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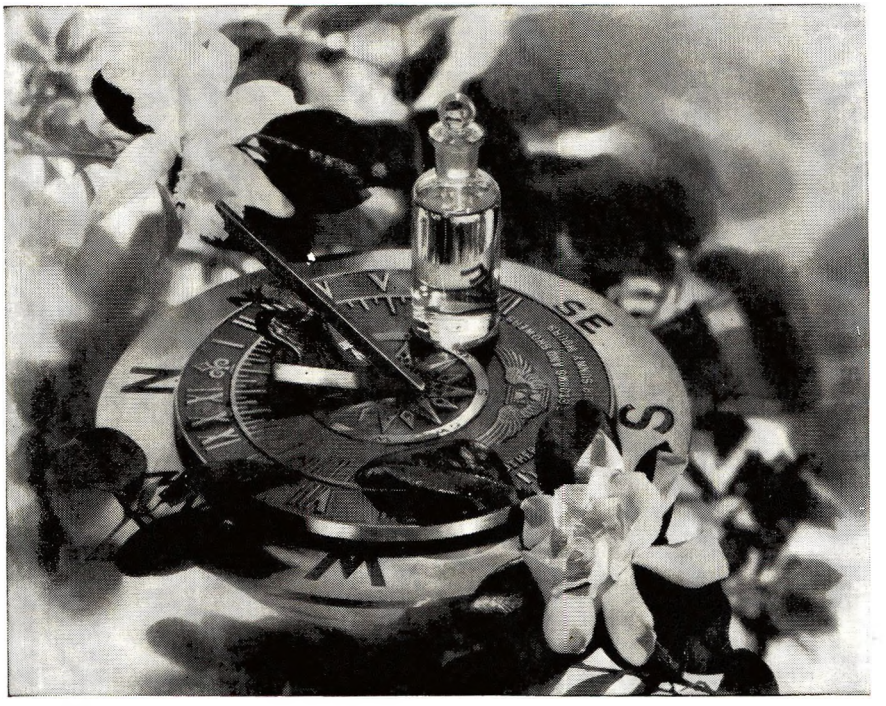

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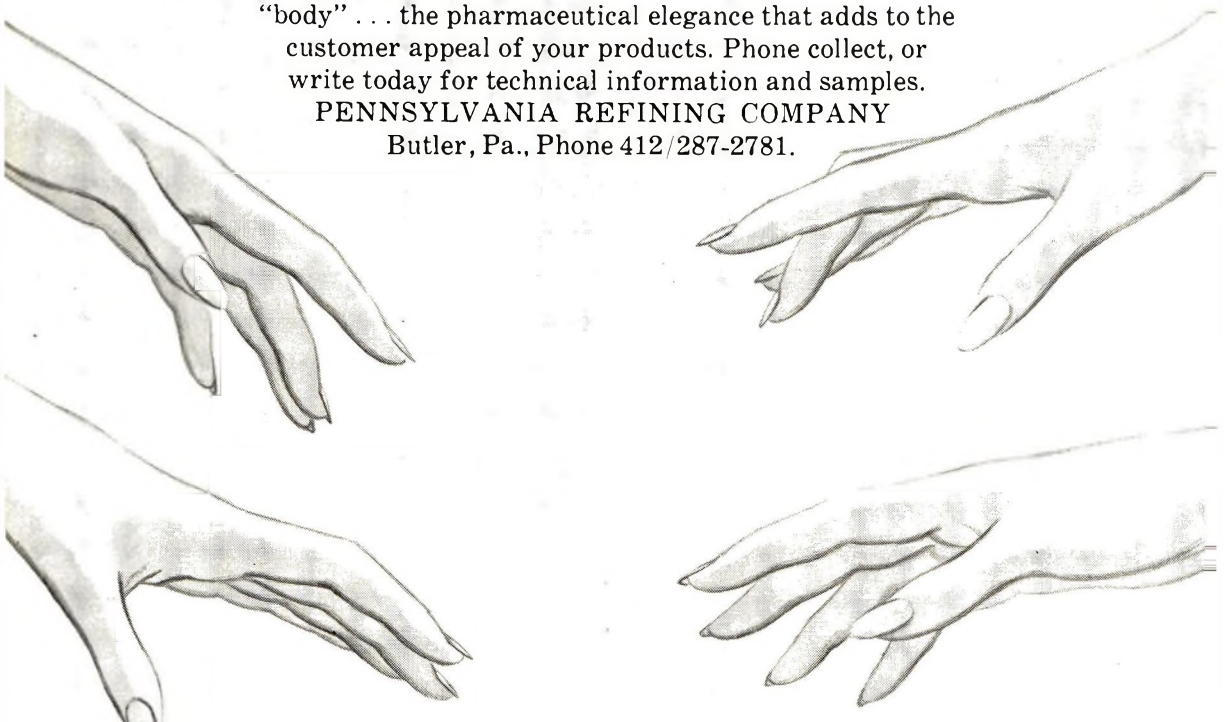

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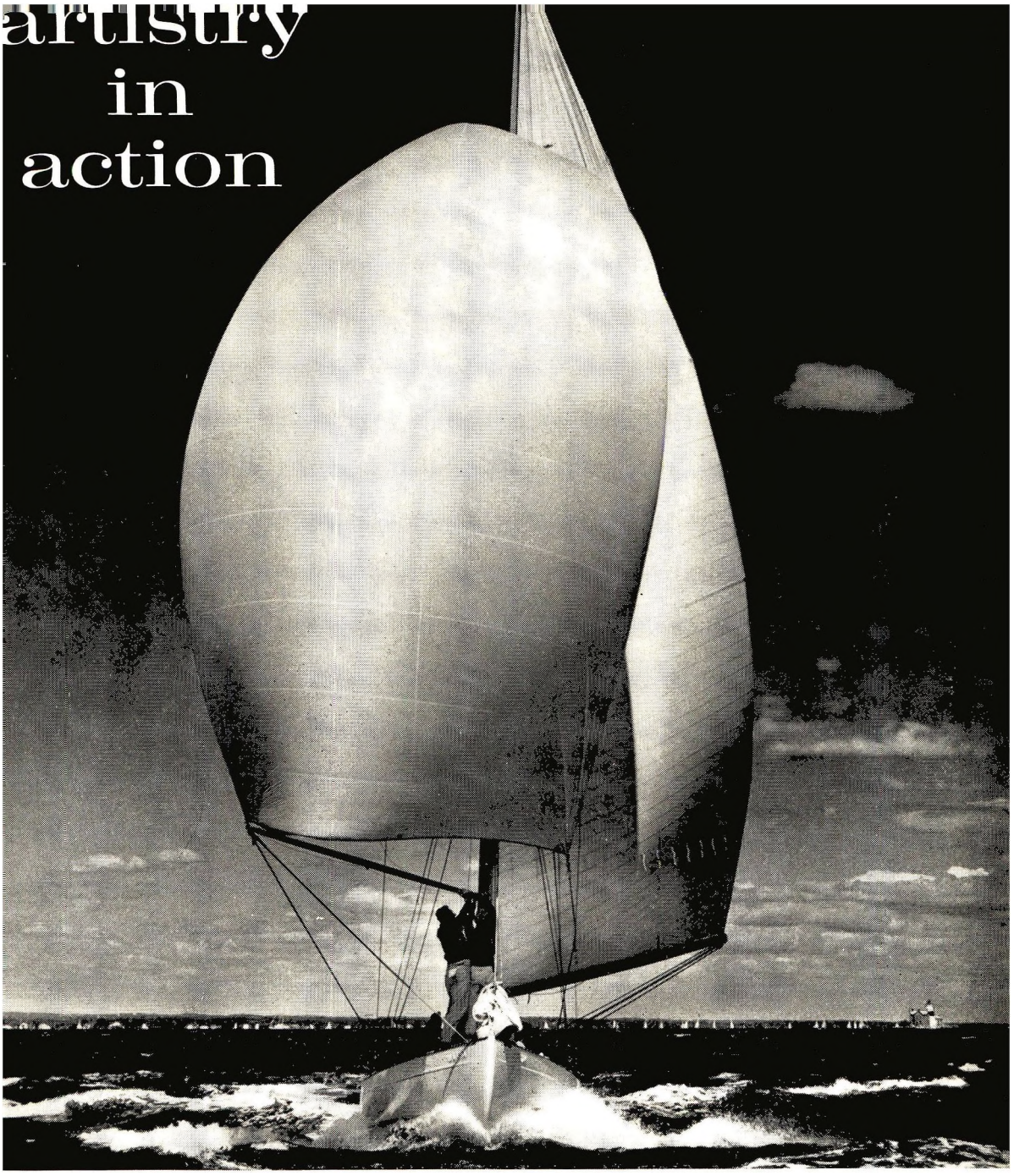

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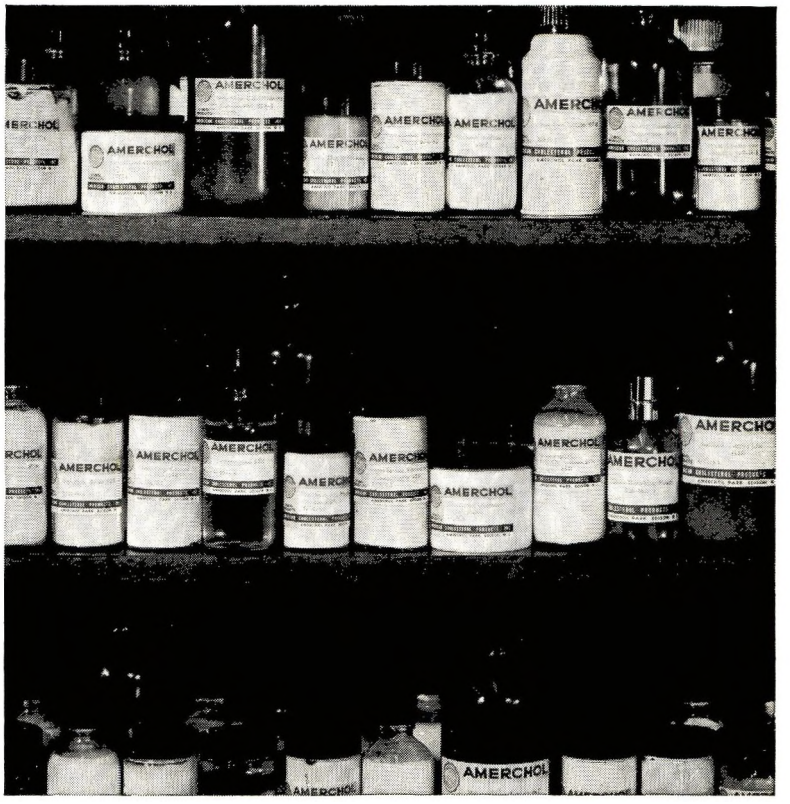

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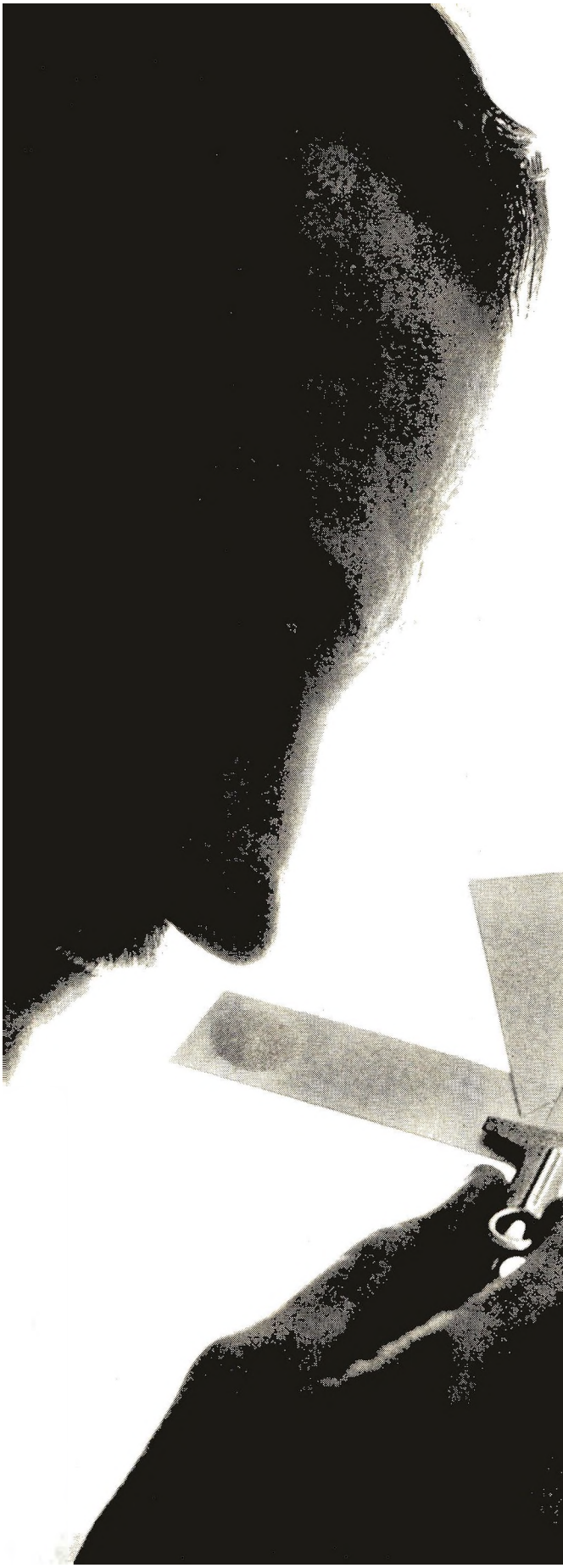

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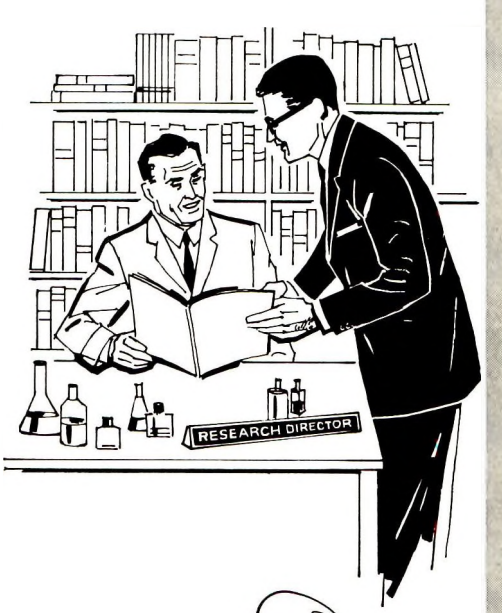

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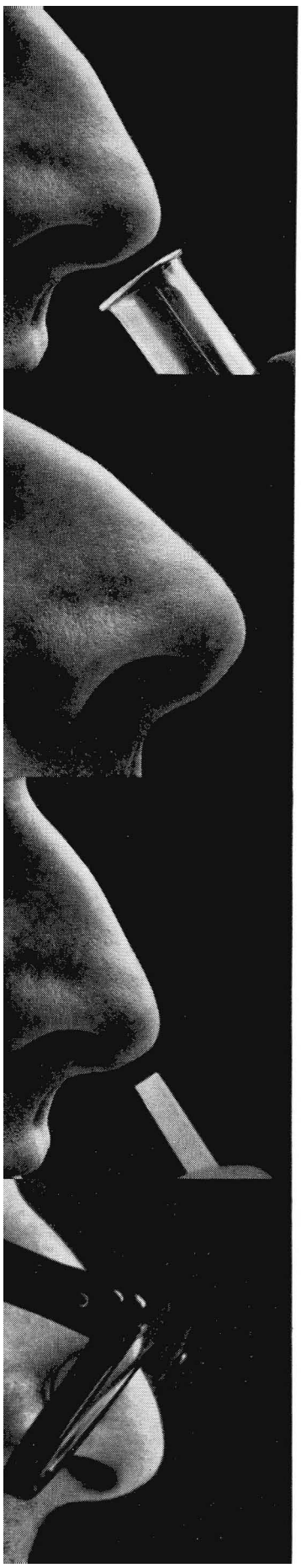

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SYNOPSES FOR CARD INDEXES

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

Product stability: Prognostication, placement, parameters—Part I: Lloyd Kennon. *Journal of the Society of Cosmetic Chemists* **17,** 135 (1966)

Synopsis—Chemical kinetics provides the basic principles which can help study of the deterioration of pharmaceutical and cosmetic products. Principles of kinetics, which could be used to predict long-term stability of finished formulations, are reviewed, and techniques are described which can be used in programming stability studies. Finally, those properties of emulsions, suspensions, and solids are discussed which are amenable to measurement and can be used as parameters for establishing and predicting deterioration of finished consumer products.

Lanolin allergy?: E. Allen Newcomb. *Journal of the Society of Cosmetic Chemists* **17,** 149 (1966)

Synopsis—A review of the literature indicates that only about 100 cases of lanolin sensitivity have been documented during the last 30 or 40 years. It is concluded that lanolin presents no hazard in cosmetics and is not a sensitizer. Possible reasons for the occasional lanolin allergy are reviewed, but no definite conclusions can be drawn from data available so far. It is noted that no specific fraction of lanolin is implicated in this sensitivity.

Surface modifying effects of lanolin derivatives: Lester I. Conrad, Henry F. Maso, and Shirley A. DeRagon. *Journal of the Society of Cosmetic Chemists* **17,** 157 (1966)

Synopsis—The influence of lanolin derivatives on the physical aspects of dispersions is discussed. Particular reference is made to pigment wetting, rheological patterns in emulsion systems, solubilization, emulsification, and spreading coefficients. Practical applications of these phenomena are illustrated by typical cosmetic formulations.

Instrumental method for the determination of hair raspiness: William C. Waggoner and George V. Scott. *Journal of the Society of Cosmetic Chemists* **17,** 171 (1966)

Synopsis—As comb teeth arrange hair fibers in a parallel manner and rub along hair scales, vibrational frequencies are emitted and play a role in the "feel" of hair. The audible frequencies, which denote raspiness, may be cosmetically undesirable. In an attempt to record and evaluate hair raspiness, an electronic comb, specifically designed to pick up frequencies by contact, was constructed. Several groups of hair tresses, which were treated with cosmetic chemicals, rinsed and dried, were combed with the instrument. Computer analysis of the data showed the expected differences between tresses; and some differences reflected excellent probabilities of test reproducibility. The method lends itself to rapid laboratory screening of agents designed to reduce friction during combing.

LITERATURE SURVEY*

Analytical

Conductometric Rapid Determination of Sulfates in Surface Active Substances and Other Compounds. Kiemstedt, K., and Pfab, W., *Z. Anal. Chem.* **213,** 100–07 (1965).

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An Improved Method of Calculating Particle Size Distribution from Centrifugal Sedimentation Experiments. Murley, R. D., *Nature* **207,** 1089–90 (Sept. 4, 1965).

Analytical and Quality Control Methods for Emulsion Polymers. Tynan, J. F., and Merken, H. *Specialties* **1,** 12–16 (August, 1965).

Identification of Organic Compounds. Chromatography of Polyethylene Oxide Compounds. Borecky, J., *Collection Czech. Chem. Commun.* **30,** 2549–57 (August, 1965) (German).

Quantitative Estimation of Isomeric Monoglycerides by Thin-Layer Chromatography. Thomas, A. E., *et al., J. Am. Oil Chemists' Soc.* **42,** 789–92 (September, 1965).

Bacteriology

Post-Irradiation Recovery of Escherichia Coli. Lee, J. S., and Sinnhuber, R. O. *Nature* **207,** 1212–14 (Sept. 11, 1965).

Repression of Staphylococcus Aureus in Associative Culture. Iandolo, J. J., *et al., Appl. Microbiol.* **13,** 646–49 (September 1965).

Related Bacteria Differentiated by GC. (150th ACS Meeting) *Chem. Eng. News* **43,** 69 (Sept. 27, 1965).

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Mutants of Escherichia Coli with High Minimal Temperatures of Growth. O'Donovan, G. A. *et al.*, *J. Bacteriol.* **90,** 611–16 (September, 1965).

Effect of Ethylenediamine Tetra-Acetate on the Resistance of Pseudomonas Aeruginosa to Antibacterial Agents. Brown, M. R. W., and Richards, R. M. E., *Nature* **207,** 1391–93 (Sept. 25, 1965).

Application of the Ryter-Kellenberger Fixation Method to Electron Microscopic Study of Bacteria on the Skin Surface. Montes, L. F., *et al.*, *J. Invest. Dermatol.* **45,** 93–98 (August, 1965).

Efficiency of Chlorine Dioxide as a Bactericide. Bernarde, M. A., *et al.*, *Appl. Microbiol.* **13,** 776–80 (September, 1965).

Factors Affecting the Antimicrobial Activity of Vitamin K_3. Merrifield, L. S., and Tang, H. Y., *Appl. Microbiol.* **13,** 766–70 (September, 1965).

Where Research Leads Us. Inhibition of Dental Caries. Kailis, D. G., *Australian Dental J.* **10,** 119–202 (June, 1965).

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Fractionation of Biological Materials by Magnetically Stabilized Electrophoresis. Nelson, S. S., and Hadermann, A. F., *Am. J. Med. Electronics* **4,** 107–12 (July-September, 1965).

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Literature Survey

The Literature Survey, a service initiated by the New York Chapter of the Society, will now appear in this JOURNAL.* It is apparent that the number of published papers which may be of interest to readers of the JOURNAL is increasing so rapidly that it has become difficult to keep abreast of the literature. It is hoped that the Survey will serve as an up-to-date guide to articles which appear to have interest and information for cosmetic chemists.

This Survey is not a complete list of technical articles pertaining to cosmetics. No attempt will be made to abstract or elaborate on the material surveyed. Hopefully, readers will find this Survey interesting and can use it as a valuable tool in expanding their occupational efficiency.

Joseph H. Kratochvil
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* The Survey appears on pages xxxiii–xxxix following the Synopses.

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Product Stability: Prognostication, Placement, Parameters—Part I

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Presented before the Eleventh Annual Seminar, September 14–15, 1965, Los Angeles

Synopsis—Chemical kinetics provides the basic principles which can help study of the deterioration of pharmaceutical and cosmetic products. Principles of kinetics, which could be used to predict long-term stability of finished formulations, are reviewed, and techniques are described which can be used in programming stability studies. Finally, those properties of emulsions, suspensions, and solids are discussed which are amenable to measurement and can be used as parameters for establishing and predicting deterioration of finished consumer products.

Introduction

To begin a discussion of a topic such as product stability and chemical kinetics, it probably would be fitting to start with several appropriate quotes from the Old Testament, or failing this, we might record some of the musings of such all-time-greats as Aristotle or Archimedes. Probably most effective, however, would be to have found a log-log plot on a bas relief in the Egyptian pyramids. Upon such a foundation one then could build a chronological historical outline which would connect the work of antiquity with that of today. However, except for one brief bow to tradition, we will dispense with the historical approach. This brief lapse entails mentioning the observation, probably not his alone, of Heraclitus (Heracleitos of Ephesos), who in about 500 B.C. said "panta rhei," or, all is flux, everything flows. Certainly,

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this fact is one which appears to be relatively immutable. Possibly this Ionian Greek philosopher was stimulated to make this observation because he was living in a time in which fire was thought to be one of the (if not *the*) primordial substances; we too have, of course, observed that a flame, being such a changeable thing, may well be a symbol (possibly a clue?) that all things are subject to a general and ceaseless process of alteration. Regardless, Heraclitus stressed the constancy of change, and here we wish to discuss change as it affects the products we create.

Prognostication

The purpose of this section will be to review basic, classical chemical kinetics, to indicate the rationale behind choosing certain of the pertinent principles from this segment of physical chemistry, and to demonstrate how these new tools may be used.

For our purposes, the basic aim is to learn how to follow reaction rates in an efficient and orderly manner, i.e., in a way that makes possible prediction of the future behavior of the system being observed. By reaction rate we mean the rate of degradation of a material. We will equate the degradation of a material to the disappearance or lowering with time of the concentration of a component of the formulation under observation. Basically, we can review the possible happenings by considering two concepts: molecularity and order.

Consider first the molecularity of reactions. A unimolecular reaction is one in which only one molecule takes part, as in, e.g., a dissociation or rearrangement. In a bimolecular reaction two molecules are involved, and collision of the two is needed. Most of the familiar reactions of formation would fall into this class. A termolecular interaction in which three molecules are involved in simultaneous collision is rare and is not unlike the problems acknowledged by the familiar "three is a crowd" adage. For practical purposes, molecularity is most easily interpretable, i.e., cast into useful form, by *observing experimentally* how a rate of reaction or degradation is influenced by the concentrations of the reacting or degrading materials, regardless of how the actual happenings are taking place on a molecular scale.

The next concept needed then is that of reaction order; definitions follow:

First Order. The rate is directly proportional to the concentration of the material reacting. Mathematical treatment yields an equation describing this situation:

$$k = (2.303/t) \log (c_0/c) = (2.303/t) \log (a/a - x)$$

where:

t = time
c_0 = c at $t = 0$,
c = c at $t = t$,
k = specific reaction rate constant; units = time^{-1},
a = original amount,
x = amount reacting in time t.

By substituting $c_0 = 100$ and $c = 50$ the familiar half-life equation and concept is developed:

$$t_{1/2} = 0.693/k$$

Obviously, one can use these equations after enough data are available to evaluate the specific reaction rate constant; after this either other times or other concentrations can be substituted into the equations to determine unknowns. Graphically, the most useful method involves a plot of log c *vs.* time; k then equals (-2.303) times the slope, which is negative.

Second Order. The rate is proportional to the concentrations of two materials or ingredients, e.g., A and B. Mathematically, two results are possible. Lower case "a" and "b" represent corresponding concentrations of A and B.

When $a = b$: $k = (1/t)\, x/a(a-x)$;
When $a \neq b$: $k = [2.303/t(a-b)] \log[b(a-x)/a(b-x)]$;
Units of k = volume amount^{-1} time^{-1}.

Graphically, log $[b(a-x)/a(b-x)]$ is plotted *vs.* time; k then equals $(2.303/a-b)$ times the slope, which is positive.

Pseudo First Order. If one reactant is in great excess in a second order reaction, the reaction may be bimolecular, but it will appear to be first order; in fact, it *will* actually be first order by definition. Order is an experimentally made observation which is not necessarily connected to the reality of any particular molecularity.

Two more orders are worthy of mention, even though they may not be applicable to the techniques which may ultimately be required.

Zero Order. The rate is not affected by concentration, but rather it is set by some outside limiting factor such as the absorption of light, the rate of diffusion in a surface reaction, or somewhat similarly, the maintenance of a constant concentration due to the involvement of a saturated solution.

Third Order. The rate is proportional to the concentration of three reacting substances. For these purposes, third order reactions are considered to be too rare and will not have to be considered.

Other complex reactions are noteworthy, but similarly, they will not affect our use of chemical kinetics. By complex reactions are meant consecutive reactions, competing reactions, and reverse reactions in which equilibria are set up which mass-wise are neither near to the beginning nor near to the point of completion. The reason confusion does not run rampant, considering the many realistic possibilities, is that, in general, some limiting step predominates such that *experimentally* we are able to observe the behavior of some single entity or parameter.

Before we try to organize and use the just-discussed physical-chemical information, one more concept, the role of temperature, should be noted. That reaction rates increase with temperature is a well-known observation amply illustrated by every-day experience. This fact has been quantitated and incorporated in the scheme of chemical kinetics by the well-known Arrhenius equation:

$$\log (k_2/k_1) = (\Delta H_a/2.303R)(T_2 - T_1/T_2T_1)$$

where:

ΔH_a = heat of activation
R = gas constant
T = absolute temperature (°C + 273°)

Graphically, a straight line of negative slope results when log k is plotted *vs.* 1/T; the slope = $(-\Delta H_a/2.303R)$.

Now that the foundation has been laid, we must choose which type of edifice to build and then justify the nature of the architecture.

First, it is obvious that the role of temperature can be incorporated into the scheme of things by employing the well-known "accelerated studies" in which formulations are stressed by storage at various elevated temperatures. Secondly, a variation of the half-life concept will be used in which a t_{90} is employed, i.e., the time it takes for 10% degradation or for a drop to 90% of the original concentration of a material. This will be illustrated later. Thirdly, first order kinetics will be utilized because of the ease of application. Amplification of these points will be effected in reverse order.

First, the validity of using first order kinetics should be verified. One should be sure that use of this order will not be misleading if the system under observation is, in fact, degrading according to second order kinetics. The existence of confusion or the lack of it, which would enter

Table I
Calculated Results of Model Second Order Kinetic Rate Equation Illustrating Degradation of A and B; Initial Concentration of $A = 10$, $B = 1$

x	$t \times 10^2$	(A)	(B)	log (A)	log (B)
0.1	0.46	9.9	0.9	0.996	−0.046
0.2	0.98	9.8	0.8	0.991	−0.097
0.3	1.58	9.7	0.7	0.987	−0.155
0.4	2.27	9.6	0.6	0.982	−0.222
0.5	3.10	9.5	0.5	0.978	−0.301
0.6	4.12	9.4	0.4	0.973	−0.398
0.7	5.46	9.3	0.3	0.968	−0.523
0.8	7.36	9.2	0.2	0.964	−0.699
0.9	10.66	9.1	0.1	0.959	−1.000

Table II
Calculated Results of Model Second Order Kinetic Rate Equation Illustrating Degradation of C or D when Initial Concentration of $C = D = 1$

x	t	(C)	log (C)
0.1	0.11	0.9	−0.046
0.2	0.25	0.8	−0.097
0.3	0.43	0.7	−0.155
0.4	0.67	0.6	−0.222
0.5	1.00	0.5	−0.301
0.6	1.50	0.4	−0.398
0.7	2.33	0.3	−0.523
0.8	4.00	0.2	−0.699
0.9	9.00	0.1	−1.000

into an attempt at analysis of a system which was degrading in second order fashion but which was treated as first order, could be determined by setting up model systems, as will be illustrated next.

The second order model data shown in Table I may best be examined by plotting them as if the system were following first order kinetics. These data were obtained for the case in which $a \neq b$ letting:

a = original concentration of A = 10,
b = original concentration of B = 1,
x = amount of degradation = 0.1, 0.2, . . ., 0.8, 0.9, and
k = 2.303.

Then: $t = \frac{1}{k} \log (0.1)\ (a-x)/(b-x)$ in arbitrary units.

Solving for t as A decomposes to about 90% and B to about 10% of original concentrations produces the figures of Table I.

Figure 1 shows the data of Table I graphically. It can be seen that in the case of "A," a first order plot exhibits considerable curvature after about 4% degradation has taken place. This is not too good from the point of view of needing a straight line relationship. However, this case, in which the original concentration of $A = 10$ and its nemesis, so

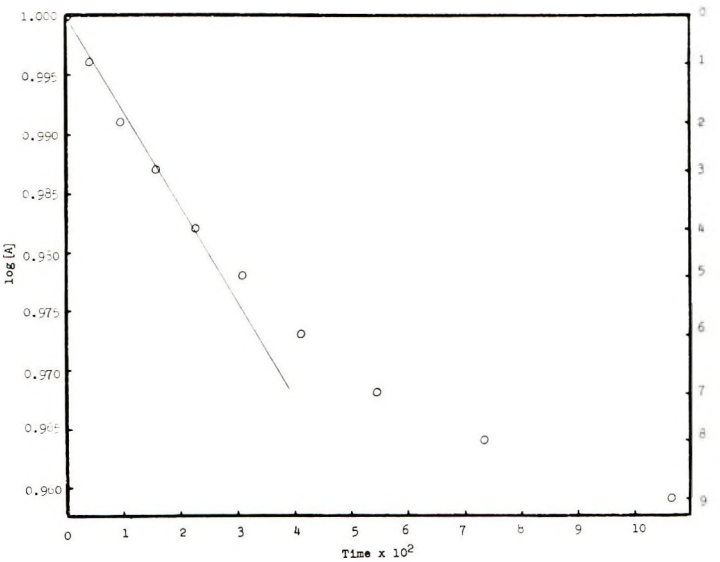

Figure 1. Percent Degradation of A

to speak, is B which initially existed at a concentration 10% of that of A, leads to some comfort in two respects: First, it is more likely that a significant nemesis would have a higher concentration, and secondly, the degradation of A will stop after 10% decomposition from a "10% nemesis."

Additional second order model data shown in Table II illustrate some different aspects of this situation. These data were obtained for the case in which $a = b$ by letting:

a = original concentration of $C = 1$,
x = amount of degradation = 0.1, 0.2, . . . , 0.8, 0.9, and
$k = 1$.

Then: $t = x/a(a-x)$ in arbitrary units.

Solving for t as C decomposes to about 10% of its original concentration produces the figures of Table II.

Figure 2 illustrates the data of Table II. It is apparent that when the original A is attacked by "someone its own size" (line "C," $a = b$)

or by a much larger adversary (line "B," $10x$), first order kinetics prevail as the lines are straight all the way in the latter case (B) and to a point at which at least 50% degradation has taken place in the former case (C). Our conclusion is that first order plots should be applicable to our work.

With regard to the use of half-life concepts it will be, as indicated previously, useful to think in terms of t_{90} values. Half-lives represent a time unit which is too long; obviously degradation must be monitored in

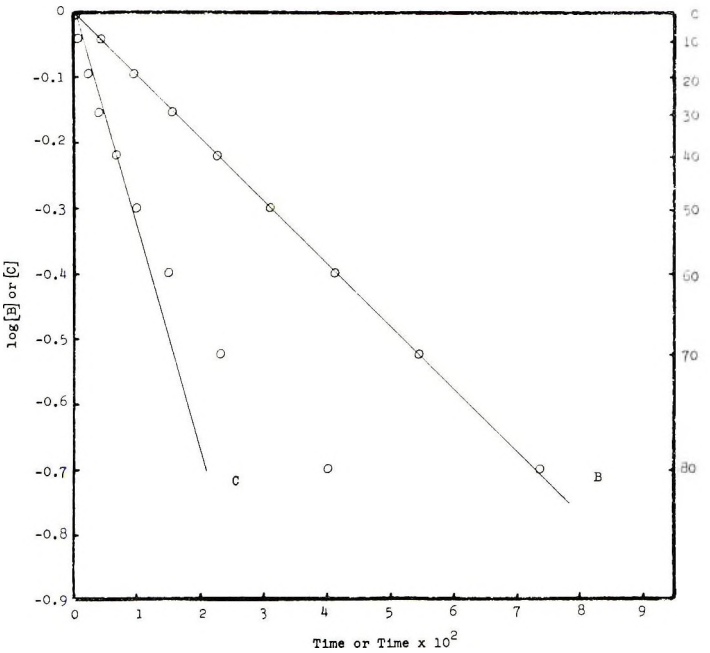

Figure 2. Percent Degradation of B or C

products during a stability study as soon as small changes develop. Therefore, the t_{90} concept, which is the time for a concentration to fall to 90% of the original, is most useful. It should be noted also that this time can be correlated (actually, it is inversely proportional to "k") to the specific reaction rate constant as indicated in the half-life equation. This means that any manipulation performed with k can also be performed with t_{90}. Finding t_{90} entails using first order equations and experimental data to find k; then having found k at any particular temperature, the same equations are used again to find t_{90} by setting $c_0 = 100$ and $c = 90$.

The role of temperature, which is the foundation upon which almost all of the accelerated stability testing procedures rest, can be brought into play by plotting the t_{90} values obtained from data taken at various temperatures *vs.* $1/T$ to get an Arrhenius-like plot but with a positive slope. The point at which the line crosses the abscissa representing room temperature is the length of time it would take the material to break down to 90% of its original concentration. Obviously, the time to reach any other desired degree of breakdown could be sought by a procedure analogous to that just described for the determination of t_{90}.

One final point involves the question of whether reactions at higher temperatures really reflect what will happen at room temperature. Obviously, higher temperatures may not if they destroy the fundamental nature of the formulation. Unfortunately, the question is not an easy one to answer conclusively. Some insight into the validity of high temperature stability studies may be gained, however, by consideration of some data already published.

Examples from the literature will be used to examine some kinetic data taken at widely different temperatures. As will be seen, the same kinetic expressions for the degradation of thiamine hydrochloride appear to be valid over a very wide temperature range; this is *not* so, however, in the cases of the degradation of glucose in acid solution or of aqueous procaine hydrochloride solutions.

Stability studies which utilize quite high temperatures are always suspect because the question always arises: Are the same or different degradative reactions predominant at these higher temperatures as at lower temperatures? The literature contains information which illustrates that, in the case of aqueous solutions of thiamine, the same reactions appear to predominate both at room temperature and at 140°C. However, no one seems to have studied this point explicitly. For example, Farrer (1–4) in his fairly extensive researches on the thermal destruction of Vitamin B_1 has never related his data obtained at 100°C to what might be happening at 25°C. Obviously, the answer to our implied question is of the utmost importance when one is considering a study of the stability of B_1 in pharmaceutical formulations. Although thiamine could not arbitrarily be declared a "typical" drug, it *is* a rather complex molecule which can (with appropriate reagents) degrade in several ways, just as many other compounds may. On this basis then, it is interesting to see the results of some calculations using data in the literature.

Macek, Feller, and Hanus (5) studied the degradation of aqueous solutions of thiamine mononitrate. The pH's were adjusted to 4 with HCl

so that the ionic species resulting were essentially the same as in the Watanabe study mentioned below; the samples were stored at room temperature and 40°C for varying periods of time up to one year. These workers did not calculate either kinetic specific reaction rate constants or the heat of activation of the degradative reaction. However, using their 1, 6, and 12 month data, approximate values can be calculated:

$$25°C: \; k = 4.80 \times 10^{-3} \text{ mo.}^{-1}$$
$$40°C: \; k = 4.05 \times 10^{-2} \text{ mo.}^{-1}$$

This situation corresponds to a heat of activation of 29,000 cal./mole. Watanabe (6, 7) carried out similar studies at temperatures of 100, 110, 120, 130, and 140°C. For his study done at pH 4.2 he lists these specific reaction rate constants:

$$100°C: \; k = 2.7 \times 10^{-2} \text{ hr.}^{-1}$$
$$110°C: \; k = 6.9 \times 10^{-2} \text{ hr.}^{-1}$$

This situation corresponds to a heat of activation of 26,100 cal./mole; Watanabe, on the basis of all his data, lists the value of the ΔH_a as 31,000 cal./mole.

It may be concluded that the agreement between the two different groups' value for the heat of activation is very good. Of course, this alone does not indicate conclusively that the degradative reaction at 25 and 110°C is the same, because the possibility of a family of lines existing on an Arrhenius plot must not be overlooked even though the slopes of the lines might be the same. However, even with the conversion factor 720 hours = 1 month, the data from the different temperatures do form a single linear Arrhenius plot. Considering the different investigators, the variability of the assay method for thiamine, and the approximation of time values in the year-long study, agreement between the two studies is surprisingly good. The data indicate that the same kinetic situation predominates both at very high and at low temperatures. This then is one case which can be considered neither completely typical nor completely atypical but in which studies at high temperatures prove to be significant.

It is easy for anyone who has studied the kinetics of relatively complex pharmaceutical formulations to cite examples wherein the results of high and low temperature studies do not present such a tidy picture as in the thiamine case just discussed. It is possible also to cite examples which concern systems with only one degrading ingredient to illustrate such situations. Heimlich and Martin (8) in a detailed study of the degradation of glucose in acid solution have shown that a change in

mechanism appears to take place at temperatures at and below 100°C as compared to studies done between 100 and 150°C. Similarly, Ooteghem and Steiger (9) showed that the hydrolytic process in degrading aqueous procaine hydrochloride solutions is not the same at 20°C and above 80°C, so that, e.g., a study done at 100°C will not permit calculation of the degradation rate at 20°C.

Finally, although the kinetic basis upon which stability studies rest is not absolutely unequivocal, we may still conclude that chemical kinetics gives us a potentially useful tool.

Placement

The preceding section covered the basic structure of methods which use chemical kinetics to predict product stability. Central to predictive techniques is, of course, the necessity of placing samples at various elevated temperatures—or stressing them in some way such as exposing them to freeze-thaw cycles. Normally, storage temperatures have been chosen more or less arbitrarily, although the evolution of the choices has resulted in a very reasonable, useful, and workable system for most formulators.

The purpose of this section is simply to call attention to the fact that there exist certain theoretical—and practical—reasons which have been used by some workers to develop particular systems of storage temperatures and assay schedules for stability studies. Examples which illustrate this will now be cited.

Tootill (10) based his suggestions of storage temperatures on a slope ratio experimental design. This is a statistical term for a certain experimental design which facilitates the application of statistical methods to the analysis of the results. This system is valuable when, of necessity, imprecise assay methods must be used. Here the aim is loose in the sense that the exact path of degradation is not determined, but rather statistics are used to estimate expiration dates. The design corrects the situation in which one obtains equivocal k values and Arrhenius plots due to a large number of unreplicated sampling times with a minimum number of storage temperatures. Tootill's method requires six time-temperature combinations in addition to the initial assay. The temperatures of storage are chosen so that the reciprocal absolute temperature values are in arithmetical progression. This will cause, if the Arrhenius relationship holds, the slopes of the individual degradation lines to be in geometric progression; this fact is expressed as the slope ratio. Fur-

Table III
Suggested Stability Storage Temperatures (Tootill)

Series							
1		2		3		4	
°C	°F	°C	°F	°C	°F	°C	°F
39	102	42	108	52	126	60	140
63	145	63	145	64.5	148	69	156
91	196	87	189	78	172	78.5	173

Table IV
Suggested Stability Test Design (Kennon)

Temperature		Assay or Sampling Times (Months)			
°C	°F	1st	2nd	3rd	4th
60	140	1	3	4	..
45	113	3	4	6	8
37	99	6	8	12	..
RT	RT	8	12	18	24

Table V
Suggested Stability Test Design (Lordi and Scott)

Temperature		Assay or Sampling Times (Months)		
°C	°F	1st	2nd	3rd
41.5	107	0.84	2	5
60	140	0.35	0.84	2
46	115	0.43	1.3	4
70	158	0.14	0.43	1.3

thermore, the time scales to get the same amount of breakdown at each temperature will also be in geometric progression in the opposite direction from the temperatures (as the higher temperatures require less time). The times are set on the basis of an estimate of the slope ratio. Thus, one needs an estimate of the slope ratio to start the experiment. This may be obtained from literature data or from a preliminary study. The experimental design will then result in approximately the same amount of degradation at the times samples are withdrawn and assayed regardless of temperature. The design calls for samples to be withdrawn at two times for each of three temperatures, with the second time being set for 50% decomposition.

Tootill has shown that, following this arrangement, each individual degradation curve is estimated with approximately equal precision and

that this simplifies both the statistical analysis and the task of judging the degree of conformity of the results to the Arrhenius equation. Table III shows four series of suggested storage temperatures which fit Tootill's design. Times and temperature set chosen would be determined depending on the degradation rate, to get the length of the experiment to a manageable or convenient length.

Kennon (11) illustrated the utility of mathematical models in determining chemical stability. The construction of the reference reaction paths he used was based on considerations involving heats of activation and shelf-life goals. From these paths a logical assay schedule arose. The schedule is actually based on the temperatures chosen for sample storage and would change if another set of storage conditions were used. An example of a set of suggested storage conditions and an assay schedule are shown in Table IV.

Lordi and Scott (12) reported on their development of nomographic stability charts which were designed to facilitate the analysis and enhance the utility of data obtained from stability tests. In connection with these efforts, they also suggested a stability program design based on probable heats of activation and t_{90}'s. They suggest the times and temperatures shown in Table V. Normally only one of the sets (either the 41.5–60°C or the 46–70°C) would be used.

Two additional—and untraditional—types of stability testing procedures are also worthy of note. These methods of "placement" are quite different from those discussed so far.

Eriksen, Pauls, and Swintosky (13) investigated the accuracy of heating-time measurements as they are affected by time lags during the heating and cooling of samples during a stability study. They developed an equation relating sample heating or cooling rate, storage time and temperature, and the heat of activation. This provided the ETTE or "equilibrium temperature time equivalent," and this information enabled one to get better data for kinetic calculations. These techniques may not appear to be especially useful for our purposes, but they are most valuable when one works with high temperatures for short times, or with very large bulks, or when heat conductivity factors are not ideal. In a subsequent paper these authors (14) presented some additional information concerning applications of this technique in a tablet stability study.

Some years later Eriksen and Stelmach (15) devised and illustrated with appropriate data a "one step" method of implementing a kinetic study. The technique uses a "reciprocal heating machine" to make a

single nonisothermal run which is considered to be equal to a complete stability study. Essentially, the sample is subjected to a programmed change of temperature-time conditions. Some function, then, which represents both temperature and concentration, is obtained from samples removed and analyzed during the run. Plotting of the function *vs.* time produces a straight line from which both the heat of activation and the specific reaction rate constant may be calculated. Rogers (16) also presented a similar accelerated storage testing technique in which both the heat of activation and the room temperature reaction rate constant could be obtained from analyses made on samples withdrawn while the temperature of the system was raised in accordance with a certain program.

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J. Soc. Cosmetic Chemists, **17**, 149–156 (1966)

Lanolin Allergy?

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Presented before the New England Chapter, November 18, 1965
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Synopsis—A review of the literature indicates that only about 100 cases of lanolin sensitivity have been documented during the last 30 or 40 years. It is concluded that lanolin presents no hazard in cosmetics and is not a sensitizer. Possible reasons for the occasional lanolin allergy are reviewed, but no definite conclusions can be drawn from data available so far. It is noted that no specific fraction of lanolin is implicated in this sensitivity.

Historical Use of Lanolin

For centuries lanolin and/or its derivatives have been and continue to be some of the most consistently appearing single components in cosmetic and toiletry formulations. While lanolin is added to formulas occasionally by a manufacturer for "magic" appeal of the word, the continued wide use of the material over such a long time can only be related to its functional value in the management of dry skin. Literally millions upon millions of pounds of lanolin and its derivatives have been applied to the skin and hair of millions upon millions of people over a period of centuries.

The use of crude wool grease as an emollient has a history that may predate even recorded civilization. There are indications that this precursor of lanolin found its way into the beauty aids and medical balms of the early Egyptians. Some speculate that the material was known to the early Chinese. Even the Old Testament makes reference to crude wool wax. The use of crude wool wax as an ointment base has been

* Malmstrom Chemical Corp., Linden, N. J.

traced to the days of Pliny in the first century before the birth of Christ (1).

Lanolin as we know it now had its birth in the centrifuge of two German scientists, Brown and Liebrich, who prepared the first refined neutral wool grease and obtained a patent on the process in the year 1882(2). These researchers are also credited with conferring the name lanolin on their refined hydrous product. Up until World War I the United States depended to a great extent on the importation of lanolin from Germany. At the start of the war these supplies became unavailable. This shortage led to the rapid growth of the lanolin industry in this country.

In the years since First World War, a boom has taken place in the use of lanolin and, more particularly, of its derivatives. The trend toward development of the newer derivatives of lanolin comes from a desire to create new materials from the already proved valuable lanolin—new products more specific in function, more versatile in use and more esthetically elegant than lanolin. By fractionation and by chemical reaction, such as ethoxylation, new derivatives are created, laboratory and clinically tested, and finally judged in consumer use to demonstrate their worth in the fields of cosmetics and dermatology.

Incidence of Dermatitis Attributed to Lanolin

Following the increasing wide spread use of the material, instances of cutaneous reaction were discovered and presumed to be caused by lanolin; it is only natural that dermatologists and allergists would attempt to study this phenomenon. Among the first in this country to report cases of allergy attributable to lanolin were Ramirez and Eller (3) (one case) and Sulzberger and Morse (4) (two cases). Sezary (5) made a similar report of three cases in France. Bonnevie (6) in 1939 reported one case in 2358 patients thoroughly investigated in Copenhagen. Ellis (7) later reported a case of allergic contact dermatitis due to wool fat and cholesterol. Schwarzfeld (8), in reporting on some ten cases sensitive to lanolin and Aquaphor* (a lanolin ester and alcohol absorption base), felt that the Ellis work gave some physicians the impression allergic reaction to lanolin was rather common. No statement in the Ellis report could be so construed. Sulzberger and Lazar (9) in reporting on four patients reacting to lanolin made the statement that this type of reaction "occurs surprisingly rarely." Sulzberger *et al.* (10) in later studies found 12 lanolin-sensitive patients out of some 1048 allergy pa-

* Duke Laboratories, Inc., Stamford, Conn.

tients—an incidence of 1.1% in this *select* population. Warshaw (11) in a report continuing this study added three more lanolin-sensitive patients discovered at the New York Skin and Cancer Unit plus seven other patients from private practice.

Hjorth (12) in Denmark described 21 lanolin-sensitive patients out of 25,000 *allergy* patients examined over a *twenty year period* or, in this *select* population of allergy cases, an incidence of lanolin sensitivity of less than 0.1%. It must be stressed that in this situation, as in the case of Sulzberger's patients, he was dealing not with normal healthy individuals but rather with individuals with predisposition to sensitivity.

Truter (13) in reporting on one case of dermal reaction to lanolin held that, from the dermatological literature, it was apparent that cutaneous hypersensitivity to lanolin is "extremely uncommon." In 1955 Baer *et al.* (14) claimed to have observed 28 lanolin-sensitive patients out of 637 tested. Then in 1962 Calnan (15) reported 11 cases.

A recent report by Wereide (16) in Oslo merits consideration because of the unusual test procedure used and the broad conclusions reached. He tested 270 eczema patients with anhydrous lanolin, Eucerin* (7 per cent lanolin alcohols† in soft paraffin) and mixtures of the two. In each test 5% of salicylic acid was added. He reported two reactions to the lanolin and three to Eucerin but 15 to the mixture of the two; he concluded that lanolin sensitivity was common in eczema patients. It is well recognized that single materials may be innocuous by themselves but toxic in combination. However, one can't help but suspect the possibility Wereide observed some other kind of primary irritation due to the rigor of the test or a possible synergistic phenomenon rather than a true lanolin sensitivity.

Carney (17) reported that in fifteen years he had seen only one proved case of lanolin sensitivity. Klauder and Ellis (18) reported five cases in private practice. Orentreich (19) in treating a series of some 154 dermatological cases with the oil soluble liquid fraction of lanolin and preparations made from it found no instances of intolerance. He did report one case discovered in routine patch testing at the Hair Clinic in N. Y. (20). Masters (21), in discussing cosmetic allergies, felt that lanolin and its derivatives are not primary irritants and that allergic manifestations to their use are small. In the regulations issued following the color additive legislation which were published in 1963, lanolin is included in the

* Beiersdorf & Co. A. G.

† Superhartolan-Croda, Ltd.

list of "safe" diluents for cosmetic use. The report of the European Committee on Chronic Toxicity Hazards (Eurotox) (22) lists lanolin as completely acceptable in the category of vehicles and solvents.

It should be pointed out that this review of the literature of reported instances of lanolin sensitivity yields a total of about 100 odd cases—reported over a period of 30 years and from several countries. In spite of all these data lanolin continues to be suspect in some quarters and with some dermatologists.

Pretesting of Cosmetics and Ingredients

Under these circumstances it seems unnecessary that the cosmetic manufacturer should be greatly concerned with the problem of cutaneous reaction to lanolin because the reported instances of such reactions are so infinitesimally low. However, no reputable manufacturer of cosmetics and toiletries would want to place on the market a product that was unsafe for use. With the exception of 1960 legislation requiring the pretesting of the class of cosmetics defined as color additives, Federal legislation does not require the pretesting of cosmetics for safety. The law as it stands provides for the seizure of dangerous cosmetics, but *only* after the Government has proved they are dangerous. As pointed out by Miller (23), the Food & Drug Administration has urged that, just as in the case of new drugs and color additives, there be a requirement for pretesting *all* cosmetics. The Harris Bill now pending before Congress would require such pretesting.

Levenstein, Draize *et al.* (24–26) describe several of the animal tests currently in use to screen cosmetics and ingredients for possible toxicity and irritation. Levenstein feels there is enough correlation between animal pretesting and human use experience to warrant such tests. Rieger and Battista (27) point out that it is not always possible to correlate between animals and human tests but urge that both be used. The following are basic screening tests considered to be a reasonable minimum for most topically used ingredients.

Primary Dermal Irritation

Primary irritation, or a skin reaction following a single contact with a substance, is usually determined by patch testing the material on both the intact and abraded skin of rabbits. A more realistic approach is the use of human subjects where possible. In the instance of lanolin and the oil soluble liquid fraction of lanolin,* Shelanski (28) reported that

* Lantrol®—Malmstrom Chemical Corp.

tests on 50 human subjects indicated they are not primary irritants. Kligman (29) reported another test for irritancy before the SOCIETY OF COSMETIC CHEMISTS. Tested with this procedure both lanolin and the liquid lanolin showed "a remarkably low order of irritancy... extraordinarily innocuous for human skin" (30).

Acute Oral Toxicity

This is a basic test for any cosmetic or ingredient which may be ingested, even if accidentally. Rats are fed successively increasing doses of the materials to determine the minimum amount, if any, required to kill 50% of the animals. In the instance of lanolin, its liquid fraction and other lanolin derivatives relatively massive doses are tolerated (31).

Rabbit Eye Irritation

The usual method of test for eye irritation is that described by Draize (26). Such tests on lanolin and some of its derivatives consistently show a very low order of irritation (32). Goldemberg (33) pointed out the possibility of formulating with anti-irritants, that is, substances which might reduce the irritancy of other materials. Russell and Hoch (34) reported that the addition of the liquid fraction of lanolin to detergent systems seems to reduce the eye irritation of the detergent system.

Sensitization and Allergenicity

One test for sensitization involves the intradermal injection of the test material in guinea pigs over a period of days, followed by a challenging injection. Areas of the wheals resulting from the final injection are compared with average responses in the previous ones. A substantial increase in response to the final injection is considered evidence that the material is a sensitizer. Human testing is generally considered more desirable. Klauder (35) feels that such predictive patch testing using as many as 200 human subjects would only begin to detect allergenicity at about the mid-region of a scale of materials "where at one end of which allergenicity is very rare (lanolin) and at the other end it is frequent (paraphenylenediamine)." Regardless of this feeling, the repeated insult test is considered desirable. In the case of lanolin and the liquid fraction of lanolin such tests on 25 human male and 25 human female subjects (36) indicate these materials are not sensitizers. Silverman (37) studying a suppository base containing 40% of the liquid fraction of lanolin reported a similar result.

Causative Factors in Lanolin Allergy

With respect to the relatively few cases of allergy attributed to lanolin it is significant to note the lack of agreement as to the causative factor involved. Some researchers have made fairly definite statements as to the nature of the allergen. However, the results have been at best contradictory. Sulzberger and Lazar (9), for example, in their report on four lanolin sensitive patients stated that the allergen was a constituent or constituents of the mixed alcohols. It did not seem to be present in other fractions of lanolin such as the mixed fatty acids, cholesterol, or lanosterol. Then Sulzberger *et al.* (10) and Warshaw (11) in their continuing studies felt they had isolated the allergen in the mixed aliphatic alcohols. They also got occasional positive reactions from the extracted fatty acids of the same source which could cause some doubt both as to the purification of the fractions and to the nature of the allergen. They also reported that modification of the lanolin and the aliphatic alcohols with acetyl radical reduced the incidence in some but not in all cases. Schwarzfeld (8) in his report of ten cases found that two were sensitive to lanolin and Aquaphor, four were sensitive to lanolin alone and four were sensitive to Aquaphor alone. Then, Fanburg (38) cited a case of contact dermatitis due to Aquaphor. This patient gave a positive reaction to "purified cholesterol esters" derived from lanolin but gave a negative reaction to lanolin itself.

Following the Sulzberger *et al.* reports, Everall and Truter (13) tested further successive fractions on their one lanolin-sensitive patient—going beyond the Sulzberger experiments. The patient reacted negatively to extracted aliphatic alcohols; on the other hand, there was a positive reaction to the crudely extracted cholesterol. Then, on purification of the cholesterol, they got a negative reaction. They finally isolated a yellow, glassy solid which they considered an impurity and to which the patient had a positive reaction. This material was not further identified. Acetylation of the "impurity" gave a negative reaction. Klauder and Ellis (18) tested their five lanolin-sensitive patients with the oil soluble liquid fraction of lanolin. All five were negative to the liquid lanolin. They tested four of these patients with the solid waxy fraction* obtained from lanolin by the same process and *also* got negative results. Ellis tested one of the patients with wool wax fatty acids and aliphatic alcohols and got a negative reaction; another gave a positive reaction to cholesterol.

* Lanfrax®–Malmstrom Chemical Corp.

From the above it would seem difficult to make a positive statement concerning the nature of the causative agent involved. In the case of the fractionated lanolin, that is, fractionated into the oil soluble liquid and the waxy solid, the mixed alcohols and aliphatic alcohols must be presumed present in both fractions. If, as Truter suggests, the allergen may be an impurity, then it is conceivable that further purification or other treatment is one answer. At best, available literature does not clarify the causative factor which results in a reaction attributed to lanolin in the relatively few subjects discovered and tested.

It must be remembered, too, that lanolin is a very complex natural material which is never completely identified. It may even vary seasonally. There can be wide variations in the grades and the purity of lanolin on the market. One cannot possibly know the effect of these variables on the results of reported cutaneous reactions, attributed to lanolin. It is known, however, that lanolin and its derivatives of vastly improved purity are available on the market today as a result of newer refining techniques.

Summary

The cosmetic chemist must be on the alert for possible allergic reaction to or irritation from many materials. Also, it is a generally accepted fact that no material is universally safe. In the case of lanolin, however, the bulk of the evidence seems to indicate that it is not a potent sensitizer. The known incidence of allergy attributed to lanolin as reported in the literature is extremely low. The evidence on the nature of the causative factor in so-called lanolin allergy does not seem to be conclusive. The further purification of lanolin, the fractionation of lanolin, and the development of the new derivatives may contribute to a reduction of the already very low incidence of reaction. However, reduction of the relatively infrequent cutaneous reactions to lanolin has not been a prime objective of research, which instead is concerned with the development of new cosmetic and pharmaceutical materials.

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Surface Modifying Effects of Lanolin Derivatives

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Presented March 10, 1965, Australian Society of Cosmetic Chemists, Sydney

Synopsis—The influence of lanolin derivatives on the physical aspects of dispersions is discussed. Particular reference is made to pigment wetting, rheological patterns in emulsion systems, solubilization, emulsification and spreading coefficients. Practical applications of these phenomena are illustrated by typical cosmetic formulations.

Introduction

This presentation is concerned primarily with the influence of lanolin derivatives on the physical aspects of dispersions. Lanolin is known to contain many chemical groups and configurations which are potentially surface-active. However, due to the manner in which these groups are chemically bound, they cannot achieve that potential. As a result, lanolin itself is relatively poor when considered from the viewpoint of surface activity. Fortunately, by means of chemical and physical procedures lanolin can be converted into very useful functional derivatives of predictable surface activity. Whereas formerly lanolin was employed mostly for the marketing advantages of having "Contains Lanolin" on the label, derivatives of lanolin are now widely used for their ability to modify the surfaces of dispersed systems as well as for emollient effects on the skin.

* American Cholesterol Products, Inc., Edison, N. J.

Chemistry of Lanolin

For a clear understanding of the subject it is necessary to review briefly the chemistry of lanolin and its derivatives. Unfortunately, the composition of lanolin fluctuates widely, both qualitatively and quantitatively, from lot to lot. Variables such as heredity, environment, and food supply affect the complex chemistry of this natural secretion of the sheep's sebaceous glands. Additional variations are introduced by aging, wool storage conditions, and scouring methods.

Esters

Lanolin consists of approximately 95% esters, 4% free alcohols, and 1% free fatty acids and hydrocarbons. The ability of lanolin to form W/O emulsions is due to the small free alcohol and fatty acid content.

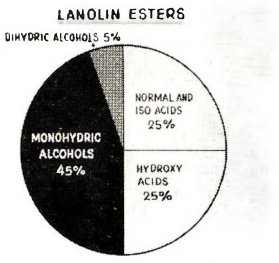

Figure 1. Composition of lanolin esters

The ester fraction contributes very little to surface activity but is important as a chemical intermediate and raw material of unique composition for the synthesis of derivatives. The nature of the esters is presented graphically in Figure 1, which shows a 50/50 division of the alcohols and acids which compose the esters. There are present both mono- and dihydric alcohols as well as normal, branched, and hydroxy acids. This assortment of reactive groups in compounds having a wide range of molecular weights (C_9 to C_{31}) results in an extremely large variety of esters.

Alcohols

The composition of lanolin alcohols is detailed in Table I. Cholesterol, of course, is the best known of these, but there are many other useful alcohols present. It is interesting that squalene, the highly unsaturated hydrocarbon characteristic of human sebum, is not found in the unsaponifiable fraction of lanolin. Glycerol is also completely absent.

Table I
Composition of Lanolin Alcohols

Aliphatic Alcohols		
Normal (C_{18} to C_{26})		18%
Branched chain (C_{17} to C_{26})		
Diols (C_{16} to C_{24}) five members isolated in 1951		4–5%
Sterols		
Cholesterol	$C_{27}H_{45}O$	25%
Dihydrocholesterol (cholestanol)	$C_{27}H_{48}O$	5%
Cerebrosterol	$C_{27}H_{47}O_2$	small amount
Triterpene Alcohols		
Lanosterol	$C_{30}H_{50}O$	10%
Dihydrolanosterol	$C_{30}H_{52}O$	10%
Agnosterol	$C_{30}H_{48}O$	1%
Dihydroagnosterol	$C_{30}H_{50}O$	4%
Hydrocarbons		<1%
Unclassified—at present		20%

Table II
Composition of Lanolin Fatty Acids (from Weitkamp)

Number of Acids	Series	Structural Formula	%
9	Normal	$CH_3—(CH_2)_{2n}—COOH$ (n = 4 to 12 incl.)	9.5
2	Hydroxy	$CH_3—(CH_2)_{2n-1}—CH(OH)—COOH$ (n = 6, 7)	4.2
10	Iso	$CH_3—CH(CH_3)—(CH_2)_{2n}—COOH$ (n = 3 to 11 incl.)	29.3
11	Anteiso	$CH_3—CH_2—CH(CH_3)—(CH_2)_{2n}—COOH$ (n = 2 to 13 incl.)	37.3
		Distillation Loss	6.0
		Residue	13.0
			99.3

Acids

Table II presents data on the composition of the lanolin acids as obtained by Weitkamp (1). Since his publication many additional acids have been identified. This laboratory found that hydroxy acids can comprise as much as 40% of the total lanolin acids (2). These fatty acids offer interesting opportunities for the synthesis of functionally active preparations for use on skin and hair.

Flow Diagram

The Lanolin Derivatives Flow Diagram (Fig. 2) graphically portrays the chemical and processing relationships between the various deriva-

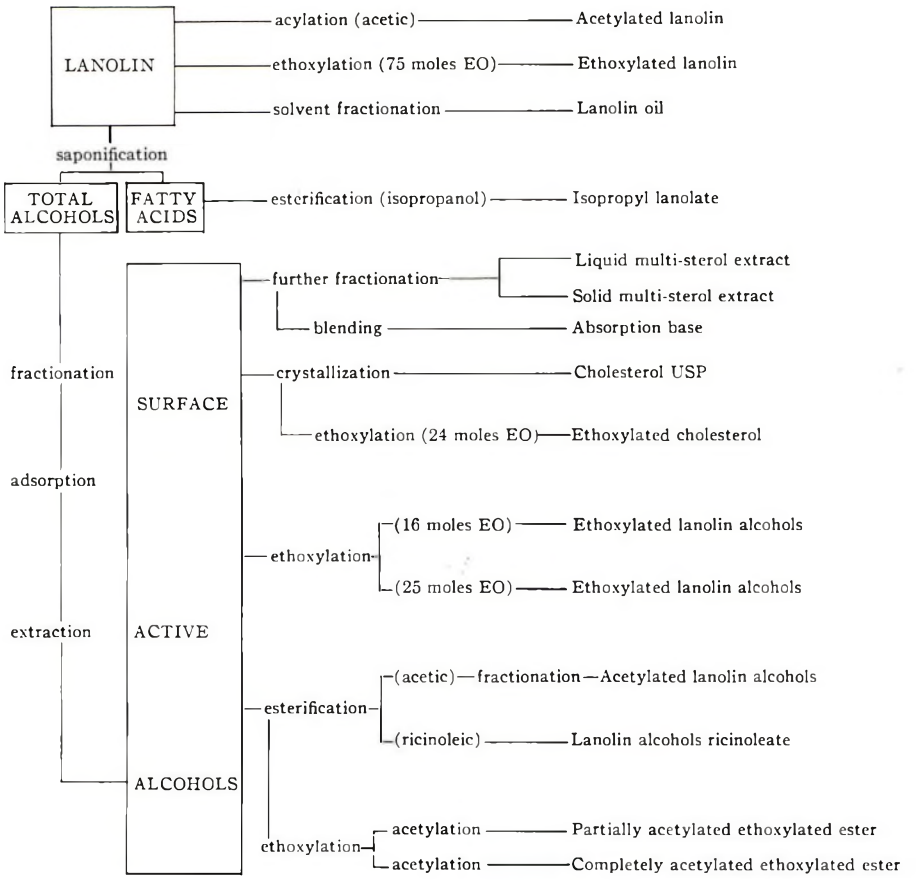

Figure 2. Flow diagram showing the usual processes employed for the manufacture of different lanolin derivatives

tives. It will be noted that there are four general processes applicable to lanolin directly. These are acylation, ethoxylation, solvent fractionation, and saponification. An additional process, rearrangement, is also being used to produce new products by the acidolysis of lanolin (3).

The lanolin fatty acids lend themselves to esterification, neutralization to form soaps, and ethoxylation. The lanolin alcohols are subjected to many processes including fractionation, adsorption, and extraction

to obtain the surface-active fraction, which can then be processed further to form multi-sterol extracts and absorption bases. Cholesterol is produced from this fraction by crystallization. By ethoxylating cholesterol, a derivative with hydro-alcoholic solubility properties is obtained. Other lanolin alcohol products are prepared directly from the surface-active alcohol fraction by ethoxylation. Another process employed is esterification. Steps such as ethoxylation and acetylation are then carried out on esterified lanolin alcohols. Quaternization has resulted in interesting experimental products with unusual substantivity when applied to skin and hair.

RESULTS AND DISCUSSION

Pigment Wetting

The effect of lanolin derivatives on the wetting and dispersing of finely ground solids in various liquid vehicles has been explored extensively. Lanolin products differ considerably in their pigment wetting action, a number of them being outstanding in this regard. It was assumed that wetting and dispersing implied deflocculation or reduction of agglomerated particles to the primary particle state. Consideration was given to the role of the derivative in terms of its orientation to and adsorption on the particle surface. The hydrophilic-lipophilic contrast within the molecule and association tendencies of portions of the derivative molecule were all regarded as important factors contributing to compatibility between the particle surface, the lanolin derivative, and the vehicle. Lanolin products probably also function by lubricating the particle surface and by displacing therefrom materials which might interfere with their adsorption onto the surface.

Wetting is regarded as a significant interfacial phenomenon involved in dispersing solids. After preliminary studies, a simple technique was selected to evaluate the comparative wetting performance of lanolin derivatives. The method employed was adapted from the paint industry where it has been used extensively (4). Recent studies have also applied this method to materials of interest in cosmetics (5).

The test consists of adding increments of vehicle from a burette to powders containing lanolin derivatives as additives. The incorporation of each increment is accomplished manually, and the mixture is worked to a uniform consistency. When a cohesive mass is formed, an end point is read, referred to as the "Wet Point." Further vehicle additions soften the mixture until a point is reached at which it flows; this volume is called the "Flow Point."

The Wet Point and the Flow Point are indicative of the wetting ability of a particular additive for a specific system. Since the wetting activity is inversely proportional to the volume of liquid vehicle added, a lower value signifies greater activity.

The ratios of derivatives to powders employed were in practical ranges for eventual use in finished formulations. The Wet and Flow Points were found to be reproducible and demonstrated a quantitative relationship in each specific system.

Table III shows the comparative efficiency of three lanolin derivatives in the wetting of several powders in mineral oil (70 Saybolt).

Table III

Wet and Flow Points in Mineral Oil (70 Saybolt)

	TiO_2		Talc		Oxy Red		D&C Red #9	
Deriv./powder ratio	Wet Pt.	Flow Pt.	Wet Pt.	Flow Pt.	Wet Pt.	Flow Pt.	Wet Pt.	Flow Pt.
Amerchol L-101								
10% of powder	30	238	31	174	30	113	28	105
20% of powder	12	47	18	165	7	58	16	83
Acetulan								
10% of powder	34	242	28	198	30	129	32	98
20% of powder	14	34	15	184	7.5	109	18	86
Amerlate P								
10% of powder	23	61	27	127	11	43	35	93
20% of powder	16	51	18	106	3	35	20	81
Control (Min. Oil)								
10% of powder	44	258	33	259	38	124	33	108
20% of powder	36	249	23	247	26	112	23	96

The results are given in terms of cc. of mineral oil per 100 g. of powder. Controls at 10 and 20% show the effect of using mineral oil instead of the derivative in the powder mixture. The data in Table III represent only one phase of the work on pigment wetting and are included here to show the value of the test method as a screening technique. Differences in wetting performance are shown. These are validated by actual experience with finished formulations employing the above materials.

Microscopic examination was also employed and found to be very useful for supplementing Wet and Flow Point data. Systems examined microscopically at the Flow Point exhibited complete deflocculation and good dispersion when the Flow Point was low. At high Flow Points

incomplete deflocculation and poor dispersion were apparent under fairly low magnification (100×). Sedimentation studies were utilized for estimating the influence of lanolin derivatives on the deflocculation of agitated liquid dispersions. It is apparent at this stage of the investigation that Amerlate P is an outstanding dispersing agent for pigments in both emulsified and anhydrous systems. This may be attributed to its chemical composition, consisting of the isopropyl esters of branched and hydroxy lanolin fatty acids in a broad range of carbon lengths. The unique lubricity resulting from this composition may play a significant role in the dispersing activity of the product. These factors also contribute to a reduction of shear requirements in formulations containing Amerlate P. The data in Table III confirm empirical findings which had led to the extensive use of this material in pigmented products.

The following formulas (*a* and *b*) illustrate the practical application of these principles in makeup items:

(*a*) *Anhydrous Makeup*	
Acetulan	6%
Amerlate P	3
Mineral oil (70 Saybolt)	36
Microwax, m.p. 170° F	15
Talc, TiO_2, Pigments	40
Perfume	q.s.

(*b*) *Liquid Cream Makeup (Highly Pigmented)*	
Amerchol L-101	4.0
Amerlate P	3.0
Stearic acid, XXX	2.0
Glyceryl monostearate	1.0
Mineral oil (70 Saybolt)	15.0
Triethanolamine	0.8
Propylene glycol	5.0
Water	69.2
Perfume	q.s.
	100.0 Parts
Pigments	15–25 Parts

These are elegant emollient preparations with good application properties on skin. They spread well with matte coverage and without streaking or feathering. Acetulan in the anhydrous makeup acts as a degreasing agent for the waxy vehicle. The lubricant properties of Amerlate P help to overcome the frictional drag of the high pigment levels of these two formulations.

Rheological Activity

Lanolin derivatives influence the rheological pattern of emulsion systems in a profound manner. They participate as emulsifiers in the formation and stabilization of an emulsion and can also affect development of its ultimate viscosity. Such viscosity trends are often thought of only in terms of the external phase. Elementary emulsion considerations point to crowding of the external phase by the volume of the dis-

persed phase and the use of external hydrocolloids as the prime sources of viscosity control. These studies show that the incorporation of lanolin derivatives in the interfacial film is an effective way to modify viscosity behavior and simultaneously add emollient properties.

The formulations shown in Table IV utilize Solulan C-24, an O/W emulsifier, together with cholesterol, a W/O emulsifier, in various ratios which determine the viscosity pattern of a cosmetically elegant O/W lotion. Brookfield readings show the dramatic influence of slight ad-

Table IV

Viscosity Changes in O/W Lotion

Cholesterol USP	...	0.5%	0.5%	0.5%	0.5%
Solulan C-24	...	...	0.15	0.3	0.75
Stearic Acid XXX	3.0%	3.0	3.0	3.0	3.0
Glyceryl monostearate (pure)	3.0	3.0	3.0	3.0	3.0
Mineral oil (70 Saybolt)	25.5	25.0	25.0	25.0	25.0
Triethanolamine	1.0	1.0	1.0	1.0	1.0
Propylene glycol	4.0	4.0	4.0	4.0	4.0
Water	63.5	63.5	63.35	63.2	62.75
Observations after one month:					
Appearance at room temp.	medium heavy flow	no flow	heavy flow	medium heavy flow	medium flow
Viscosity readings Brookfield—cps. #3 spindle @3 rpm	23,000	off-scale (solid)	39,000	26,000	9,400
Room temp. stability	good	good	good	good	good
Incubator stability (42°C)	good	good	fair	good	fair

justments in concentration of Solulan C-24 [ethoxylated (24 moles) cholesterol] on the reduction of the viscosity of the system. Extended time studies of this formula show that an optimum concentration of 0.3% Solulan C-24 prevents the undesirable thickening of this formula while maintaining its stability. This antigelling effect is a very useful property which may be applied to many lotion systems.

Solubilization

Transparent gels involve the use of microemulsions in modern cosmetic technology. Lanolin derivatives are essential components in many of these interesting systems in which the dispersed phase is invisible to transmitted light (theoretically a particle size of less than one-

fourth of the wavelength of light). Extensive studies of this type of solubilization have been reported previously (6). The following formulas (*c* and *d*) illustrate some of the transparent gels; in these cases, the lanolin derivative promotes stability in the presence of a large amount of both oil and water phases at a relatively low surfactant to oil ratio, important from irritation considerations.

Emollient Clear Gels (c and d)

Solulan C-24	15%	Solulan 16	10%
Isopropyl myristate	25	Atlas G-1292	10
Oleyl alcohol	5	Mineral oil (70 vis.)	20
Atlas G-1292	15	Oleyl alcohol	4
Propylene glycol	5	Propylene glycol	5
Water	35	Hostaphat KL340	4
		Water	47

Experience with transparent colloidal dispersions indicates that, although they are generally considered to be thermodynamically stable, they must be formulated very carefully if they are to survive the temperature extremes to which commercial products are normally exposed. Aging tests with microemulsions should take this into consideration, and the formulator should examine his experiments closely for changes in their physical state indicated by gradual opacification, loss of consistency, and a loss of their resonant or vibrating character. The latter often appears first and may precede other adverse changes.

Emulsifying Effects

The performance of lanolin derivatives as emulsifiers has been reported previously in some detail (7). More recently these laboratories have been concerned with the participation of lanolin derivatives in association phenomena related to the construction of emulsion interfaces. Much of this work has been of an empirical nature, and many formulas have been developed in which so-called theoretically balanced systems (e.g., HLB) utilizing conventionally paired O/W and W/O emulsifiers have been supplemented by the addition of lanolin derivatives. For example, use of one of the Amerchols (W/O) together with a Solulan (O/W) will add stability by associating at the interface with the other hydrophilic and lipophilic emulsifiers. This can be demonstrated in both nonionic and ionic systems and, in addition, leads to added benefits in terms of improved feel and texture. This work is actually an outgrowth of the classical experiments demonstrating the interfacial coupling of cholesterol with anionic emulsifiers of the sodium alkyl sulfate type (8). Examples of emulsion formulas (*e*, *f*, and *g*) having well as-

sociated interfaces, with lanolin derivatives as the key auxiliary emulsifiers, are given below:

(e) Anionic Lotion O/W Hair Dressing		*(f) Cationic Lotion O/W*		*(g) Nonionic Lotion O/W Roll-On Antiperspirant*	
Waxolan	5.0%	Amerchol L-101	5.0%	Amerlate P	1.5%
Amerchol L-101	4.0	Solulan 98	2.0	Amerchol L-101	3.5
Amerlate P	3.0	Cetyl alcohol	1.0	Solulan 98	2.0
Stearic acid	2.0	Arlacel 165	4.0	Cetyl alcohol	2.0
Mineral oil (70 Saybolt)	10.0	Emcol E-607S	0.1	Glycerol	2.0
Glyceryl monostearate	1.0	Glycerol	2.0	Polyoxyl 40 stearate	4.0
Ucon 50 HB 660	5.0	Water	85.9	Veegum HV	1.0
Water	68.86	Perfume	q.s.	Water	38.0
Carbopol 941	0.15			Chlorhydrol, 50%	36.0
Triethanolamine	1.0			Alcohol	10.0
Perfume	q.s.			Perfume	q.s.

Formula *e* is a heavy bodied lotion with good grooming qualities for hair. It behaves like a cream-oil type but is washable and non-oily. The cationic lotion *f* may be used for general hand and body applications or for removing static from hair for good manageability. The roll-on *g* is a relatively non-tacky system which resists crystallization on the ball applicator and deposits a flexible antiperspirant film on skin.

Spreading Properties

Surface activity can be expressed in terms of spreading coefficient (S) calculated from the following equation:

$$S = \gamma_B - \gamma_A - \gamma_{AB}$$

where γ_B is the surface tension of water; γ_A surface tension of the oil; and γ_{AB} is the interfacial tension between oil and water. The following Table V presents surface and interfacial tension data determined on mineral oil solutions of several products; these data are compared with the calculated spreading coefficients.

The higher the value of S, the greater the tendency for the oil to spread over the water surface. It is interesting to note here that several lanolin derivatives, which do not fit the classical description of emulsifiers because their molecular configurations show no hydrophilic-lipophilic contrast, nevertheless reduce interfacial tension considerably and show correspondingly high spreading coefficients. This indicates that there are other factors which may determine the interfacial activity of lanolin derivatives. An example of this is a comparison of the value of Acetulan with that of isopropyl myristate: Acetulan demonstrates a

Table V

Spreading Coefficients (S)

	γ_A(oil)	γ_{AB}(oil/water)	S(calculated for γ_B = 72.3 for water)
5% Solutions in mineral oil (70 Saybolt)			
Acetulan	32.0	21.2	19.1
Amerchol L-101	32.8	7.6	31.9
Modulan	32.5	15.0	24.8
Polylan	31.7	16.8	23.8
Ricilan B	32.6	19.1	20.6
Ricilan C	32.4	21.7	18.2
Viscolan	31.8	5.7	34.8
Isopropyl myristate	31.7	32.9	7.7
PEG 400 dilaurate	32.7	0.4	39.2
100% Materials			
Acetulan	32.9	17.2	22.2
Isopropyl myristate	30.9	16.7	24.7
Mineral oil (70 Saybolt)	32.4	45.3	−5.6

depressant effect on interfacial tension even after dilution to 5% in mineral oil; isopropyl myristate does not show this effect.

The following formulas (h, i and j) for bath oils utilize these principles to promote their spreading characteristics on water. This action of the lanolin derivatives can be fortified, if desired, by the addition of an oil soluble surfactant which will, in turn, promote emulsification of bath oil throughout the bath water. The above formulas are surface orienting. Reducing the surfactant, in this case polyethylene glycol 400 dilaurate, favors migration of the dispersed oil droplets to the surface of the water.

Emoilient Bath Oils

	h	i	j
Acetulan	5%	...	...
Modulan	5	...	...
Viscolan	...	10%	...
Polylan	...	...	3.5%
PEG 400 dilaurate	5	5	4.5
Isopropyl myristate	25	25	37.5
Mineral oil (70 Saybolt)	60	60	54.5

Summary

Various aspects of studies concerned with the participation of lanolin derivatives in surface phenomena were presented. These surface active effects are valuable supplemental properties to the established emollient character of these derivatives.

Data on pigment wetting performance were presented utilizing a simple technique which permits the comparative evaluation of lanolin derivatives in a quantitative manner.

The influence of lanolin derivatives on the rheological pattern of emulsion systems was illustrated by the viscosity and stability behavior of these systems.

Solubilizing and emulsifying effects of lanolin derivatives were discussed, and formulas were presented illustrative of the principles involved.

Finally, data on the spreading properties of several lanolin derivatives along with their practical applications were presented.

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Appendix

Raw Materials Used

(A) Lanolin Derivatives*

Acetulan®	Acetylated lanolin alcohols
Amerchol® L-101	Liquid multi-sterol extract
Amerlate® P	Isopropyl lanolate
Modulan®	Acetylated lanolin
Polylan®	Lanolin alcohols linolcate
Ricilan® B	Lanolin alcohols ricinoleate
Ricilan® C	Acetylated lanolin alcohols ricinolcate
Solulan® 16	Ethoxylated lanolin alcohols
Solulan® 97	Completely acetylated, ethoxylated lanolin alcohol-esters
Solulan® 98	Partially acetylated, ethoxylated lanolin alcohol-esters
Solulan® C-24	Ethoxylated cholesterol
Viscolan®	Lanolin oil
Waxolan®	Lanolin wax

* The above products are manufactured and the Trade Marks are owned by American Cholesterol Products, Inc., Edison, N. J.

(B) Miscellaneous Ingredients

Arlacel 165	Glyceryl monostearate, acid type, self emulsifying, Atlas Chemical Industries.
Carbopol 941	Carboxy vinyl polymer, B. F. Goodrich Chemical Co.
Chlorhydrol 50%	Aluminum chlorhydroxide complex, Reheis Co., Inc.
Emcol E-607-S	N-(Stearoyl colamino formyl methyl) pyridinium chloride, Emulsol Division, Witco Chemical Co.
Atlas G-1292	Ethoxylated hydrogenated castor oil, Atlas Chemical Industries.
Hostaphat KL340	Tertiary ester from o-phosphoric acid and lauryl tetraglycol ether, Hostachem Corporation.
Microwax (m.p. 170°F)	Microcrystalline hydrocarbon wax, white, 170°F m.p., Bareco Wax Co.
Ucon 50 HB 660	Polyalkylene glycol, Union Carbide Chemicals Company.
Veegum HV	Magnesium aluminum silicate, R. T. Vanderbilt Co.
Oxy Red	Purified grade of ferric oxide, Whittaker, Clark and Daniels.

Society of Cosmetic Chemists 1966 Meetings

The Society of Cosmetic Chemists will hold the following meetings in 1966:

Date	*Meeting*	*Location*	*Program*
May 10, 1966	Semiannual	Americana Hotel, New York, N.Y.	To be announced later
Sept. 20, 1966 Sept. 21, 1966	Seminar	Americana Hotel, New York, N. Y.	Pediatric Cosmetics Geriatric Cosmetics Perfume Psychology Cosmetic Safety Testing
Nov. 30, 1966	Semiannual and medal award dinner-dance	Americana Hotel, New York, N.Y.	To be announced later

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Instrumental Method for the Determination of Hair Raspiness

WILLIAM C. WAGGONER, Ph.D., and GEORGE V. SCOTT, Ph.D.*

Presented December 1, 1965, New York City

Synopsis—As comb teeth arrange hair fibers in a parallel manner and rub along hair scales, vibrational frequencies are emitted and play a role in the "feel" of hair. The audible frequencies, which denote raspiness, may be cosmetically undesirable. In an attempt to record and evaluate hair raspiness, an electronic comb, specifically designed to pick up frequencies by contact, was constructed. Several groups of hair tresses, which were treated with cosmetic chemicals, rinsed and dried, were combed with the instrument. Computer analysis of the data showed the expected differences between tresses; and some differences reflected excellent probabilities of test reproducibility. The method lends itself to rapid laboratory screening of agents designed to reduce friction during combing.

Hair raspiness, which is the property of a substance producing grating, harsh sounds and feel, is probably most noticeable during the combing process. As the comb moves through the hair and arranges it in a parallel manner, friction at the tooth-hair interface generates frequencies and conveys to the individual an impression of general hair condition. It has been shown (1) that subjective judgments of handle and combing ease correlate very well with frictional measurements. A literature survey (2) has revealed the existence of many fiber frictional measurement methods, some of which may be applied to human hair studies. Others (3, 4) have measured the spectral distribution of sound produced by fibers in friction.

In an attempt to investigate characteristics of hair sound and feel as experienced by an individual during the combing process, an electronic

* Colgate-Palmolive Co., Research and Development Dept., Piscataway, N. J. 08854.

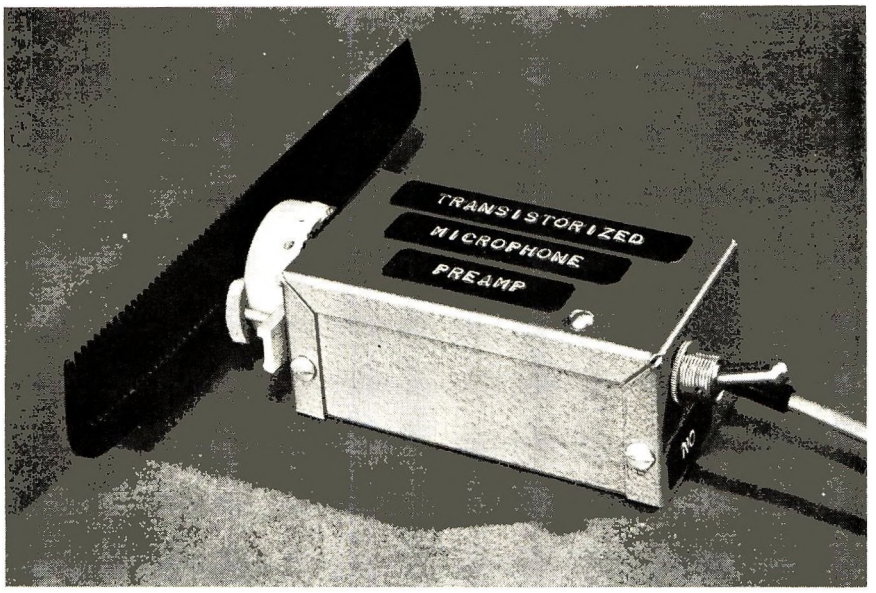

Figure 1. Comb, microphone, and pre-amplifier

comb which measures frequencies generated by tooth-hair interface friction was developed, with the following objectives:

a. The method should quantitatively compare product effects on hair raspiness.
b. The results should be in a form suitable for the application of statistics.
c. The method should be practical enough in test conditions to provide a routine evaluation of hair products.
d. The method should provide an additional parameter for tress quality control.

Materials and Methods

A crystal contact microphone* which is specifically designed to pick up frequencies by contact and at the same time remains oblivious to extraneous noise was chosen for the study. An Ace Wavesetta hard rubber comb (#1033)† was affixed to the contact microphone (Fig. 1) by two small bolts. A third bolt, which had been placed through the comb

* Hamlin, Inc., Lake Mills, Wis.
† Ace Comb Co., Butler, N. J.

frame, served as a pressure adjustable contact bridge between the comb and microphone. In this situation, any sound frequencies received by the comb are carried to the contact microphone *via* the steel bolt. This complete assembly was mounted onto the end of a minibox. The microphone output was delivered to the single-ended input of a transistorized four stage pre-amplifier (Fig. 2) which has a self-contained power source, has an approximate gain of 100 and is contained within the aforesaid minibox. Signals from the complete unit were monitored on an oscilloscope during several tress combings. From the noise patterns on the

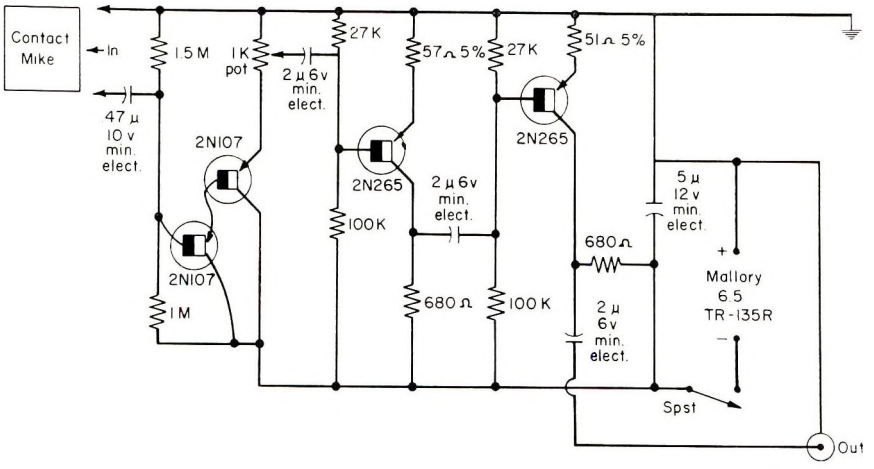

Figure 2. Diagram schematic of comb pre-amplifier

screen, the unit appeared to perform satisfactorily and provided a nucleus for all subsequent work. When the unit was monitored on a loudspeaker system, tress combings sounded similar to a rasping file on a sound board; hence the choice of the name, raspiness.

Initially, the transistorized pre-amplifier output was connected (single-ended) to a Grass 5B Polygraph* (Fig. 3) utilizing a 5P3 integrator pre-amplifier, which will integrate the complete incoming signal whether it is procured with a fast sweeping comb stroke or a slow methodical stroke; each record reveals the same area under the curve. As an option, the integrating pre-amplifier was monitored with a DuMont 411 oscilloscope.† A driver amplifier received the output of the integrating pre-amplifier and delivered the signal to an

* Grass Instrument Co., Quincy, Mass.

† DuMont Laboratories, Clifton, N. J.

oscillograph, where recordings were produced on strip-chart paper with curvilinear pens. Since the area under the curve has a direct relationship to frequency amplitude, chart curves were cut out with scissors and weighed on an analytical balance. Planimetering of the curves was found to be less accurate and, therefore, unsatisfactory. Integrator pre-amplifier calibration with a known input voltage makes possible comparisons between results taken at different times.

Secondly, the comb pre-amplifier was connected to an oscilloscope (Fig. 4) to which outside electronic capacitors had been applied to

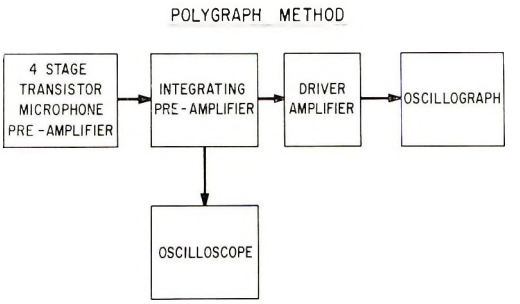

Figure 3. Block diagram of polygraph method

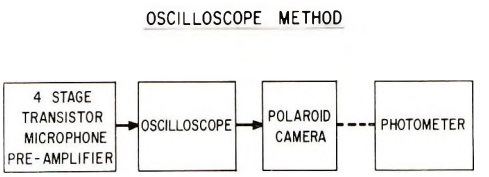

Figure 4. Block diagram of oscilloscope method

slow the sweep. Deviations of the electron beam were recorded on positive film using a Polaroid®* camera. After film development, a photometer reading of transmitted light through the film gave results relative to deflection amplitude of the electron beam.

For use, the transistorized pre-amplifier with the comb attached is held in the hand. A rigidly mounted tress or the subject's hair is combed with even strokes. Alternatively, tresses may be mounted on a constant speed rotating wheel and pulled through the rigidly mounted comb. Before the test combing is initiated, the comb is run through the hair several times to ensure no snarls and to establish timing.

* Polaroid is a trade mark of Polaroid Corp., Cambridge, Mass.

At least ten comb strokes at one-second intervals comprise the test. Tests have been run on wet and dry preparations. All tresses weighed 2.0 (±0.1) g.

Initially, damaged (bleached) and undamaged clean tresses were compared. In a second study, shampooed tresses were compared to tresses which had been shampooed and treated with a cationic rinse. Still further, in a third study, shampooed tresses were compared to tresses which had been treated with an experimental shampoo, which had been shown in previous subjective tests to increase hair manageability. A cross-over of the latter tress treatment supplemented this study. All results were analyzed by a Control Data® 160-A Computer,* using statistical FORTRAN† programs written by one of the authors (W. C. W.). Outcoming data from the hair combing device fit a normal distribution pattern.

Results

Figure 5 gives representative recording examples. At the top left (*A*) is a compressed direct readout of three tress combings using the polygraph method. It is a series of positive and negative deflections; and although not utilizable for quantitative interpretation, it is evidence of noise generation. However, pen response time prevents recording frequencies above 60 cycles/sec. If the three previous signals are each electrically integrated, the record at the top right (*B*) is obtained. To increase sensitivity of the method, paper speed of the strip chart recorder may be accelerated to give an expanded integrated readout, as seen in recording *C*.

Records of control and treated tresses appear in the lower recordings of Fig. 5. Recording *D* is that of a clean, dry tress examined with the polygraph method (1 comb stroke). Record *F* is obtained from a similar tress examined by the oscilloscope method (4 comb strokes). If a dry tress which has been treated with a cationic rinse after shampooing is combed at the same amplifier settings used with control tresses, it may be readily observed from records *E* and *G* that the signal drop from the controls (*D* and *F*) is considerable with both methods of recording.

As seen in Table I (polygraph method), control tresses were compared to cationic rinse treated tresses, which when combed with the coarse

* Control Data is a trade mark of Control Data Corp., Minneapolis, Minn.

† FORTRAN is an abbreviation for FORmula TRANslation and was originally developed for International Business Machine equipment.

comb teeth showed a 77.72% drop in sound levels. Statistically, on the basis of the null hypothesis, there was a 5% chance that the control and experimental tresses were from the same population as a result of treatment. When the tresses were combed with the fine comb teeth and the results compared, there was an 84.31% drop in sound levels of the treated tress group. Here, there was only a 1% chance that the control and experimental tresses were from the same population as a result of treatment.

Table II (oscilloscope method) compares two groups of tresses which were treated with a control shampoo and an experimental sham-

Table I
Control Tresses and Cationic-Treated Tresses (Polygraph Method)

Tress	N	Mean	Std. dev.	*t* Value	Level of Sig.	% Change
			A. Coarse teeth			
Control	3	4.09	1.98	...	...	...
Cationic	3	0.91	0.24	3.70	.95	−77.72
			B. Fine teeth			
Control	3	14.98	3.55	...	...	...
Cationic	3	2.84	0.47	5.87	.99	−84.31

Table II
Control Shampoo Tresses and Experimental Shampoo Tresses (Oscilloscope Method)

Tress	N	Mean	Std. Dev.	*t* Value	Level of Sig.	% Change
Control (A)	6	40.81	7.21	...	...	...
Experimental (B)	6	36.02	5.88	1.261	.70	−11.87
Control (B)	5	54.23	9.78	...	...	...
Experimental (A)	6	51.67	4.27	0.545	.40	− 4.73

poo, respectively. The experimental shampoo had the same detergent base as the control shampoo; however, it contained two additives which have been shown subjectively to increase hair manageability. The tresses which were washed in the experimental shampoo showed an 11.87% drop in sound levels when compared to the control group. Accompanying this is a 30% probability that the two groups are from the same population as a result of treatment. When the tress groups are crossed over, as seen in the bottom half of Table II, the experimental shampoo group exhibits only a 4.73% drop in sound levels when compared to the control group. However, there is a 60% probability that

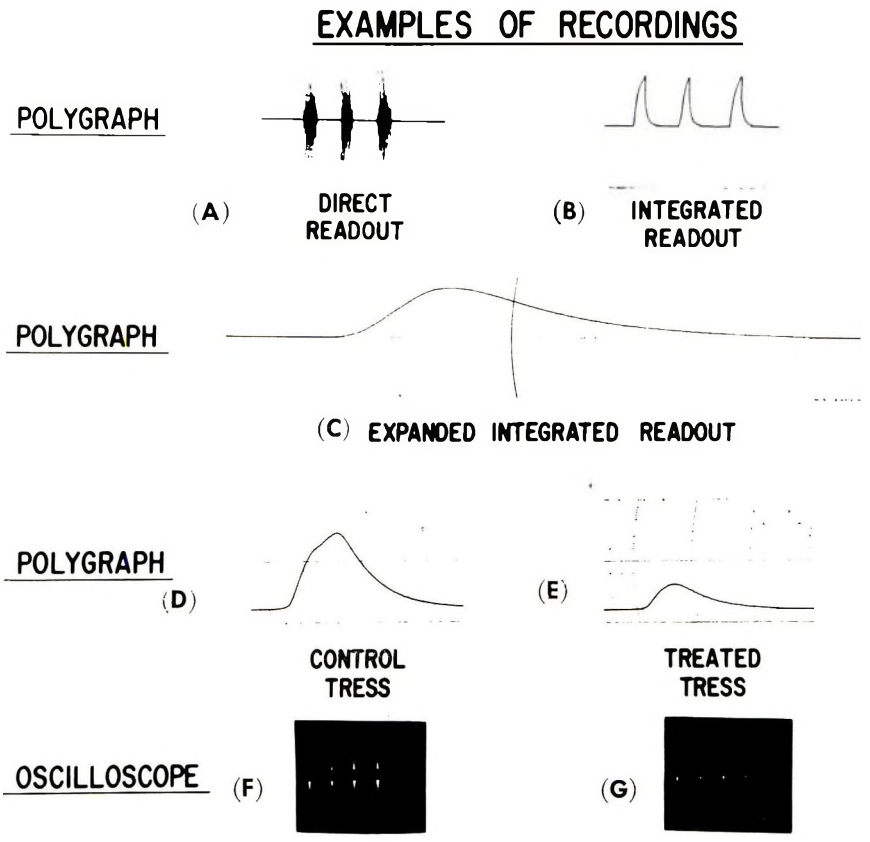

Figure 5. Representative examples of tress recordings

the two groups are from the same population as a result of treatment. In the cross-over, one tress was eliminated in group *B* due to obvious contamination.

In addition, when dry bleached hair was compared to dry unbleached hair in early studies, there were greater sound levels during combing of the former based on subjective evaluation of the records. Some holding sprays tend to increase combing sound levels. Furthermore, it is difficult to differentiate between similar control and experimental products on wet hair.

Discussion

The method as shown in Fig. 5 and monitored on audio output appears to reflect sound levels (raspiness) as a result of comb-tooth and frame interface friction during the combing process. The method appears to

be practical for use in both tress and *in vivo* work, since the initial sensing element is a common hard rubber comb.

The polygraph method and oscilloscope method give comparable results. The former method appears to have advantages from an *a priori* standpoint because the integration system will more faithfully register complete signals; whereas the oscilloscope photos register only those points in the flying spot path for which residence time is sufficient to affect film emulsion. However, the polygraph method is more time consuming in cutting and weighing of records. A digital voltmeter which would display the integrated signal would rectify this situation.

From the data in Table I, tresses treated with a cationic rinse gave about one-fifth the raspiness levels as those recorded in the control tresses; and this change was significant at the 0.05% level with the coarse comb teeth and significant at the 0.01% level with the fine comb teeth. This is in contrast to previous work (1), which found a cationic rinse to have relatively little effect on dry friction of hair.

Table II compares two groups of tresses, which were treated with a control shampoo and an experimental shampoo, respectively. The experimental shampoo contains two ingredients which have been shown subjectively to increase hair manageability. In the first test, the 12% drop in raspiness values is not significant at an acceptable level. After the cross-over, the experimental group again shows a raspiness value drop, which is not significant at an acceptable level. However, a trend is noticeable, and the data of the first experiment in Table II show enough promise to warrant increasing the degrees of freedom (numbers of tresses) to anticipate better confidence limits of probability. In the second experiment, tress group *B* may have had some carry-over from the first treatment, as reflected in the lower relative changes in sound levels.

The finding that bleached hair gives much higher raspiness levels than unbleached hair correlates with other studies (1). These present tests were examined subjectively by strip-chart recorder and audio outputs; however, the difference was highly discernible.

In addition, electronic comb measurement is now being used as another parameter for selection of homogeneous tress groups, thereby establishing better tress quality control.

In conclusion, the method presented appears to offer the hair investigator a tool for the exploration of the parameter, raspiness. It is possible that the method may find better use after further development. It has an advantage in that the primary probe is the common comb and

the electrical integrating system is designed to normalize readings independent of sampling technique. The disadvantages lie in the inability to sample a standard tress after different treatments. In one case the hair may be highly charged with static, spread out, and representative combings difficult to obtain; and with other treatments the hair fibers may tend to mat together and involve more fibers than in the first case. However, this may be a blessing in disguise for these situations do more closely depict actual user conditions.

Several other aspects can be considered in future studies. The effects of materials of construction of combs would be of interest to comb manufacturers. This study would be feasible if the combs were produced in similar molds. The hair-on-hair *versus* comb-on-hair noise ratio should be explored. Our assumption that the major noise component is a result of tooth-hair interface friction may be vulnerable. In spite of apparent shortcomings the method appears to have some potential which will be borne out by future studies.

Summary

1. A method to evaluate frequencies, which are produced during hair combing, has been developed.

2. Data from the output devices may be handled statistically.

3. The method provides a basis for routine screening of hair products.

4. The method provides an additional parameter for tress quality control.

(Received December 10, 1965)

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(3) Thorsen, W. J., and Veneklasen, P., *Ibid.*, **31**, 804 (1961).
(4) Thorsen, W. J., *Ibid.*, **32**, 670 (1962).

Translations Available

English translations of the following papers may be obtained by writing to Mr. Robert A. Kramer, Evans Chemicals, Inc., 250 East Forty-third Street, New York, New York 10017.

"Studies of the Phenomenon of Permanent Waving of Human Hair," by Dr. Hans Freytag.

"Alteration of Hair Keratin by Cosmetic Processing and Natural Environmental Influences," by Dr. Peter Berth and Dr. Gunter Reese.

"New Information about the Morphological Structure of the Hair," by Dr. Rudolf Randebrock.

"The Application of the Analytical Methods of Sulfur Chemistry to Permanently Waved Hair," by Prof. Dr.-Ing. Helmut Zahn, Dr. Tarsilla Gerthsen, and Dipl.-Chem. Marie-Luise Kehren.

Book Reviews

THE ART OF RESEARCH, by B. E. Noltingk, Elsevier Publishing Company, Inc., New York, 1965. 142 pages, illustrated. Price $5.75.

This book is aimed primarily at the "lowlier research worker" and the graduate student who is beginning a career in research. Naturally, the volume is directed to British readers; but very little imagination is needed to make this book of interest to an international readership.

A volume of this size cannot possibly cover methods and principles which should be followed in order to do worthwhile research at an appropriate pace. The author's major thesis, in this reviewer's opinion, is summarized in the following quote from this book. "He [the scientist] should, therefore, also keep himself generally educated on a broad front in preparation for what the future may bring forth." Admittedly, modern society demands a degree of specialization of the researcher which, at times, certainly is undesirable. Thus, Noltingk quotes Lavoisier as follows: "Most of the work still to be done in science and the useful arts is precisely that which needs the knowledge and cooperation of many scientists—that is why it is necessary for scientists and technologists to meet—even in those branches of knowledge, which seem to have the least relation and connection with one another." Two further quotes from Noltingk will serve to emphasize this point. "The all-too-prevalent attitude: 'This is not relevant to my current work; I cannot afford to take notice of it.' is a vicious one." Later on, Noltingk refers to the need for extensive and broad reading in the researcher's field; "the research worker must keep himself informed of world progress, both before and while he makes his own contribution to it."

A second point which struck this reviewer as particularly noteworthy is Noltingk's comments on criticism. It is not sufficient that the research worker examine his own work and conclusions critically to eliminate flaws and mistakes; there is also a second area of criticism which extends beyond the research worker's own activities. Thus, Noltingk states: "Familiarity [with other people's work] should even have bred an element of contempt! since

an instinctive respect for the printed word makes it difficult for most people to appreciate that it is occasionally completely false. Such wisdom is not difficult to come by, provided a consious [*sic*] effort is made to cultivate it."

It would deprive the reader of enjoyment to highlight more of the interesting points that the author makes. Instead, this reviewer feels that any research worker who will spend two or three hours reading this book will be the richer for it and a better scientist.—M. M. RIEGER, Warner-Lambert Research Institute.

DIE NORMALE UND PATHOLOGISCHE PHYSIOLOGIE DER HAUT by Günter Stüttgen. Gustav Fischer Verlag, Stuttgart, Germany. 1965. 577 pages, illustrated and indexed. Price 88 M.

In contrast to other textbooks of dermatology, Stüttgen's book uses skin physiology to differentiate between normal and pathological conditions. Thus, deviation from the normal function of the skin is used as the basis for describing its pathological changes. As a result, one finds relatively little in this volume on morphology and skin anatomy. Instead, the chemical and physical properties and the metabolism of the normal skin are described in detail. It is for this reason that this volume should indeed be of particular interest to cosmetic chemists.

The volume is divided into 24 chapters of widely varying lengths. Most of these chapters are further subdivided into minor headings. Each chapter is followed by extensive literature references, which include not only original research papers but also books and review papers. It is a special credit to the author that references—considering the formidable subject and the number of citations—are quite up-to-date. As noted above, this book differs from other books on the same subject in approach; it is also unusual in style and arrangement. The author has managed to keep the size of the book to a minimum by making tables, listings, flow diagrams, classifications, etc., intrinsic parts of the text. By this technique, unnecessary repetition is avoided, and an unusual amount of information has been crammed into relatively little space.

Of particular interest to the cosmetic chemists is the chapter on penetration and absorption. The graphic approach to molecular and ionic size and the tabulation of those chemicals the penetration of which has been studied are unique and instructive and deserve special mention. Other excellent chapters of immediate value to cosmetic chemists are the chapters on the influence of light on skin and on the reactivity of human skin.

This volume is not only an excellent introductory text to dermatology but should prove useful as a definitive reference work to the vast literature which pertains to the physiology of skin. The price of about $19 is high but still less than that of many American books on

related subjects which offer less. Study of this book can be recommended highly to all who can read German even if they need a dictionary for assistance. Perhaps, the publisher might translate this book into English for those who are unable or unwilling to struggle through the German text.—M. M. RIEGER, Warner-Lambert Research Institute.

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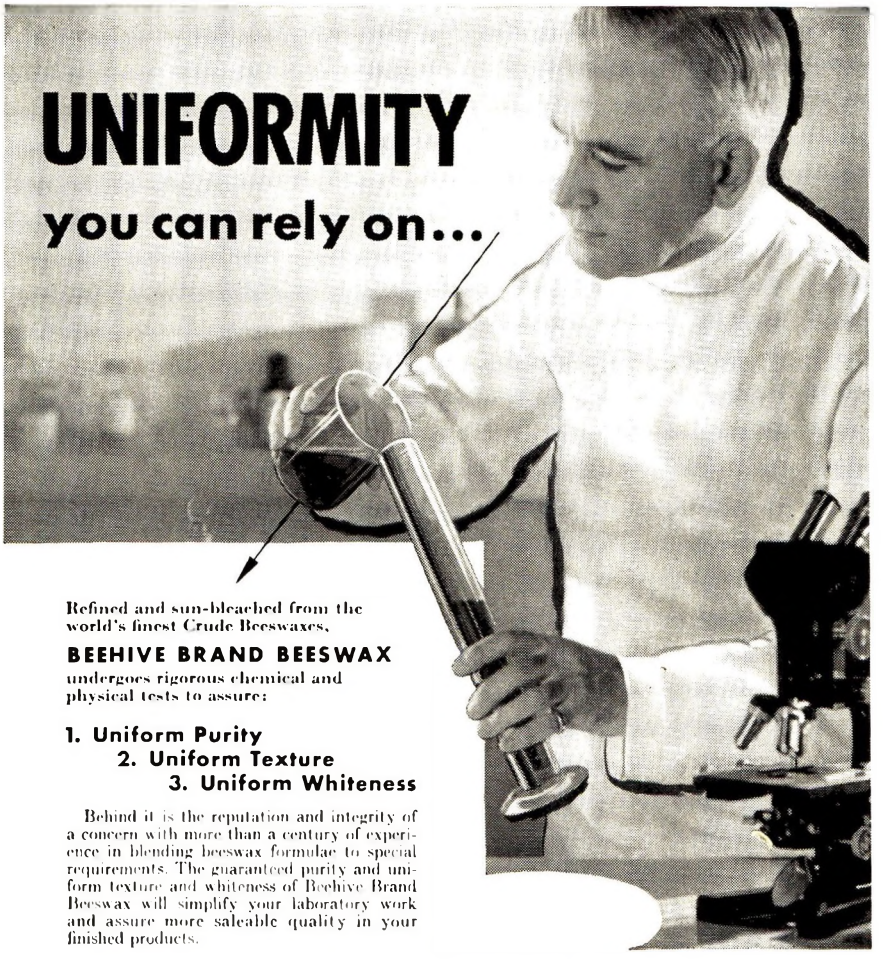

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