ineinander überführbare Systeme, bestehend aus Wasser (W), Öl (O) und Micellenbildner (o—)

LITERATUR

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Society of Cosmetic Chemists Award Sponsored by Shaw Mudge and Co.

The 1973 Society of Cosmetic Chemists Award sponsored by Shaw Mudge & Co. has been presented to Dr. Alexander A. Fisher, New York University Medical Center, for his work on contact dermatology.

The award, consisting of a scroll and a $1000 honorarium is presented annually to the author or authors for outstanding contributions to safety in the use of toiletry and cosmetic products. Formal presentation was made by Miss Rosemarie Wallisch, 1974 Seminar Chairman, at the May 9, 1974, luncheon session during the Society's Seminar at Chicago, Illinois.

Left to right: SCC President Dr. Hyman Henkin, Award Recipient Dr. Alexander A. Fisher, and Seminar Chairman Miss Rosemarie Wallisch

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Application of Rheological Studies to Product Formulation, Stability, and Processing Problems

JOHN B. WARD, Ph.D., JAMES F. KINNEY, M.Sc., and HOSNY Y. SAAD, Ph.D.*

Presented May 3, 1973, Seminar, Cinncinnati, Ohio

Synopsis—The PHYSICAL CHEMICAL PRINCIPLES involved in RHEOLOGICAL MEASUREMENTS are briefly reviewed. Instrumentation including the Brookfield Viscometer, the Brookfield with Helipath, the Brookfield Plate and Cone Viscometer, and the Rotovisco Viscometer is discussed. Comparative data are presented for typical lotion, cream, and suspension products as measured with each of these instruments. The practical application of such data to FORMULATION, STABILITY, and PROCESSING studies is illustrated. The interpretive meaning of the mathematical equations governing this phenomenon and their application in achieving the desired effect are also discussed.

Introduction

The word "rheology" was first recognized in the work of Bingham and Crawford *circa* 1929 (1). The first Society of Rheology was founded in America in that year. In the late 1940's, scientists were still debating if "rheology" was the proper word to define the study of deformation and flow of matter. This brief insight into the history of this science is offered to illustrate the newness of the field.

Scott-Blair first directed the attention of pharmaceutical scientists to this new area in 1945 when he published an article in the Pharmaceutical Journal entitled, "Rheology and the Pharmacist" (2). This worker remained active in the field for over 20 years. His thesis in all of his work was to relate that property which consumers define as "feel" to scientific measure. One of his major contributions was the publication of a dictionary of terms used in rheology (3).

*Product Development Department, Avon Products, Inc., Suffern, N. Y. 10901.

Emulsions and suspensions are important classes of cosmetic formulations. However, little is known about the correlation between the rheology of a product system and its ultimate application or use in the cosmetic field. Great emphasis is still placed on arbitrary subjective evaluation, with little predictive knowledge of how the product system will perform or be altered by processing and filling procedures.

The cosmetic scientist is interested in the rheology of his product as it affects mixing, packaging, stability, dispensing, and ultimate use characteristics. In each of these instances, the sound application of rheological studies can avoid many pitfalls. The manner in which the consumer views product performance is nicely summarized by Marriott who wrote, "In use, cosmetic products are evaluated generally by touch. A touch of the finger tells of rigidity, thixotropy, viscosity, smoothness and texture in general. Coupled with the seeing eye, simply spreading the preparation on the skin can cause the brain to appreciate uniformity, coherence, absorption and many other features of the thin film—it may be shiny, be dull or matte, or have pearly lustre. Such procedures involve some motion or flow and fall within the ambit of rheology" (4).

This paper is sharply directed toward the practical use of rheology in the development of improved cosmetic products and is intended to give a concise review of rheology and its application to cosmetic formulations. General principles will be reviewed. The capabilities and limitations of four different viscometers will be presented by utilizing them in a rheological study of three model cosmetic formulas. The application of rheological principles to formulation and processing will be discussed. Case histories from experience will be presented to show how rheology is used to solve practical problems.

Review

Figure 1 briefly illustrates the four types of flow which are encountered, with definitions developed as a function of rate of shear *(G) versus* shearing stress *(F)*. These are as follows:

1. Newtonian flow is an orderly flow pattern in which the rate of shear is directly proportional to shearing stress. Viscosity values are obtained by dividing the rate of shear by the shearing stress, all expressed in appropriate units.

2. Plastic flow is characteristic of Bingham bodies. In this type of flow a certain Yield Value must be exceeded before flow starts. This type of flow will be discussed in more detail, particularly as it relates to formulation.

3. Pseudoplastic flow is characteristic of most natural and synthetic gums. In this type of flow the rate of shear is not directly proportional to the shearing stress. The curve passes through the origin, but is rarely linear. Recently, Yakatan and Araujo (5) proposed the use of an analog computer to simulate this type of flow. Mathematically, it is the most difficult form to handle.

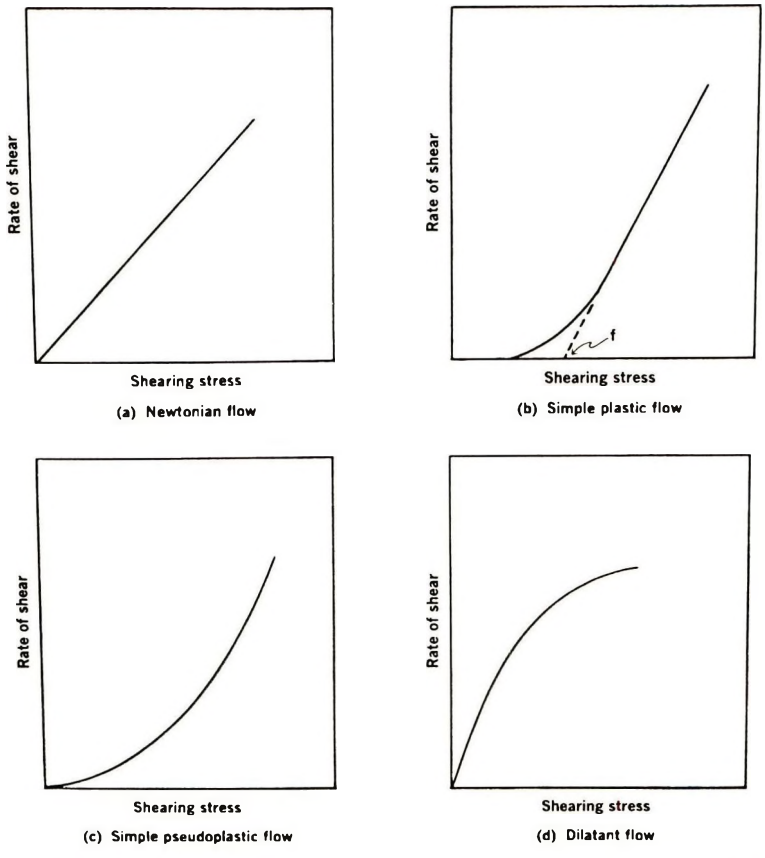

Figure 1. Examples of four types of flow (6) (reprinted with permission of copyright holder)

4. Dilatant flow is characteristic of some products containing high levels of deflocculated solids, such as oil slurries and muds. In this type of flow, an increase in viscosity is observed as the rate of shear is increased.

In Fig. 2, Martin (6) illustrates the pitfalls in relying on a single point measure of viscosity, particularly when working with non-Newtonian systems. Note that values of 20, 8.5, 10, and 5 poises are obtained, depending on the type of flow encountered.

In studying the rheology of a cosmetic system, the scientist should simulate the rates of shear which will be encountered in processing, filling, storing, removing from package, and applying.

Table I presents a variety of shear rate values taken from the cosmetic, pharmaceutical, and paint industries (7–10). Few viscometers can effectively encompass the variety of rates of shear which are cited. All values can be of interest to the cosmetic formulator.

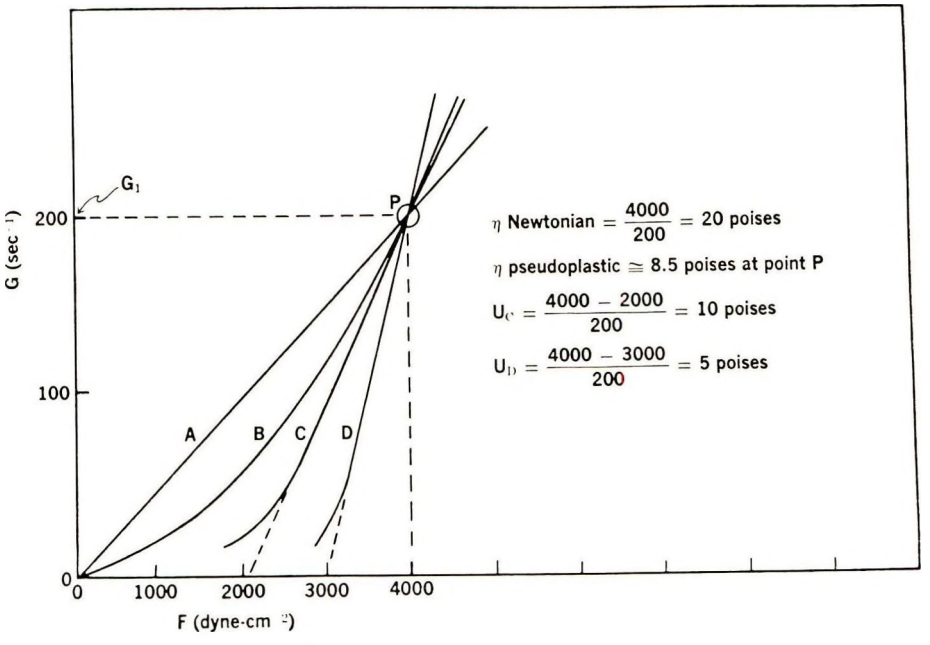

Figure 2. Illustration of single-point measure of viscosity (6) (reprinted with permission of copyright holder)

Table II illustrates the manner in which an unknown shear rate can be calculated. All that is required is a knowledge of the rate at which the application is made, and the thickness of the applied layer. This principle has been widely applied in paints, pharmaceuticals, and cosmetics (7–9). The rates of shear encountered in most processing equipment can be calculated by a bright chemical engineer.

Once the rates of shear which are encountered in the mixing, filling, extrusion, and application of a product are known, valid rheological studies can be undertaken. If the cosmetic scientist is to do an adequate job in developing his product, he must study shear with an instrument capable of making valid measurements over the entire shear range which the product may encounter in processing. Four types of viscometers are commonly employed in our laboratories including the Brookfield Synchro-Electric,* the Brookfield with T-Bar and Helipath,* the Brookfield/Wellington Cone and Plate Viscometer,* and the Haake Rotovisco.†

Figure 3 illustrates the geometry of the measuring device in each of these. With the Brookfield Synchro-Electric and the Brookfield with T-Bar and Helipath, direct scale readings are obtained which can be converted to relative

*Brookfield Engineering Laboratories, Inc., Stoughton, Mass.
†Gebrüder Haake, Berlin, Germany

Table I
Shear Rates of Cosmetic Interest

Operation	Assumptions	Rate of Shear (sec^{-1})	Source
Roller milling	Rollers 0.009 cm apart	10^3 to 1.2 x 10^4	Sherman (7)
Roller milling (2 rolls)	Rollers 0.009 cm apart Speeds of 167 and 55 cm/sec	1.2 x 10^4	Henderson (8)
Colloid milling	...	Several hundred thousand	Henderson (8)
Forcing through hypodermic syringe	Equivalent to crude homogenization	10^4	Henderson (8)
Topical application	Velocity of 10 cm/sec		Sherman (7)
	Layer of 0.1 cm	10^2	
	Layer of 0.01 cm	10^3	
	Layer of 0.001 cm	10^4	
Pouring from a bottle	...	53	Sherman (7)
		100	Henderson (8)
Aspiration of a plastic spray bottle	Small nasal tip	2 x 10^2	Henderson (8)
Passage through an aerosol valve	...	10^3 to 10^5	Sherman (7)
Extrusion	Liquid cream from plastic bottle—Flow 1 cm^3/sec, orifice 1 cm	10	Sherman (7)
	Toothpaste from metal tube Flow 1 cm^3/sec, orifice 0.5 cm	10^2	
	Makeup from plastic tube Flow 0.1 cm^3/sec, orifice 0.1 cm	10^3	
Applying paint by brush	...	5 x 10^3 to 10^4	Fink-Jensen (9)
Application of lipstick	...	2 x 10^3 - 10^4	Kinney (10)

Table II
Estimated Shear Rate Employed during Lipstick Application

A. Surface Area Measurements
   1. Testers were asked to blot lips after lipstick applications.
   2. A planimeter was then employed to calculate the surface areas involved.
   3. The mean surface area was estimated at 10 cm^2/tester.
   4. The mean application rate v was 10 cm/sec.

B. Thickness of Lipstick Layer
   1. Lipstick samples were weighed before and after single applications.
   2. The mean lipstick weight applied per tester was determined as 0.05 g.
   3. The density assumed for each formulation tested was approximated as being equal to 1 g/cm^3.
   4. From the information given above, the thickness x of the applied lipstick layer was estimated as 0.005 cm.

C. γ shear rate $= v/x$

$$\gamma = \frac{10 \text{ cm/sec}}{0.005 \text{ cm}}$$

$$\gamma = 2000 \text{ sec}^{-1}$$

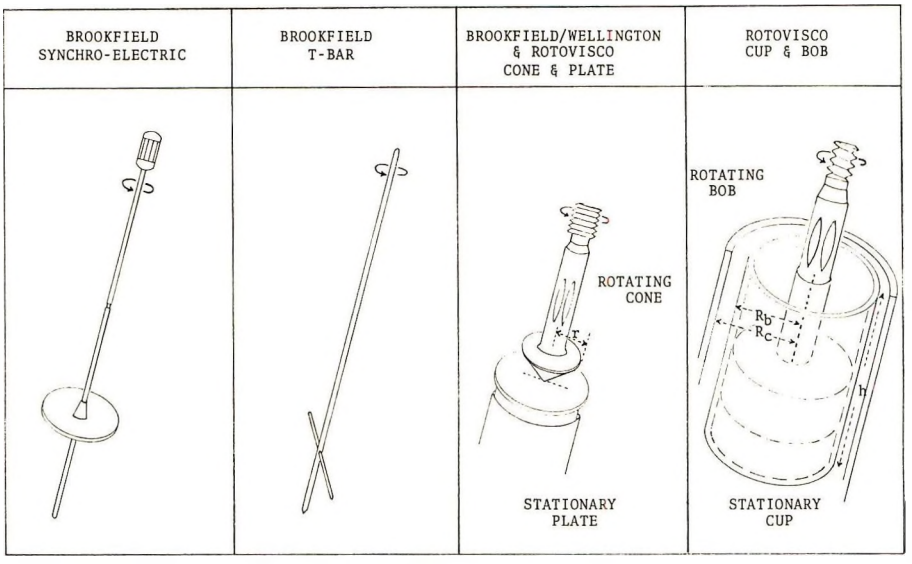

Figure 3. Viscometer geometry

viscosity. With the Brookfield/Wellington and the Haake Rotovisco, absolute values are obtained. Details of the equations and calculations involved are available in a paper by Sherman (11). These calculations are reasonably complex. In our work, the Brookfield/Wellington calculations have been programed with an 1800 IBM Computer. Note that with the conventional Brookfield Synchro-Electric, there is no sharp definition of the wall of the containing vessel. The instrument is standardized to read Newtonian fluids using a particular beaker as the containing vessel. When working with non-Newtonian systems, it is impossible to obtain accurate values in absolute viscosity. This can be done with the Brookfield/Wellington or Haake Rotovisco.

Comparative Viscometry

In order to illustrate the utility and limitations of each instrument, three model formulations of varying types for rheological study have been prepared.* Products include an emollient cream, an emollient lotion, and a liquid makeup. All are taken directly from the most recent edition of Sagarin (12) and are shown in Table III. As much as practical, all products were manufactured and studied under standardized conditions, particularly with respect to aging history.

Table IV shows the results of a series of determinations made on these formulations with the Brookfield Synchro-Electric and the Brookfield with

*Readings taken after 10 sec at cited rpm values.

Table III

Composition of Test Formulations

Ingredient	% w/w		
	Emollient Cream[a]	Emollient Lotion[b]	Liquid Makeup[c]
Part A			
Tween 40	1.00	...	...
Cetyl alcohol	2.00	1.00	...
Arlacel 83	5.00	...	...
Beeswax	5.00	...	...
Stearic acid	...	2.00	2.50
Diethylene glycol MS	...	2.00	...
Propylene glycol MS	...	2.00	6.00
Mineral oil	10.00	...	15.00
Lantrol	20.00	...	...
Lanolin	...	2.00	...
Petrolatum	20.00	...	...
Propyl paraben	0.15	0.15	...
Part B			
Methyl paraben	0.15	0.15	0.10
Borax	0.30	...	...
Water	36.10	81.40	53.10
Triethanolamine	...	1.00	1.30
Perfume	0.30	0.30	0.30
Part C			
Sodium lauryl sulfate	...	...	1.10
Bentonite	...	...	4.70
Kaolin	...	...	5.20
Dry powder (pigments, etc.)	...	...	11.00
Totals	100.00	100.00	100.00

[a] Formula 53 from reference (12), p. 63.
[b] Formula 76 from reference (12), p. 76.
[c] Formula 8 from reference (12), p. 324.

Table IV

Brookfield Synchro-Electric and T-Bar Helipath Viscosity Determinations on Cream, Lotion, and Liquid Makeup Formulas

Rpm	Viscosity (centipoise)[a]					
	Emollient Cream		Emollient Lotion		Liquid Makeup	
	Spindle #6	T-Bar C	Spindle #6	T-Bar C	Spindle #6	T-Bar C
2	197,000	172,500	22,500	65,000	35,000	43,000
4	124,500	156,250	16,000	43,750	18,750	27,500
10	71,000	76,000	10,600	21,600	8,900	14,600
20	41,750	46,300	6,300	12,700	5,150	8,200

[a] Taken in 250-ml beaker (Kimax—I.D.—2.5 in.)

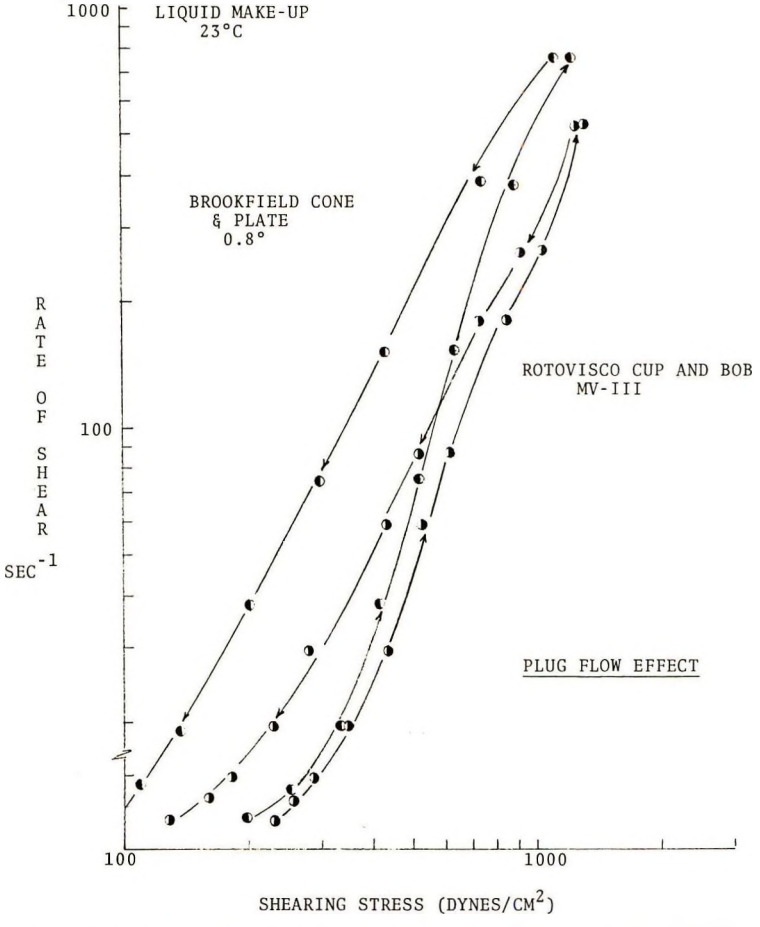

Figure 4. Comparison of measurements made on liquid makeup using Brookfield/Wellington Cone and Plate Viscometer and Haake Rotovisco with Cup and Bob

T-Bar and Helipath. Note that there is considerable variation in the viscosity of each formula measured at the same rpm. With non-Newtonian products such as these, the values obtained are only relative, not absolute. However, these values can serve as valuable benchmarks for the development chemist, when the instrument and environmental conditions are standardized as much as practical. When data are collected and viewed under these restrictions, one is able to quickly screen certain flow properties which may be useful guidelines in formulation. In addition, these numerical values may serve as valuable reference points for quality assurance in a production situation.

Figure 4 illustrates comparative data obtained with the liquid makeup using the Brookfield/Wellington Cone and Plate Viscometer and the Haake Rotovisco with Cup and Bob. At these relatively low shearing stresses, it ap-

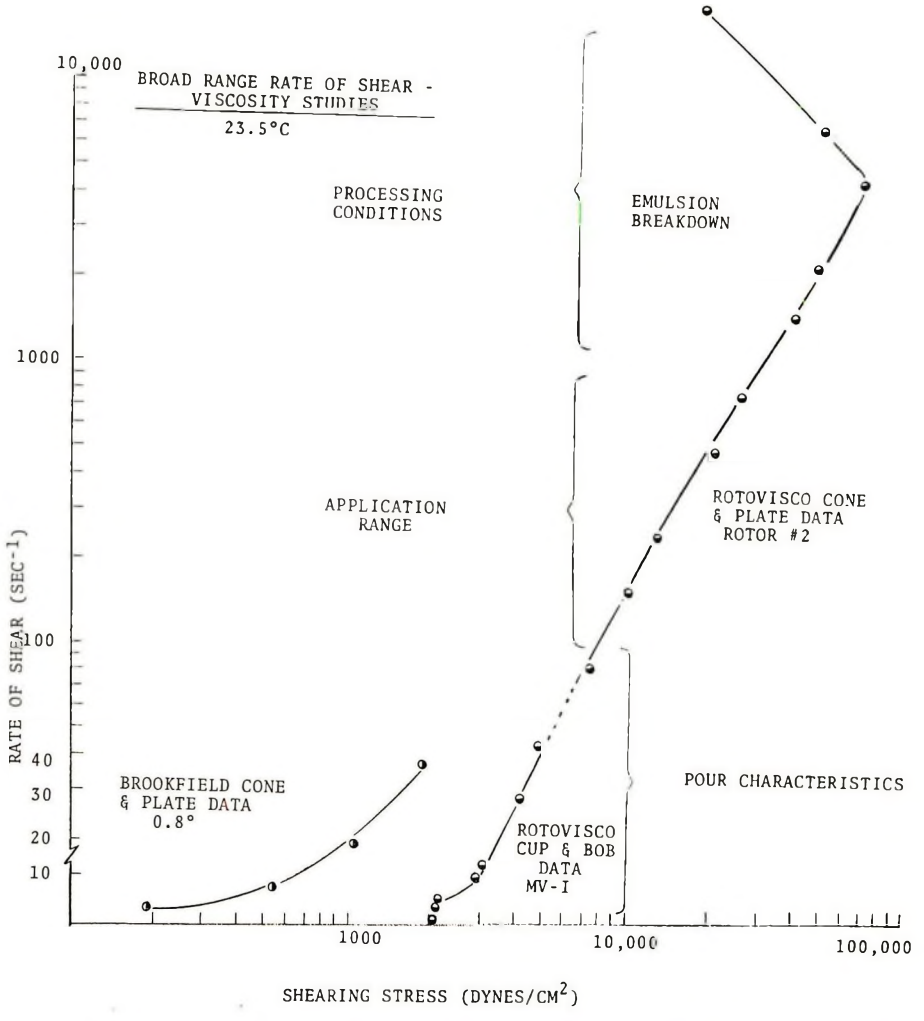

Figure 5. Comparison of measurements made on emollient cream using Rotovisco Cup and Bob, Rotovisco Cone and Plate, and Brookfield/Wellington Cone and Plate

pears that both instruments give similar initial curves. However, on downward curves, the Brookfield measurements show much greater breakdown than the Cup and Bob data. These differences are probably caused by the different geometry of the two measuring heads. When plastic flow is encountered, the Cup and Bob attachments are more likely to produce variable shear stress across the distance between the shearing head and the container walls. At a certain distance from the shearing head, the yield value of any sample may be high enough that there is no product flow at all. If a

portion of the sample receives little or no shear with a particular Cup and Bob combination, it will appear more viscous on the downward portion of the hysteresis curve. This plug effect may be partially eliminated by using the largest diameter Bob possible, or by using the appropriate Cone and Plate attachment for the Rotovisco.

Although the Haake Cup and Bob design presents some problems to the rheologist when dealing with plastic flow, its Cone and Plate attachment make it an extremely versatile instrument when a broad range of shear information is desired. Figure 5 illustrates how this attachment can be used to provide critical data on the emollient cream. Pour characteristics (10 to 100 sec^{-1}), application properties (100 to 1,000 sec^{-1}), and tendency to breakdown under processing conditions (1,000 to 10^5 sec^{-1}) can all be seen in the Rotovisco Cup and Bob and the Rotovisco Cone and Plate data. The data from one attachment lead into the next attachment on the Rotovisco.

For comparative purposes, the data obtained with the Brookfield/Wellington Cone and Plate Viscometer are included. Certain shortcomings in the response of this instrument can be noted, in that all values above about 1300 dynes/cm^2 have been lost. This can probably be attributed to poor functioning of the pneumatic strip recorder used in conjunction with this instrument. Because of the slow response time, considerable data are lost in the evaluation of a product of this type.

Considerations in Formulation

Yield Value

Meyer and Cohen presented a practical way to apply rheology to the formulation of stable suspensions (13). They demonstrated that a permanent suspension would result when the water phase exhibits a critical minimum yield value irrespective of apparent viscosity. They pointed out that settling is delayed by using ultrafine particle size, adjusting density, and adjusting viscosity. The method employed a Brookfield Synchro-Electric Viscometer, with all its limitations. They developed a value which they called the Brookfield Yield Value. This value is defined by the equation:

$$\text{Brookfield Yield Value} = \frac{\text{apparent viscosity at 0.5 rpm} - \text{apparent viscosity at 1.0 rpm}}{100}$$

Experimental Brookfield Yield Values were then established for a variety of natural and synthetic gums. An equation was developed for the yield value which was expected to produce a permanent suspension. Critical values in this equation included:

$$\text{Theoretical minimum yield value} = \frac{(\text{vol.} \times \text{density of particle}) - (\text{vol.} \times \text{density disp. medium}) \times (\text{acceleration of gravity})}{\text{cross sectional area of particle}}$$

While this is a simplistic approach, and does not consider many forces known to be at work in a suspension, it did afford these investigators a fairly reliable means of producing stable, permanent suspensions. The Carbopol resins emerged as the best suspending agents in this study, because they produced a high yield value when used in low concentrations.

Laboratory evaluation of a Carbopol®* 934 solution has shown that three types of yield value exist. This is illustrated in Fig. 6. Value B is the conventional or Bingham Value which is an extenson of the straight line portion of the curve. It is the most commonly cited value. Value A, which can be calculated, is the point at which it is presumed that laminar flow starts. Value A is sometimes referred to as the "Experimental Yield Value." This value can be obtained from measurements using a rotational viscometer. It is the same type of value reported earlier by Meyer and Cohen (13). Value C, which is perpendicular to the tangent is called calculated yield value and is very rarely used.

*B. F. Goodrich Chemical Co., Cleveland, Ohio.

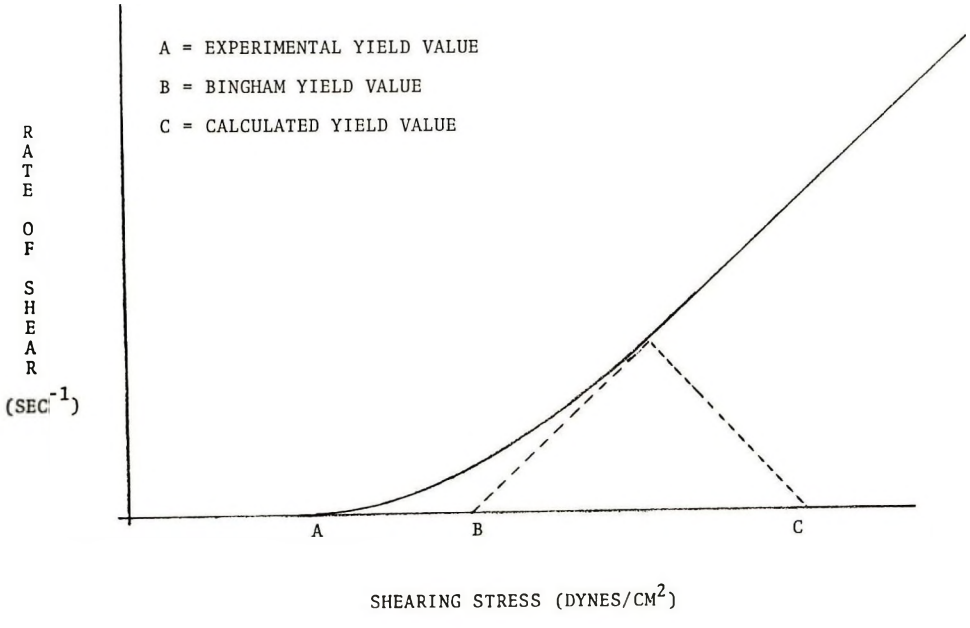

Figure 6. Yield values of a Carbopol 934 gel

The utilization of these yield values can be of great importance in evaluating drag, greasiness, and slip. It should be pointed out, however, that from a practical point of view, the Bingham Value is not unique. The experimental yield value is actually the point at which the flow or structural breakdown starts and it is the value of most concern in formulating.

Thixotropy

This phenomenon is observed to occur preferentially, although not exclusively in systems with elongated flat or long particles. For example, it can be observed in a freshly shaken suspension of iron oxide to which a little electrolyte has been added. Initially, this system behaves as a Newtonian liquid, but in the course of time, the system becomes plastic or gel-like, with a continuously increasing yield value. Here the particles adhere to each other, but the adhesion is so weak that it is completely destroyed by shaking. However, they reconstitute to form their plastic or gel-like state on standing, retaining enmeshed intermicellular liquid.

Martin (14) has indicated that the ideal suspending agent should have a high viscosity at negligible shear (shelf life) and a low viscosity at high shearing rates (free flowing during agitation). The simple system detailed above meets this description.

Electrolytic concentration and valency can effect the time of solidification or gel formation for a thixotropic system. Both tend to increase the time for solidification.

Increasing the H^+ ion concentration, or lowering the pH, increases the time for solidification. A drop of less than a unit in pH in an iron oxide suspension changed the solidification time 100-fold. In this same system, raising the temperature resulted in a shortening of the time for solidification.

Dilatancy

Dilatancy may be considered as the reverse of thixotropy; that is, lipophilic systems exhibit low resistance at low shearing rate but high resistance at high shear rates. In these suspensions, there is no permanent contact between particles.

Boylan offered the observation that dilitant flow is roughly the opposite of pseudoplastic flow (15). These substances show an increased resistance to flow with an increase in shear. Dilatant materials are highly concentrated systems, usually suspensions. The particles are fine, closely packed, and deflocculated. At rest, the particles occupy a minimum volume, with only a very small quantity of liquid filling the interstices. With increasing shear rate, the bulk volume increases and the vehicle is insufficient to fill the void spaces between particles. Interparticle friction increases, resulting in an overall increased resistance to flow.

Modern aerosol powder concentrates present a level of suspended solids in which dilatant flow can occur. Thorough rheological examination of all high solids content suspensions is strongly recommended. Such study can save problems in scale-up work, where high rates of shear may be encountered for first time.

Predicting Rheological Behavior

The prediction of rheological stability continues to plague the cosmetic scientist. It is the one area still fraught with frustration. Cosmetic interest can be traced to the work of Wood and others in 1963 (16, 17). More recently, Sherman (18) and Barry (19) have addressed the problem. Attention should be directed to a number of the factors which are at work in emulsions and suspensions as they age.

There can be partitioning of components between the oil and water phase, particularly as a function of storage temperature. pH changes can occur as a result of storage which can influence both the internal and external phases of emulsions. These can also influence the external phase of a suspension. A number of changes can occur in the internal phase of an emulsion including changes in chemical composition, globule size, size distribution, volume concentration, and ultimately viscosity. Particle interactions must also be considered, both in suspensions and emulsions. The aging of emulsions involves definite changes which Sherman (20) has described in the following order. The globules flocculate, leading to aggregates of globules. The film surrounding the individual globules is thinned, resulting in ultimate coalescence.

Temperature Effects

The cosmetic scientist likes to perform measurements at ambient room temperature, particularly because of the convenience it affords. However, his products are applied to a skin surface of perhaps 35°C, almost 100°F. They may be stored at temperatures of from −20°F to plus 120°F. He should investigate his product at some of these extremes. Boylan *et al.* (21) performed a comprehensive study on a variety of pharmaceutical ointments which looked very different in rheological properties at room temperature. However, when evaluated at about 32°C, normal skin temperature, they tended to follow a common rheological behavior pattern.

In our work, the temperature-related behavior pattern shown in Fig. 7 has been observed for a lipstick. This clearly illustrates the different temperature related viscosity characteristics.

Case Histories

Lotion Problem

In order to adequately present the manner in which proper rheological studies can avoid processing and filling problems, two case histories have

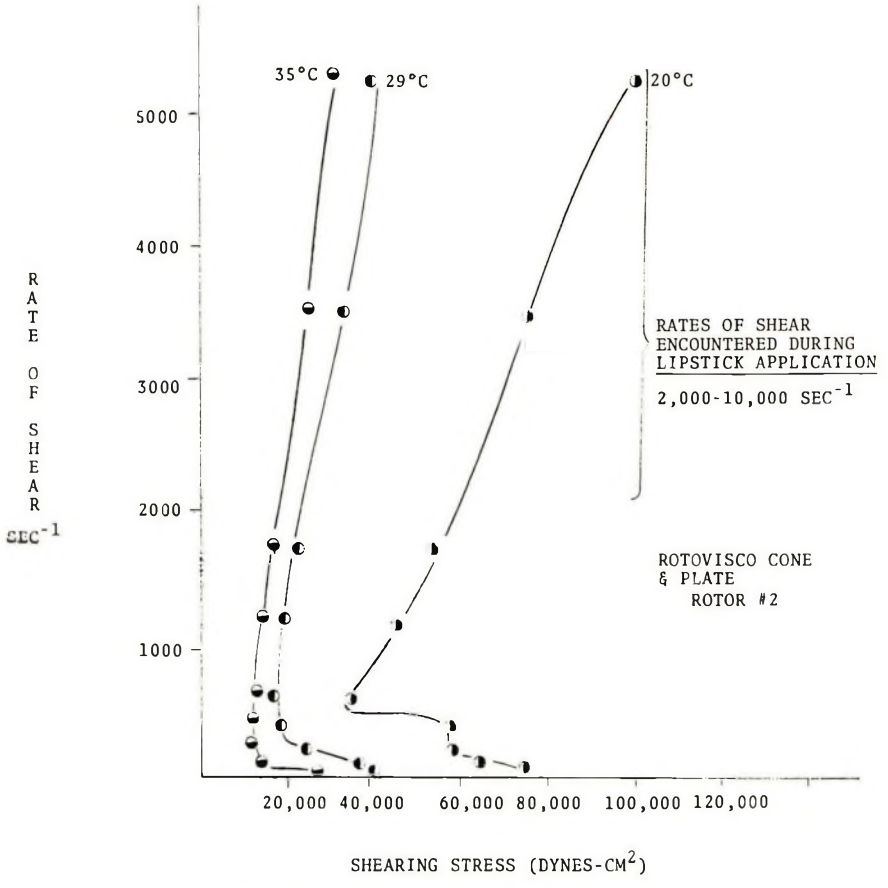

Figure 7. Variation of lipstick viscosity with temperature

been selected from experience. Figure 8 illustrates a problem encountered in the scale-up of a unique product. This particular product, as prepared on the bench, produced uniformly excellent results. However, as the process was scaled-up, problems were encountered with respect to viscosity. To establish the cause for these erratic, sometimes low, sometimes normal viscosities, the rheological behavior of several differently prepared samples was studied.

The variable which was eventually recognized as being pivotal in this viscosity problem was the order in which surfactants were added to the oil and water phase, or to the oil phase alone. On the bench, polyoxyethylene stearate −40 moles of ethylene oxide was being added to the water phase and polyoxyethylene (2) stearyl ether to the oil phase prior to melt-down and emulsification (Curve A). In scale-up, processing time became a major consideration, and in the interest of saving time both surfactants were added to the oil

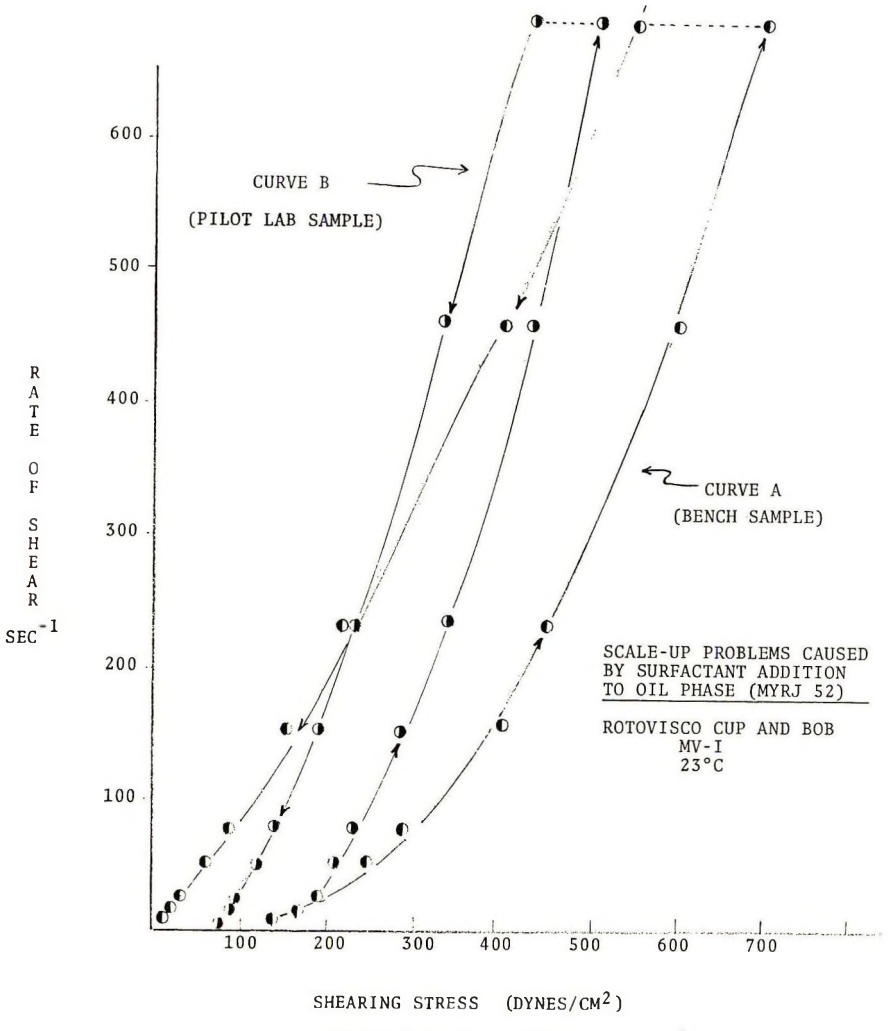

Figure 8. Lotion problem

phase. The effects of this procedure are detailed in Curve B. Obviously the bench method improved the surface active properties of both phases and resulted in a smaller particle size internal phase, with a resultant higher viscosity emulsion.

Shampoo Problem

The next case history illustrates an unexpected filling problem encountered with a shampoo formulation. When initial attempts were made to pass this product through a Cozzoli Filling Machine at a rate of 8 cycles per minute,

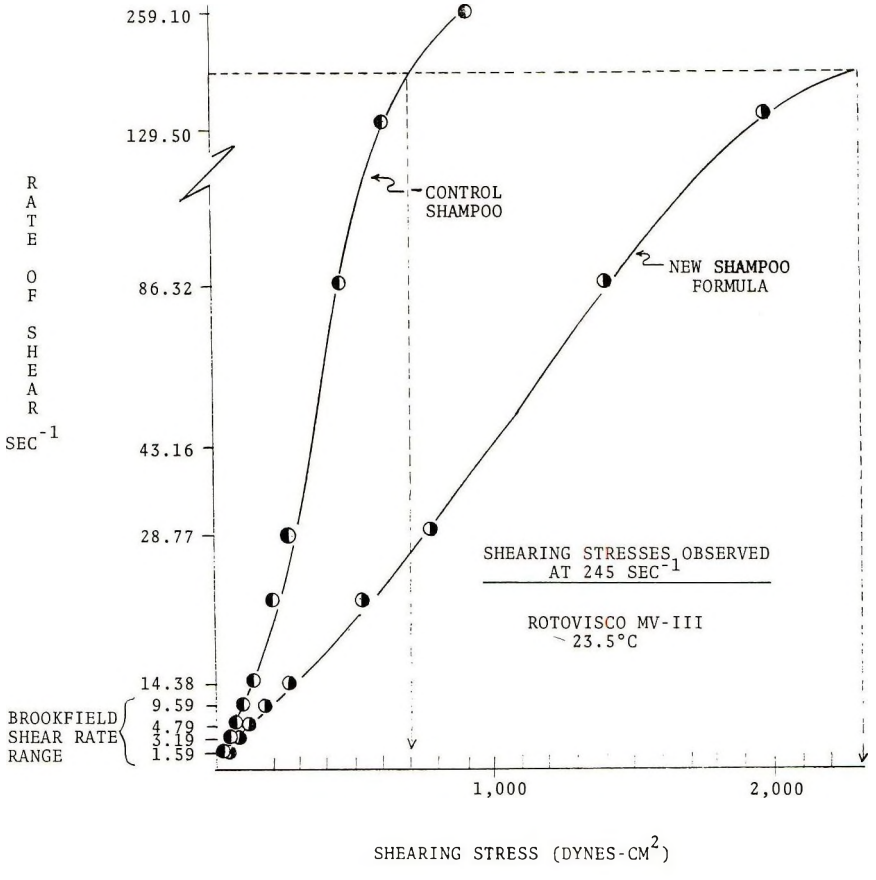

Figure 9. Shampoo problem

equipment breakdown was noted. Although the development chemist had Brookfield Synchro-Electric data which indicated that the viscosity profile of this product closely paralleled an acceptable control, a filling problem still existed.

The rate of shear which was encountered in this type of filling equipment was determined. These shear rates were approximated using the following modified Poiseuille equation which describes flow through a capillary:

$$D = 4Q/r^3 = 245 \text{ sec}^{-1}$$

where

D = shear rate
Q = volume delivered/sec
r = radius

Once this approximation had been made, performance of the product when pumped at a low rate of shear of approximately 250 sec^{-1} was investigated, using the Rotovisco. Figure 9 illustrates the remarkable difference between the control and new product when evaluated at rates of shear not encountered with the usual Brookfield Synchro-Electric test. Here we see that at 245 sec^{-1} the newly developed product had a shearing stress of 2,830 dynes/cm^2, while the control product gave a shearing stress value of 700 dynes/cm^2. Closer inspection of the Cozzoli Filler revealed a shear pin which would and did fracture at this shear stress. Once the problem was clearly recognized, it was easily solved.

Other production scale-up problems have been discussed in an article by Fujiyama *et al.* (22).

Summary

The basic principles of rheology have been reviewed. Using three model formulations and four different viscometers, the utility and the shortcomings of the instruments have been demonstrated. The problems encountered in the formulation and stability evaluation of cosmetic products has been discussed. By way of case histories we have illustrated the value of proper rheological study. The viscometer is a valuable tool for the cosmetic scientist. It should be utilized to its fullest capability.

(Received May 3, 1973)

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The 1973 Society of Cosmetic Chemists Award sponsored by Perry Brothers Fragrances, Inc., has been presented to Dr. Mary J. Marples.

The award, consisting of a scroll and a $1000 honorarium, is given annually to an individual or individuals who have made an outstanding contribution to microbiology as related to the manufacture and preservation of cosmetics. Formal presentation was made by Ms. Janet Curry, Award Chairman, at the May 9th luncheon session during the Society's Seminar in Chicago, Illinois.

Left to right: Dr. Brian Marples, husband of Award Recipient, Dr. Mary J. Marples, Award Recipient, Dr. Hyman Henkin, Society President, and Ms. Janet C. Curry, Award Chairman

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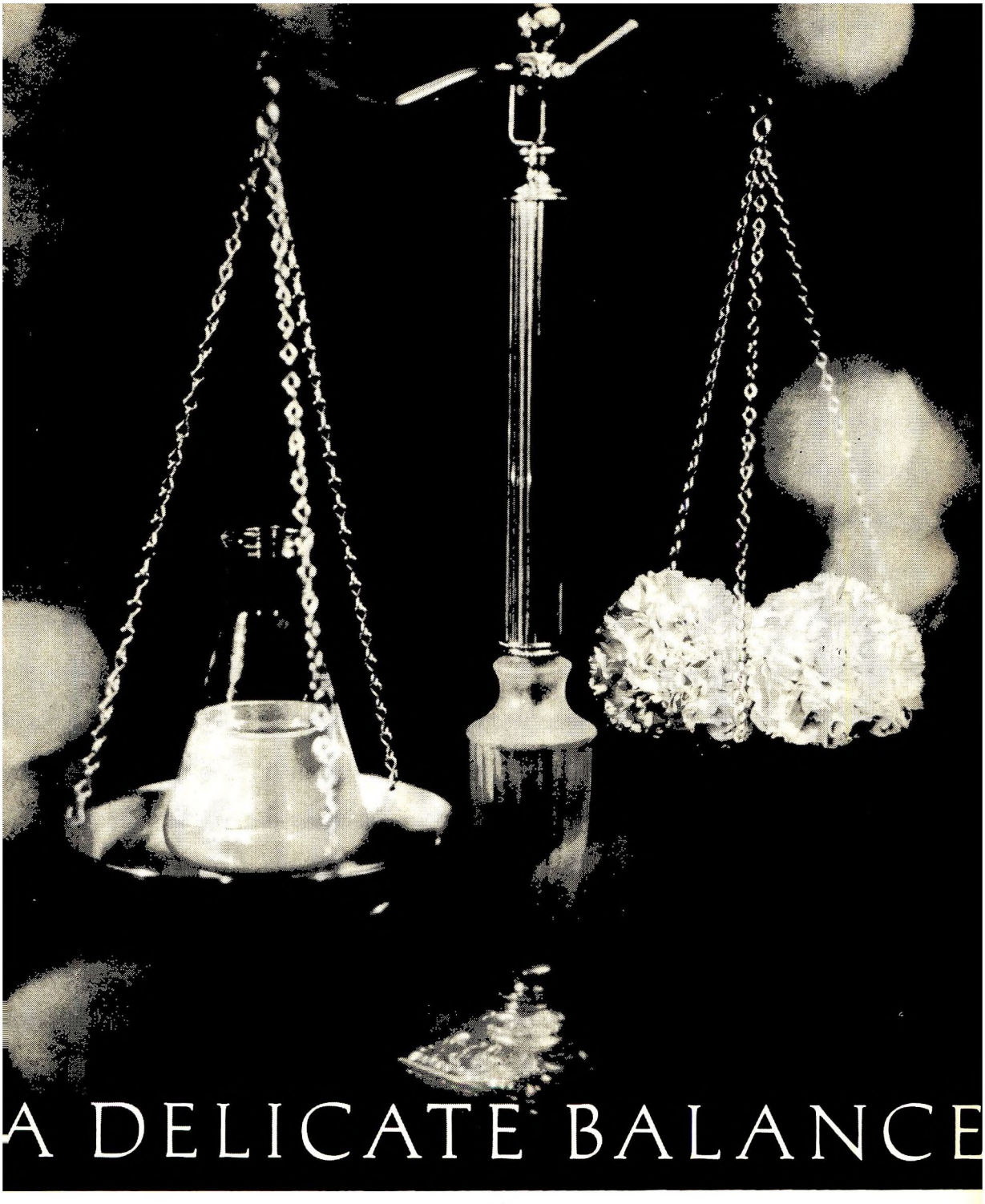

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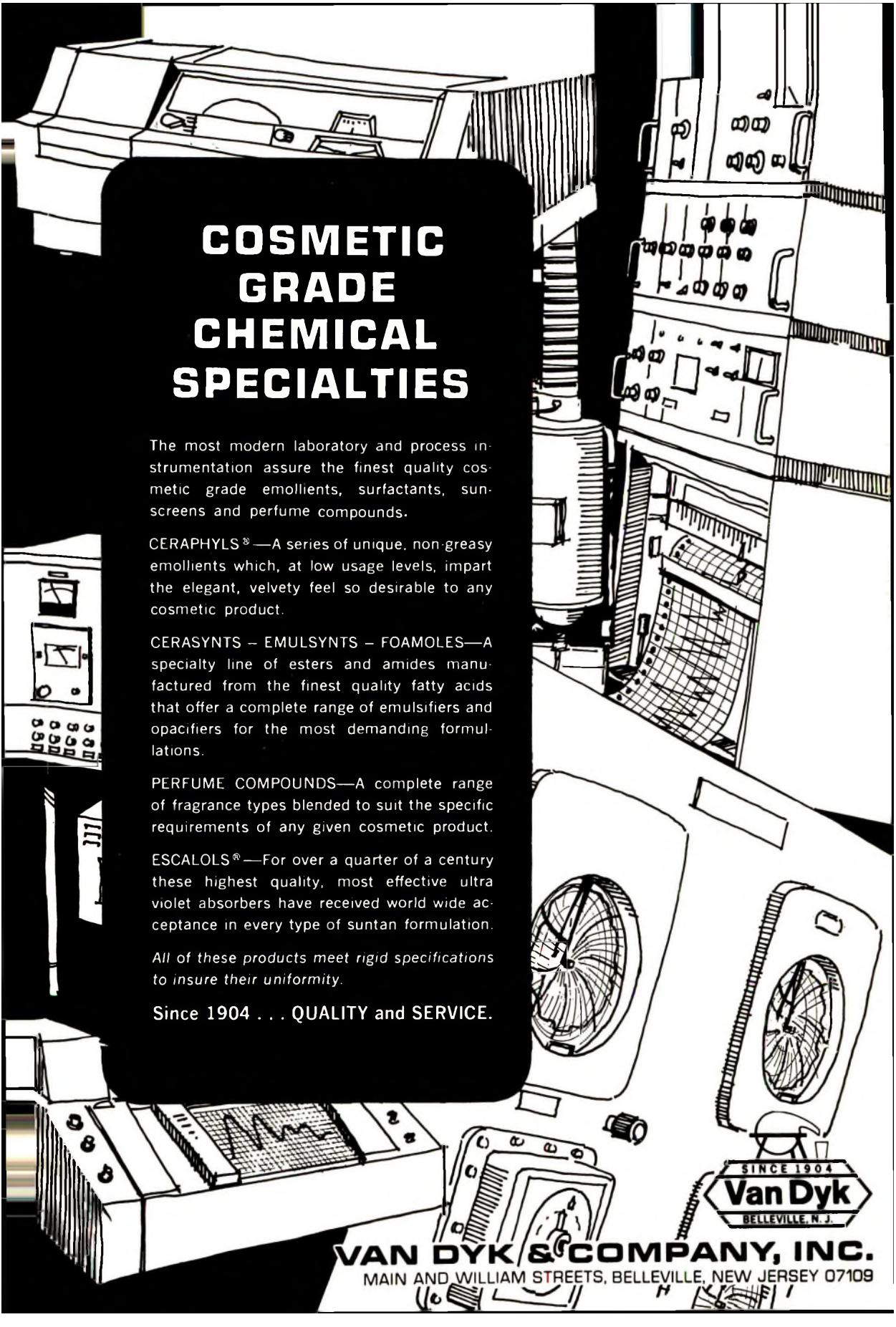

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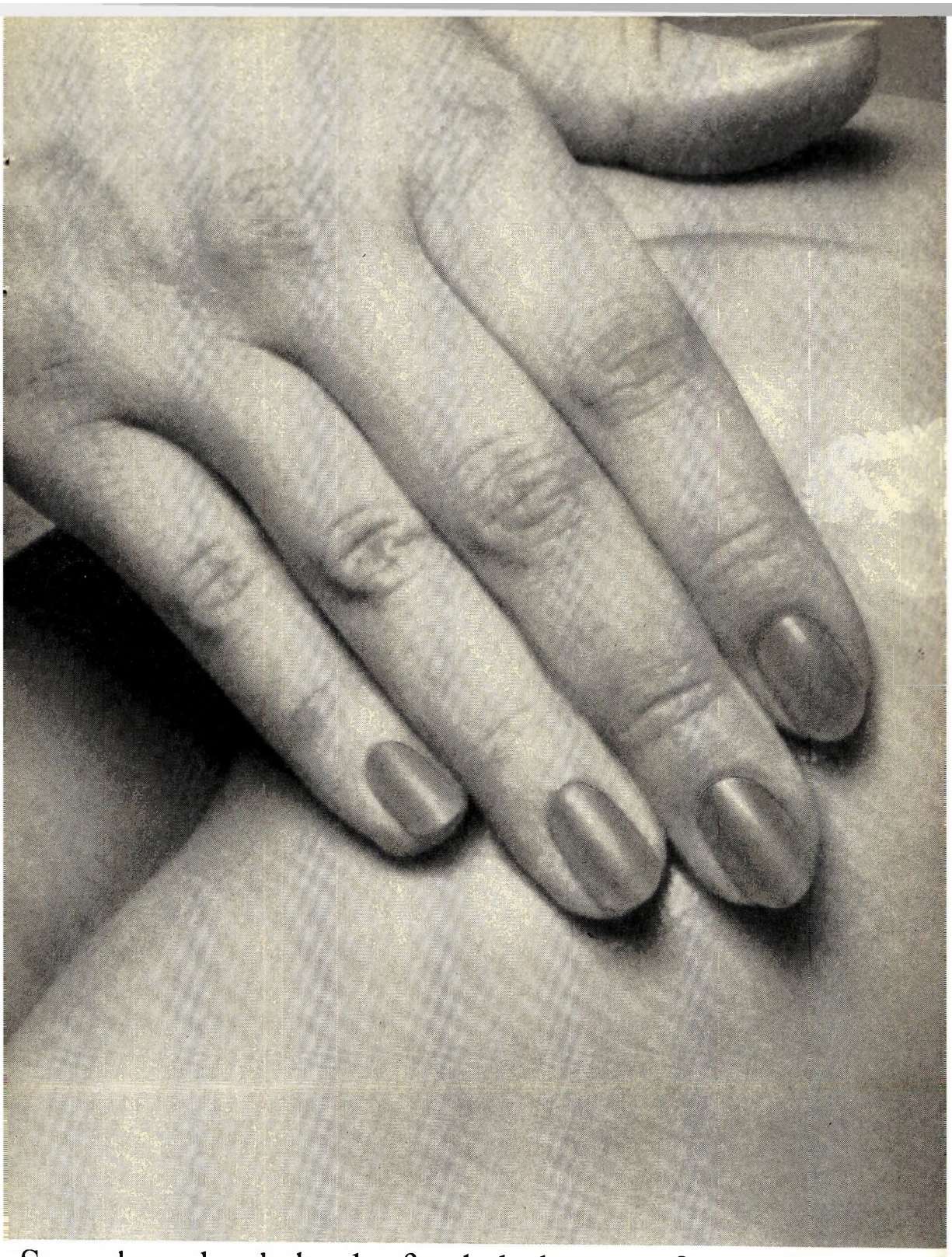

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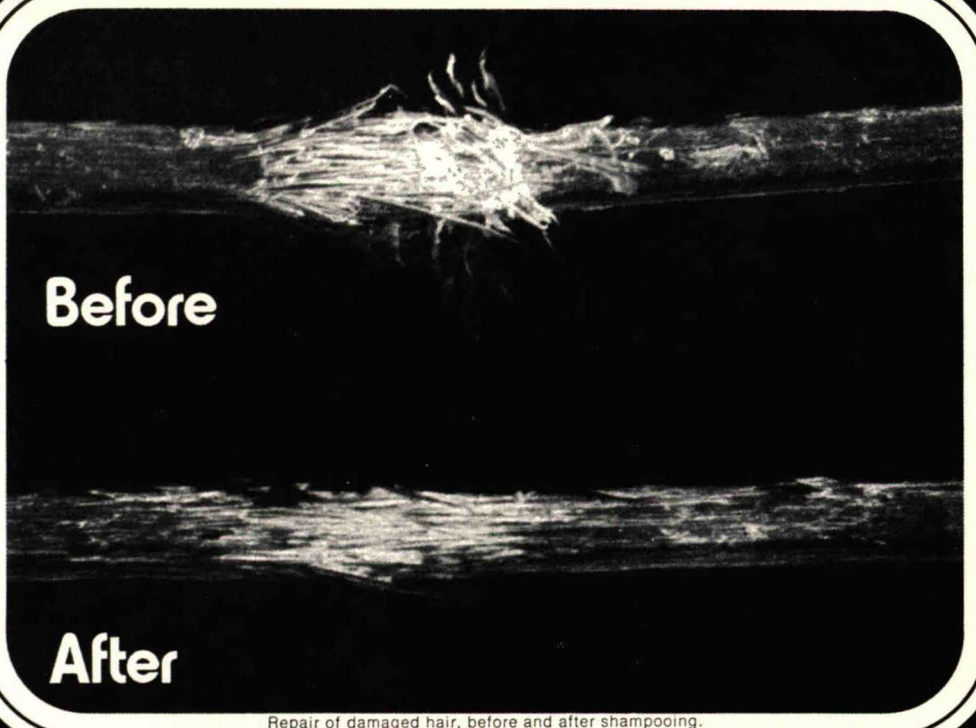

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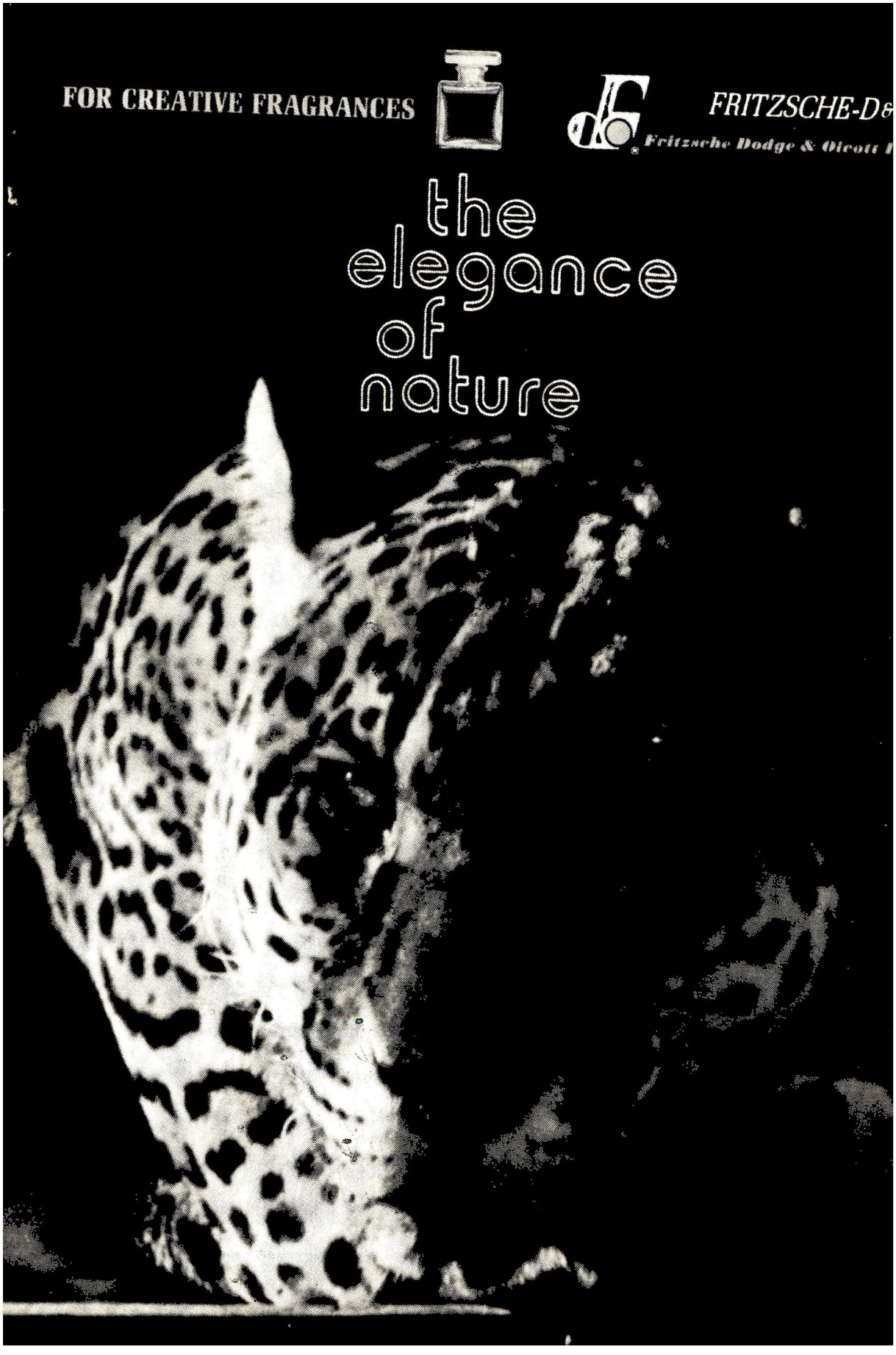
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