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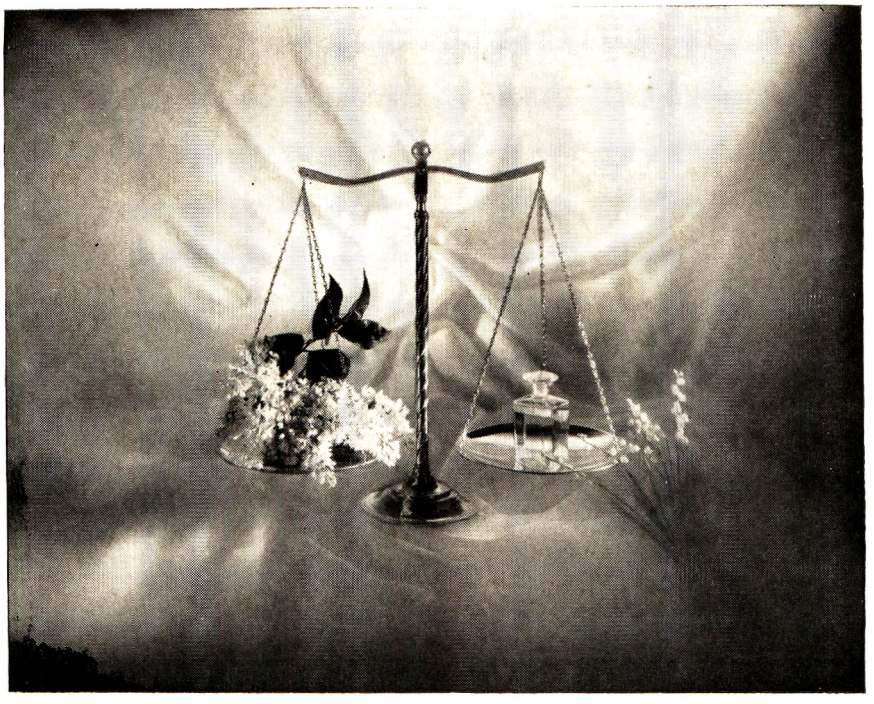
Contents



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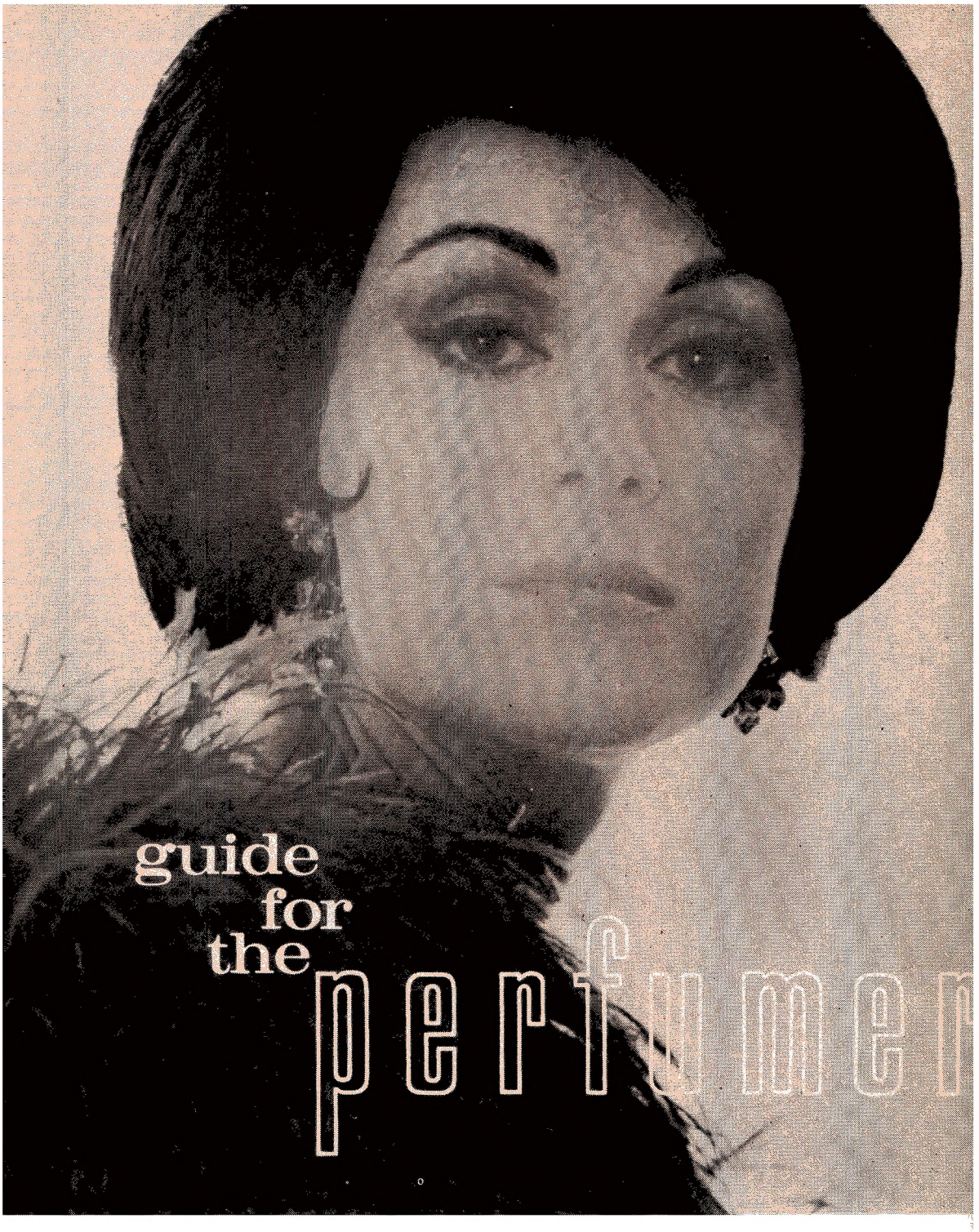

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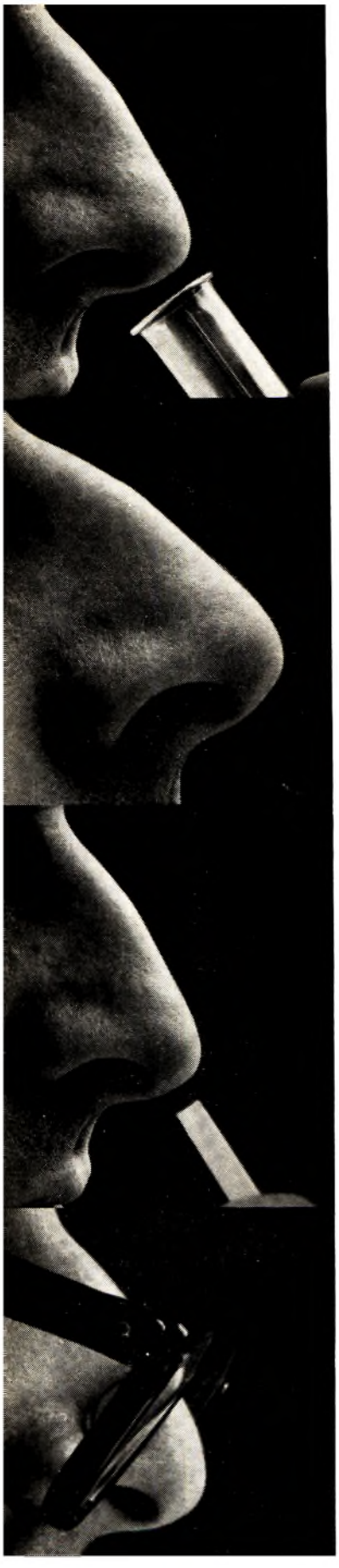

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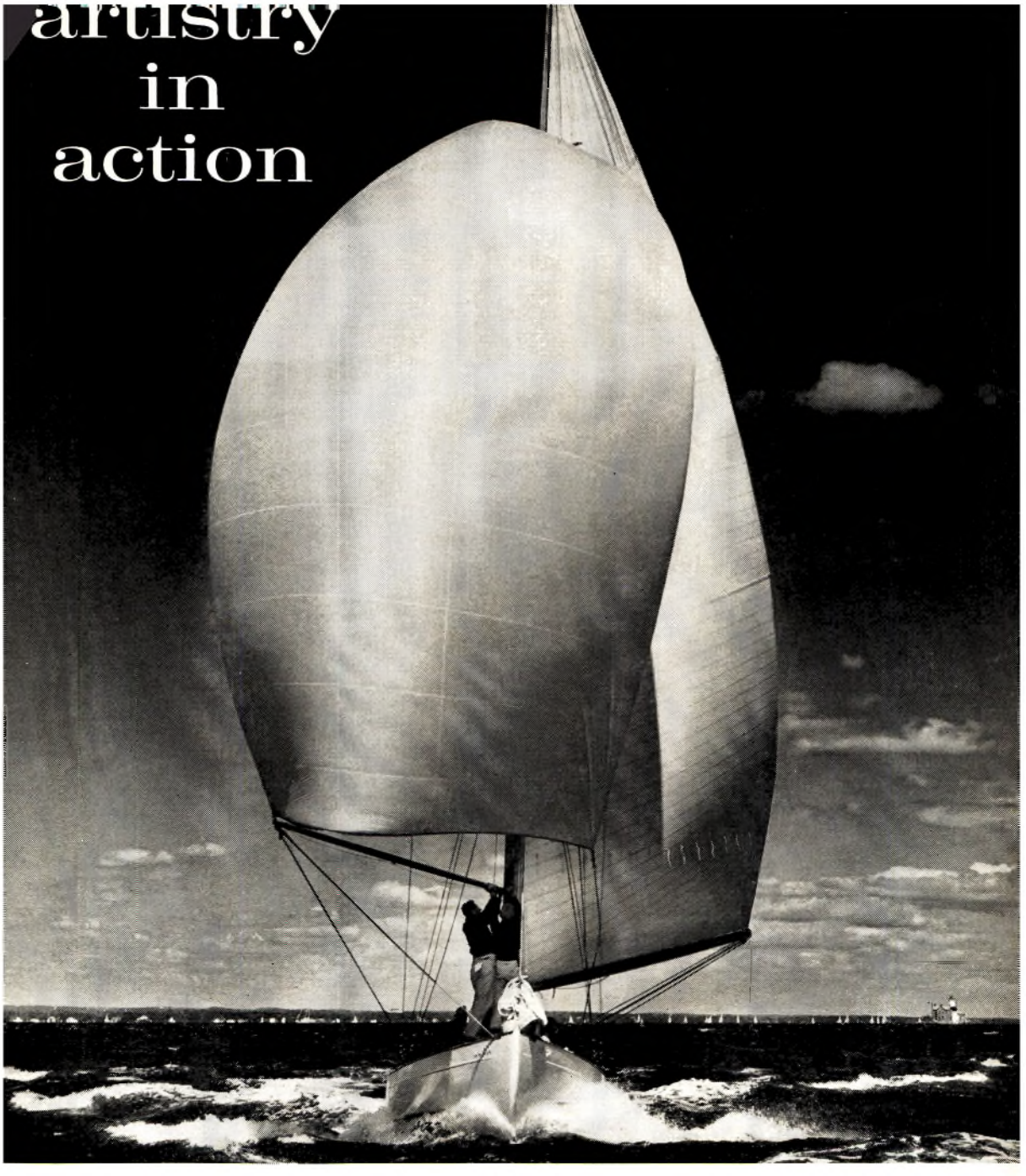

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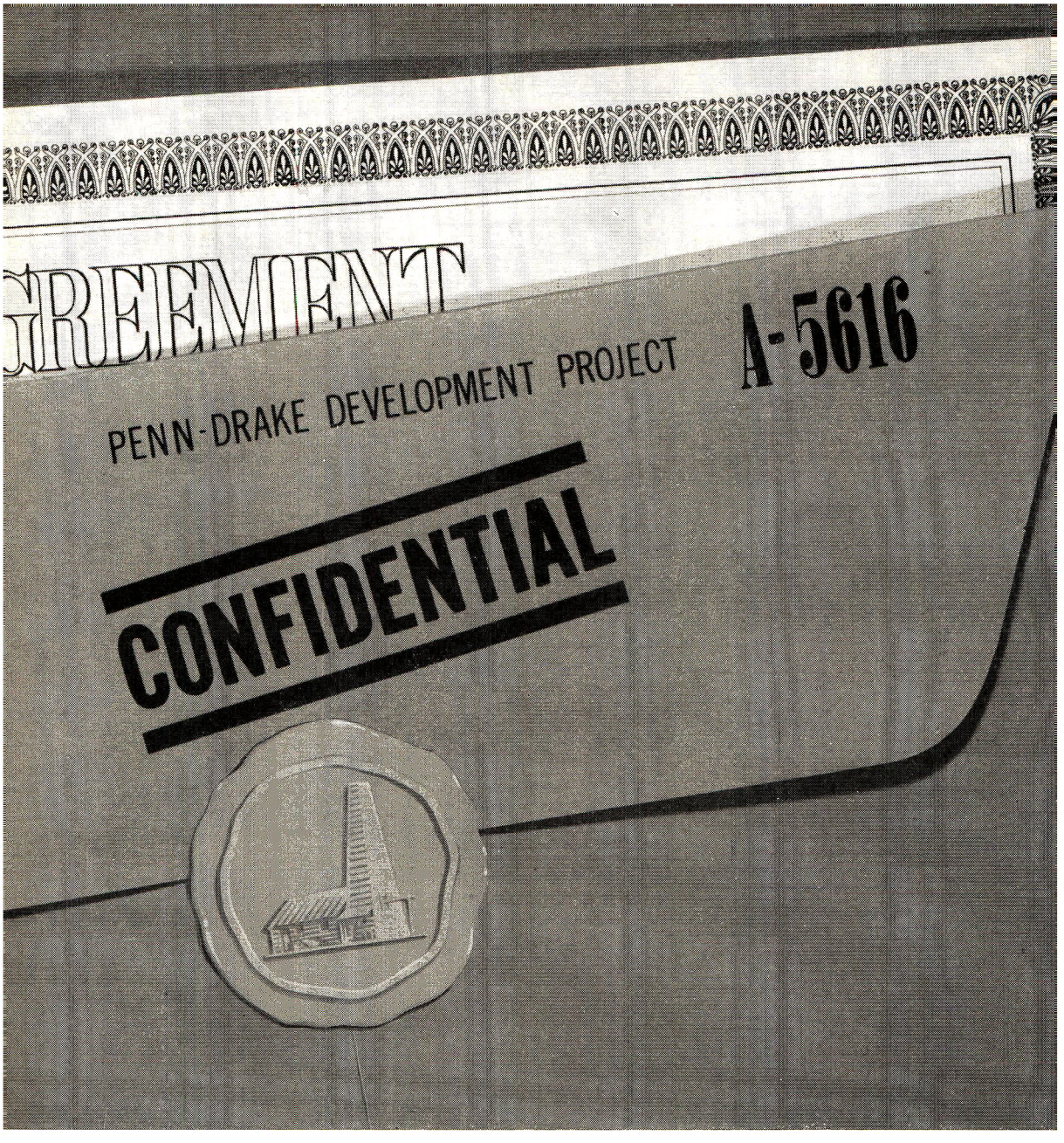

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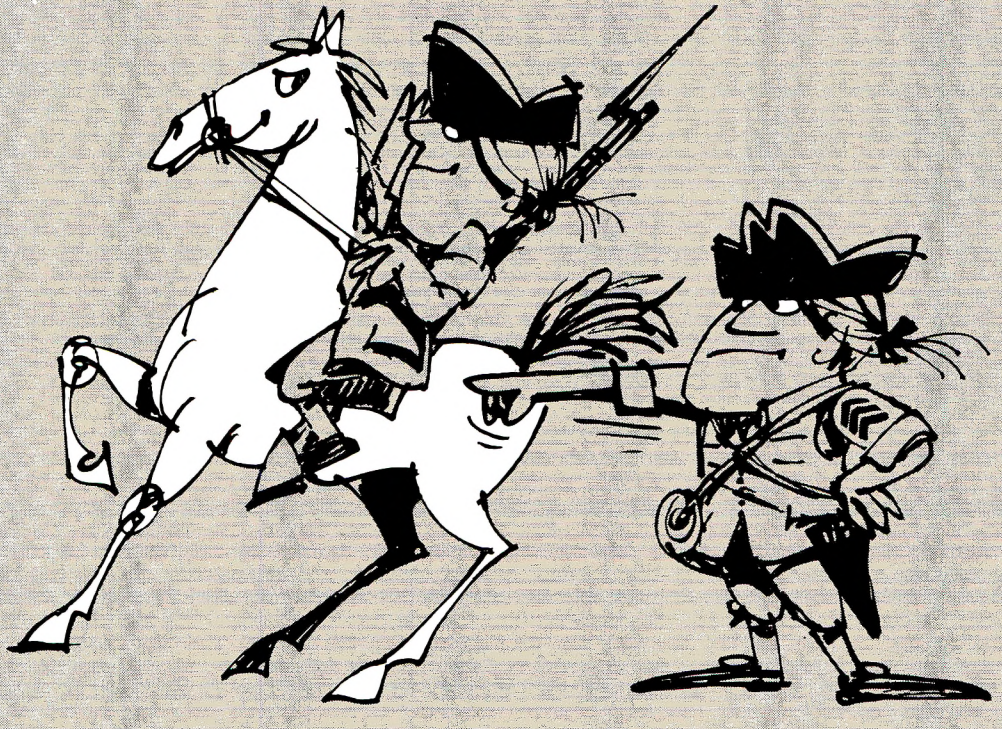

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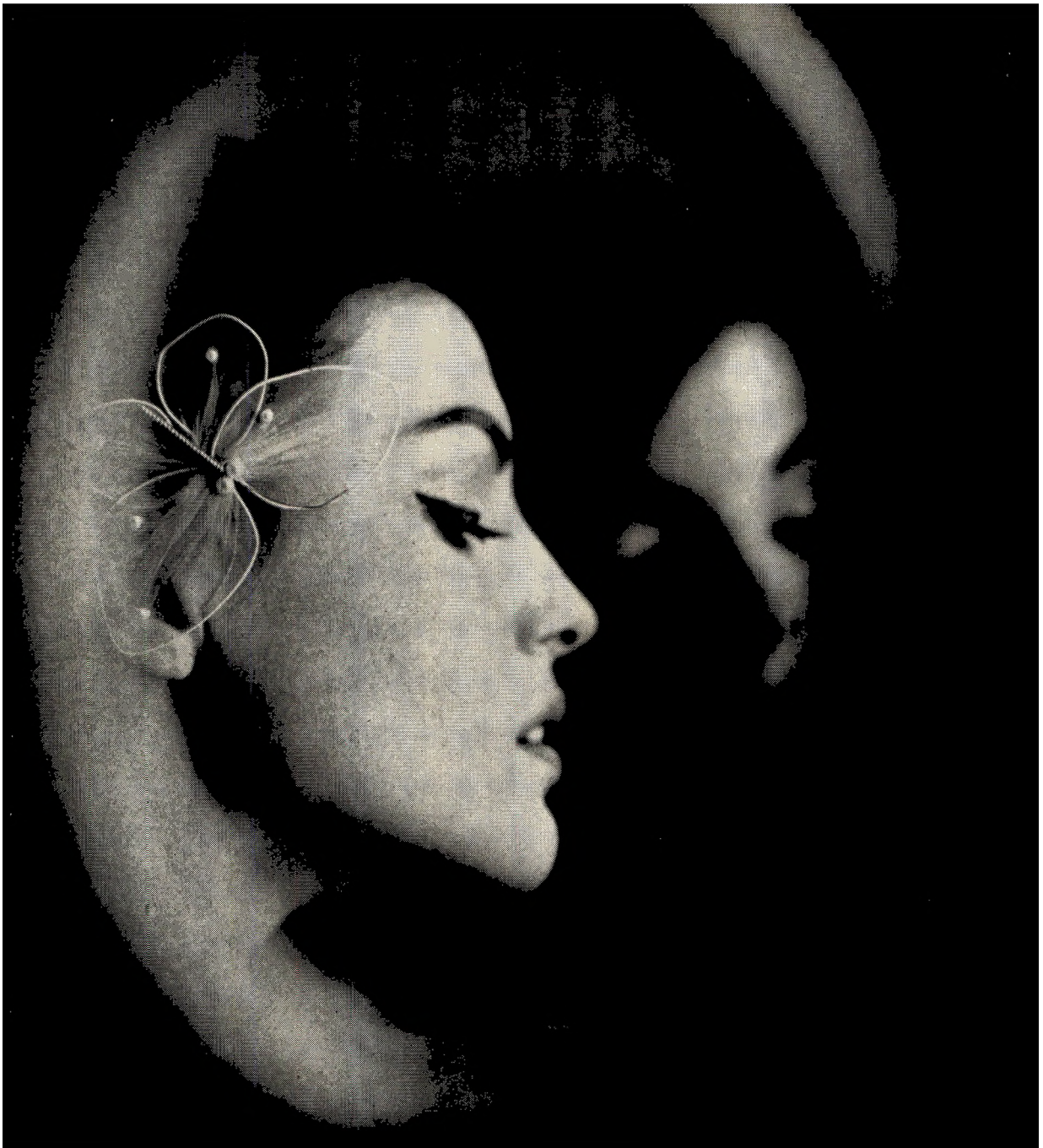

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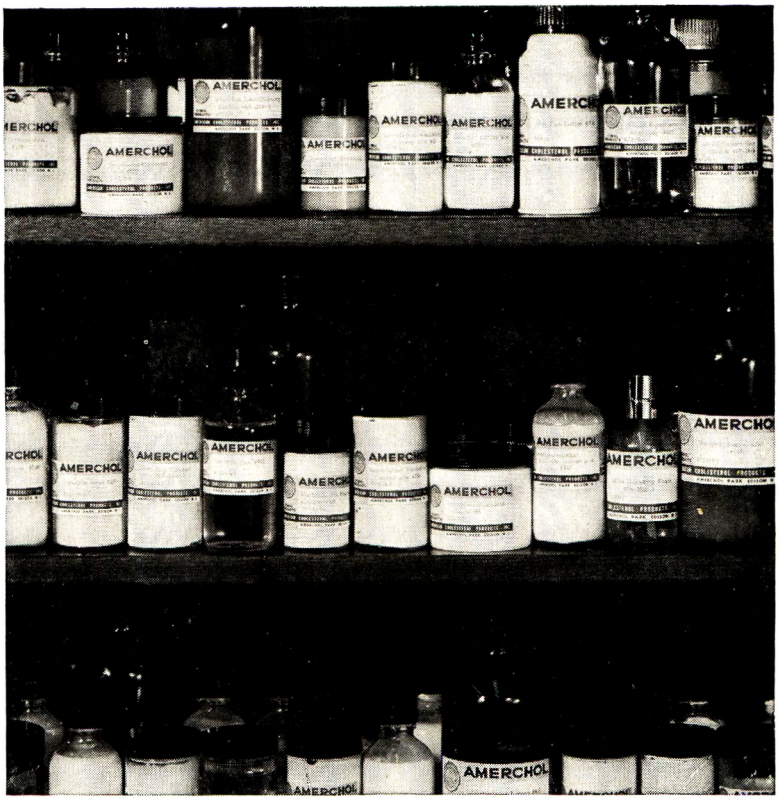

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SYNOPSES FOR CARD INDEXES

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

The effect of linear fatty amides in the benzylation of fatty alkyldimethylamines in aqueous media: Einar Birkelo and Timothy Johnson. *Journal of the Society of Cosmetic Chemists* **16,** 547 (1965).

Synopsis—Data are presented, which illustrate the reaction rates of the quaternization of benzyl chloride with stearyldimethylamine in aqueous media. The data show the presence of an induction period before a peak reaction is obtained. Using these data, the effect of the presence of a fatty alkyl amide on the reaction is illustrated. Finally, some data and observations are presented to illustrate the effect of fatty amide in the quaternary on its use as a creme rinse.

Albumin as an antiwrinkling cosmetic: Albert M. Kligman and Christopher M. Papa. *Journal of the Society of Cosmetic Chemists* **16,** 557 (1965).

Synopsis—A limited use test of an antiwrinkling preparation based on bovine serum albumin shows that it has a purely physical effect on wrinkling. The slight temporary reduction in the appearance of wrinkles is not due to physiological changes as demonstrated by microscopic examination of punch biopsies, effect on sweating, and cutaneous permeability to drugs. It is reasoned that the antiwrinkling effect of the albumin solution is due to formation of a film which lifts the furrows of the normal skin surface and elevates the wrinkles to the level of the surrounding skin.

Aqueous topical adhesives. I. Film forming base: W. E. Lange and F. R. Gonet. *Journal of the Society of Cosmetic Chemists* **16,** 563 (1965).

Synopsis—A considerable amount of interest has recently arisen with regard to the preparation of protective and medicated films for cosmetic and dermatological uses. The majority of these widely accepted preparations are aerosols containing plain or medicated resin dressings; however, they have shortcomings due to the need for an organic solvent. Thus, the development of a preparation containing a water-washable resin as the main film-forming component was considered desirable.

Polyvinyl alcohol was chosen as the soluble synthetic resin because of its apparent lack of toxicity and the relative stability of its films. Water-washable and easily peeled film-forming liquid preparations were formulated by blending various emulsions or dispersions with polyvinyl alcohol. The preparations showed good stability and could contain water-soluble medicaments.

An evaluation of the potentials of neutron activation analysis in cosmetic chemistry: George W. Leddicotte and Werner H. Wahl. *Journal of the Society of Cosmetic Chemists* **16,** 571 (1965).

Synopsis—The basic principles of activation analysis are presented. The neutron reactions used, the availability of neutron sources, and the mathematics describing the production of radioactivity during an activation and the subsequent decay of the radioactivity are discussed. The instrumental and radiochemical techniques used to complete an analysis are also described. In addition, a number of examples are cited to illustrate how cosmetic chemists might use this unique method in applications to such analytical problems as the determination of the elemental constituents in raw materials, product specifications, or the toxicity of cosmetics and related materials.

International Federation of Societies of Cosmetic Chemists

The Praesidium of the I.F.S.C.C. met in Barcelona during the Semana de Quimica Cosmetica (April 26–May 2) at the invitation of the Sociedad Espanola de Quimicos Cosmeticos. The occasion provided by the Semana de Quimica Cosmetica was most appropriate because, for the first time, a major exhibition was mounted combining scientific symposia, technical demonstrations, and the consumer attributes of cosmetics. The matters discussed by the Praesidium included the Federation policy on Legislation, recommendations on which are shortly to be published, and plans for furthering scientific education in the fields appropriate to the industry. Agreement was reached on plans for the next World Congress of Cosmetic Science, in June 1966, and that following in Tokyo in 1968.

Fall Meetings, Society of Cosmetic Chemists, New York Chapter

The Society of Cosmetic Chemists, New York Chapter, announces the following schedule of meetings for the remainder of 1965:

September 8, 1965—Dr. Leonard Harber, Dr. Milton Cahn, and Dr. Leonard Vinson, "Photosensitivity Panel Discussion." Meeting at Robin Hood Inn, Clifton, N. J.

October 13, 1965—Mr. M. J. Thomas, "Encapsulation Techniques." Meeting at Robin Hood Inn, Clifton, N. J.

November 10, 1965—Mr. Adolph Maruszewski, "Lipstick Technology" and Dr. Paul Jewel, President's Night. Meeting at the Shelburne Hotel, New York.

J. Soc. Cosmetic Chemists, 16, 547–556(1965)

The Effect of Linear Fatty Amides in the Benzylation of Fatty Alkyldimethylamines in Aqueous Media

EINAR BIRKELO, B. A., and TIMOTHY JOHNSON, B. S.*

Presented January 12, 1965, Chicago Chapter

Synopsis—Data are presented which illustrate the reaction rates of the quaternization of benzyl chloride with stearyldimethylamine in aqueous media. The data show the presence of an induction period before a peak reaction is obtained. Using these data, the effect of the presence of a fatty alkyl amide on the reaction is illustrated. Finally, some data and observations are presented to illustrate the effect of fatty amide in the quaternary on its use as a creme rinse.

Introduction

Results of laboratory experiments are presented which illustrate the effect of fatty alkyl amides on the reaction of benzyl chloride and higher fatty alkyldimethylamines in an aqueous medium. The stearyl homologue was chosen because it was of most interest in this work.

There are many references and patents in the literature indicating new and potential uses of alkyldimethylbenzylammonium salts. Morris made reference to their use for the removal of radioactive contaminants (1). Pfanmuller described solubilization of tyrothrycin and its therapeutically active components (2). Pearsall indicated the use of 0.1 to 0.5% in a formulation which aids in the removal of engine deposits

* Rayette, Inc., St. Paul, Minn.

(3). Bhorgava and co-workers reported on improved retention of polyvinyl acetate by the use of an alkyldimethylbenzylammonium salt in the paper industry (4). In addition, numerous authors have reported on the bactericidal properties of the alkyldimethylbenzylammonium salts. The first reference on the use of alkyldimethylbenzylammonium chlorides for use in creme rinses for hair was in May, 1942, by Den Beste (Rayette Research Notebook 5–203).

There has been a rebirth of interest in the amine oxides, resulting in an increased potential demand for alkyldimethylamines. As the demand for alkyldimethylamines has increased, refinements in manufacture and processing have resulted in products of greater purity, which is necessary for amine oxide preparation. According to Lake and Hoh, the conversion rate of these amines to amine oxides is dependent on the starting purity of the amine (5). Along with these improvements in purity of the fatty alkyldimethylamines, it was found that one material was removed that has a significant effect on benzylation of these amines. Initial work on the benzylation of commercial stearyldimethylamines indicated that reaction rates were somewhat unpredictable, even though the reaction conditions were precisely controlled.

Procedure

Materials Used

The following materials were used as received from the suppliers using their description, except in cases where additional purification was made:

*Coco-Amide (Armid C)**

An amide derived from coconut C_{12-18} saturated fatty acids, having a melting point of 90 °C.

Arachidyl-Behenyl Amide (Adogen 1)†

Typical chain length distribution: 2% C_{14} Myristyl, 13% C_{16} Palmityl, 30% C_{18} Stearyl, 30% C_{20} Arachidyl, 25% C_{22} Behenyl.

*Stearamide (Armid HT)**

An industrial grade hydrogenated tallow amide was further purified by two crystallizations from hot ethanol. The purified product had a m.p. of 104–106 °C.

* Armid and Armeen are registered trade marks of Armour Chemical Company.

† Adogen 1 is a registered trade mark of Archer-Daniels-Midland Company.

*Dodecyldimethylamine (Armeen DM12D)**

Distilled grade (apparent equivalent weight 220).‡

*Tetradecyldimethylamine (Armeen DM14D)**

Distilled grade (apparent equivalent weight 246).‡

*Hexadecyldimethylamine (Armeen DM16D)**

Distilled grade (apparent equivalent weight 275).‡

*Octadecyldimethylamine (Armeen DM18D)**

Distilled grade octadecyldimethylamine was redistilled through a 3 ft. column packed with Raschig rings under 2 mm. vacuum. The fraction distilling over at 167–170 °C was collected and used in the following work. Gas chromatographic analysis using an F & M 810 dual flame chromatograph with a 6 ft. column packed with 10% Carbowax 20,000§ on white acid-washed diatomaceous earth gave a purity of 99% and apparent equivalent weight 298.‡

Benzyl Chloride

A commercial grade (Tennessee Eastman) assaying 99.6% was used in all experiments.

Apparatus

The benzylation apparatus consisted of a 1.5 l. resin reactor with a four neck cover. The center opening was fitted with a Teflon Asco gland to accommodate a three-blade glass propeller, powered by a variable speed mixer. One of the ports was fitted with a long stem thermometer, and the other two ports were stoppered with glass stoppers. Sampling and addition of reactants were made through these ports. The reactor was clamped in a bath equipped for heating and cooling.

Reaction Conditions

Approximately 0.7 mole of the desired amine, along with the proper amount of fatty amide, was dispersed in 1100 g. of water, decreased by the amount of amide added, and mixed at 85 °C until homogeneous. The amine-amide dispersion was adjusted to 63 °C, and the benzyl chloride was rapidly added with as fast a mixing rate as possible to

‡ Apparent equivalent weights determined by authors.

§ Carbowax 20,000 is a registered trade mark of Union Carbide Corporation.

achieve a uniform system as quickly as possible. Samples were withdrawn at periodic intervals for analysis.

Acidimetric titrations for unreacted amine were found to give reliable and easily obtainable results. This procedure involved withdrawing a sample from the reaction mixture and pipetting the sample directly into an excess of standard 0.1N hydrochloric acid in isopropanol. The container with standard acid was weighed prior to adding the sample so the sample weight could be obtained by weighing back. The samples were immediately back titrated to a yellow end point using bromophenol blue indicator (pH 3.6).

Results and Discussion

Fig. 1 shows the log of the concentration of unreacted stearyldimethylamine (SDMA) *vs.* the time of reaction with benzyl chloride, using the following reaction mixture: 209 g. stearyldimethylamine, 87.4 g. benzyl chloride, and 1100 g. distilled water.

It is evident from Fig. 1 that this is not a simple second order reaction. There is a definite induction or a slow initial reaction rate during the first 20 min. of reaction. If the concentration of product formed *vs.* the time of reaction with benzyl chloride is plotted on linear graph paper, the curve is S shaped, typical of an autocatalytic reaction (6). This is illustrated in Fig. 2 (curve with 0 % stearamide) and indicates the product formed, in this case stearyldimethylbenzylammonium chloride, has a catalytic effect on the reaction.

Next, to determine if stearyldimethylbenzylammonium chloride (SDMBA Cl) actually has a catalytic effect on the reaction rate, an amount was added that theoretically could make the reaction start out at a peak rate. Figure 1 suggests that the presence of a 1 : 1 molar ratio of stearyldimethylamine and stearyldimethylbenzylammonium chloride in the reaction with benzyl chloride should make the reaction start out at a peak rate. Figure 3 describes the reaction between 43.7 g. benzyl chloride, 104.7 g. stearyldimethylamine, 147.7 g. stearyldimethylbenzylammonium chloride and 1100 g. distilled water. It can be seen that the induction period is eliminated and that the reaction starts out at a peak rate, verifying the catalytic effect of stearyldimethylbenzylammonium chloride.

In order to illustrate and explain the effect of the presence of an alkyl fatty amide on the reaction, the previous discussions of the reaction between stearyldimethylamine and benzyl chloride may be used. Figure 4 is a plot of the reaction between stearyldimethylamine and

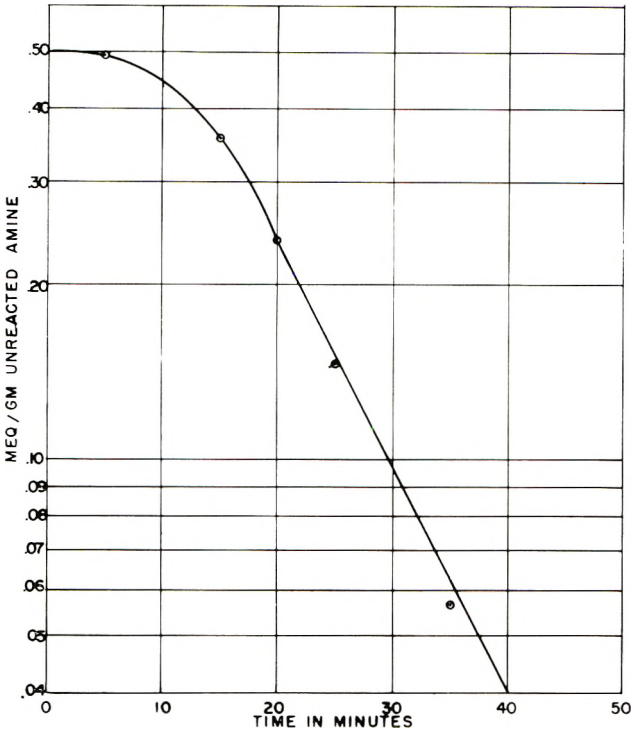

Figure 1. Unreacted amine *vs.* time for reaction of SDMA and $PHCH_2Cl$

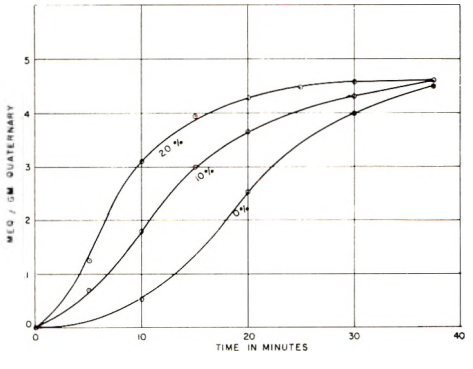

Figure 2. Concentration of quaternary *vs.* time for reaction of $PHCH_2Cl$ and SDMA with various amounts of amide present

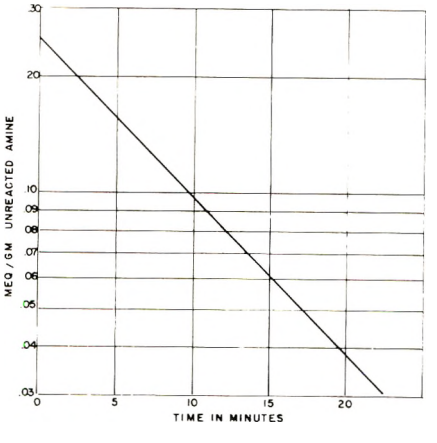

Figure 3. Unreacted amine *vs.* time for reaction of $PHCH_2Cl$ and SDMA in the presence of SDMBACl

benzyl chloride with 0, 5, 10 and 20% stearamide, based on the amine charge. The curves of the reaction with the varying amounts of amide present during the reaction indicate that the time required to obtain a maximum rate of reaction is decreased as the amide concentration is increased to about 20%, based on the tertiary amine charge. Earlier work not reported here indicated that the effect of the amide is apparent at concentrations as low as 1% based on the stearyldimethylamine

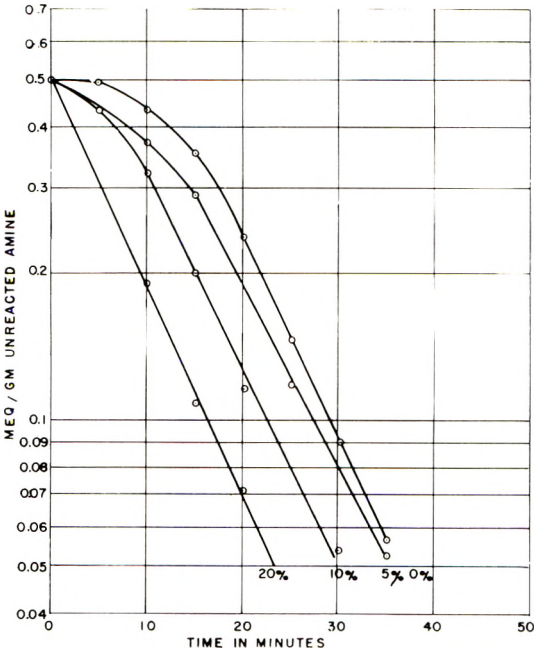

Figure 4. Reaction rate of $PHCH_2Cl$ and SDMA with various increments of stearamide present

It can be seen that, after the first 20 min., little or no effect on the reaction rate is observed; however, during the first 20 min., the effect is quite pronounced. This is illustrated better in Table I, which shows the percent completion of the reaction at various stearamide concentrations.

Figure 2 shows that the presence of stearamide decreases the S-shaped character of the reaction curve and indicates that it decreases the autocatalytic effect of the stearyldimethylbenzylammonium chloride formed in the reaction.

The effect of other fatty amides in the reaction of benzyl chloride and stearyldimethylamine is indicated in Table II, which shows the

results with and without amides. The effect of different fatty amides in decreasing the initial reaction lag is evident. There does appear to be an indication that the lower chain amides might be more effective in decreasing the initial slow rate of reactions.

Next, a study was made of the effect of stearamide in the presence of alkyldimethylamines of different chain lengths. In this case, tetradecyldimethylamine (Armeen DM14D) and dodecyldimethylamine

TABLE I

Effect of Stearamide on Quaternization Reaction

% Stearamide Based R_3N	% Stearyldimethylamine Reacted in 10 min.	% Stearyldimethylamine Reacted in 20 Min.
0	13	51
5	27	63
10	37	79
20	62	87

TABLE II

Effect of Different Amides on Quaternization Reaction[a]

Time Reaction, Min.	20% Armid C Coco-Amide	20% Stearamide	20% Adogen 1 Arachidyl Behenyl Amide	No Amide
0	0.525[b]	0.525[b]	0.525[b]	0.540[b]
10	0.268	0.286	0.298	0.495
20	0.154	0.169	0.178	0.385
30	0.126	0.130	0.145	0.262

[a] Reaction of 0.7 mole of stearyldimethylamine, 0.06 mole of stearylamine, 0.6 mole of benzyl chloride, 1100 g. distilled water, and 41.2 g. of the desired amide (i.e., 20% based on SDMA charge).

[b] Numbers refer to unreacted amine in meq./g.

(Armeen DM12D) with and without stearamide were evaluated. The stearamide decreases the reaction time to reach a peak rate with C_{12} and C_{14} alkyldimethylamine and benzyl chloride, but the effect is less noticeable in the case of the lower chain amines.

The analysis of the completed reaction mixture (after 90 min.) indicates to what degree the quaternary was actually formed along with hydrolysis of the benzyl chloride to benzyl alcohol and HCl. Table IV gives the data using the redistilled stearyldimethylamine and recrystallized stearamide with benzyl chloride. The data show that the formation of stearyldimethylbenzylammonium chloride proceeded from

96.5 to 98.2% of theoretical. The stearamide does not appear to influence the extent of quaternary formation.

The stearyldimethylamine hydrochloride is an indication of the degree of hydrolysis of benzyl chloride to benzyl alcohol and hydrochloric acid. In the six runs shown in Table IV, the range of hydrolysis falls between 1.2 and 2.4% of the reaction, with the presence of the amide showing no

TABLE III

Effect of Different Amines on Quaternization Reaction[a]

Time Reaction, Min.	Dodecyldimethylamine		Tetradecyldimethylamine	
	No Amide	6.7% Stearamide[c]	No Amide	6% Stearamide[c]
0	0.564[b]	0.560[b]	0.558[b]	0.552[b]
10	0.430	0.358	0.463	0.364
20	0.232	0.222	0.292	0.169
30	0.133	0.122	0.165	0.103

[a] Reaction of 0.7 mole of alkyldimethylamine, 0.06 mole stearylamine, 0.6 mole benzyl chloride, 1100 g. distilled water, and 10.2 g. of stearamide reacted according to the previously mentioned conditions.

[b] Numbers refer to unreacted amine in meq./g.

[c] Stearamide based on R_3N.

TABLE IV

Analysis of Reaction Mixture[a]

% Stearamide	Theoretical		At Completion (90 min.)		
	Amine Conc.	Benzyl Chloride	Quaternary	Amine HCl	Free Amine
0	0.501	0.495	—	0.009	0.016
1	0.501	0.495	0.480	0.012	0.011
5	0.501	0.495	0.476	0.007	0.007
10	0.501	0.495	0.477	0.006	0.009
15	0.501	0.495	—	0.006	0.013
20	0.501	0.495	0.487	0.009	0.008

[a] All results are expressed as meq./g. except % stearamide which is % based on the stearyldimethylamine used in the reaction.

effect on the degree of hydrolysis. Gas chromatographic analysis of the reaction mixtures, using a procedure based on the work of Metcalfe (7), gives benzyl alcohol concentrations in the range of 0.05 to 0.10% or about 0.8 to 1.6% of the total reaction.

A small amount of benzaldehyde is formed, detectable by its characteristic odor. The gas chromatographic analysis of alkyldimethylbenzylammonium chlorides using a modified procedure failed to separate

benzaldehyde from benzyl chloride. Benzyl chloride is a decomposition product during gas chromatography. Current research is aimed at the development of a procedure that will separate benzaldehyde in the presence of benzyl chloride. Based on the extent of the reaction of the quaternary and benzyl alcohol formation, benzaldehyde is formed only in trace quantities.

Stearyldimethylbenzylammonium chloride represents the main active ingredient in the majority of creme rinses. Data are presented here to illustrate the effect of a small amount of stearamide in stearyldimethylbenzylammonium chloride at typical creme rinse concentrations. Five per cent aqueous concentrations of the reaction mixtures (reacted to completion or 90 min.) with the various amounts of stearamide present were equilibrated in a water bath (26.6°C) for three weeks. Samples were centrifuged, and the supernatant liquid was filtered through Whatman #1 filter paper The clear saturated solutions at 26.6°C were titrated for quaternary. The following tabulation summarizes the results. The percentage of stearamide is based on the amount of amine used in the reaction to form the quaternary.

% Stearamide	Soluble Quaternary, meq./g.	% Actual Quaternary in Solution
0	0.00443	0.187
1	0.00765	0.324
5	0.02506	1.061
10	0.02528	1.075

Estimated quaternary added 0.0250 meq./g.

It is obvious that the concentrations of quaternary were too low to obtain the full solubilizing effect of the higher stearamide concentrations. These results were not expected to be so dramatic and were unusual because of the large effect from such small amounts of stearamide. Perhaps these results might give a little more credence to the more subjective evaluations: Blind half-head evaluations were made in the Rayette Research Beauty Salon using 5% dispersions of the reaction mixtures, diluted eight-fold just prior to use. It was decided to compare the samples with no stearamide present to those with 20% stearamide present (based on the amine used to make the quaternary) in order to obtain the maximum effect. A total of ten comparisons were made, and the results, in the opinion of the beauticians, favored the sample with stearamide present for luster, combing, and manageability in eight out of the ten evaluations.

Conclusions

The data presented indicate that:

1. There is a lag in the reaction rate during the first 10 to 20 min. when C_{12}-C_{18} alkyldimethylamines are reacted with benzyl chloride in a hot aqueous system.
2. The addition of stearyldimethylbenzylammonium chloride, added initially to a reaction mixture of benzyl chloride and stearyldimethylamine in a hot aqueous system, eliminates the initial reaction lag.
3. Higher fatty amides, added at a level of 1–20% (based on the alkyldimethylamine in a reaction between benzyl chloride and alkyldimethylamine), decrease or eliminate the initial reaction lag.
4. There is no benzylation of the amide under the described reaction conditions.
5. Stearamide increases the water solubility of stearyldimethylbenzylammonium chloride
6. The presence of the stearamide gives superior performance to stearyldimethylbenzylammonium chloride when used as a creme rinse.

Acknowledgment

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(1) Morris, F. H., *U. S. Pat.* 3,033,794 (1962).
(2) Pfanmuller, J., *U. S. Pat.* 2,643,967 (1953).
(3) Pearsall, H. W., *U. S. Pat.* 3,704,733 (1955).
(4) Bhorgava, R. L., Reiter, R. W., and Stannet, V., *Tappi*, **40**, 338 (1957).
(5) Lake, D. B., and Hoh, G. L., *J. Am. Oil Chemists' Soc.*, **40**, 628 (1963).
(6) Frost, A. A., and Pearson, R. G., *Kinetics and Mechanism*, John Wiley, New York, 1953, p. 20.
(7) Metcalfe, L. D., *J. Am. Oil Chemists' Soc.*, **40**, 25 (1963).
(8) Colichman, E. L., *J. Am. Chem. Soc.*, **73**, 1795 (1951).

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Albumin As an Antiwrinkling Cosmetic

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Synopsis—A limited use test of an antiwrinkling preparation based on bovine serum albumin shows that it has a purely physical effect on wrinkling. The slight temporary reduction in the appearance of wrinkles is not due to physiological changes as demonstrated by microscopic examination of punch biopsies, effect on sweating, and cutaneous permeability to drugs. It is reasoned that the antiwrinkling effect of the albumin solution is due to formation of a film which lifts the furrows of the normal skin surface and elevates the wrinkles to the level of the surrounding skin.

Purified solutions of bovine serum albumin have recently been introduced to produce temporary smoothing of facial wrinkles. This paper considers the effectiveness, mode of action, and safety of one such preparation.†

Procedure

The studies were conducted on institutionalized, healthy, white males and females, 35 to 95 years of age, at the Philadelphia Home for the Aged at Riverview, Philadelphia. Wrinkles were the sole criterion for admission to the study. The finer wrinkles around the eyes and those on the cheeks were the best test sites. The product was applied by an operator once daily for three months (after washing in the morning) to one side of the face of 10 subjects and for one month on 15 other participants.

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† The test agent was "Magic Secret" by Helene Curtis.

Cosmetic Effectiveness

Over 50 subjects were used for these observations. Throughout, a quantity, just sufficient to wet the facial skin, was applied by finger rubbing. As the solution dries within a few minutes, the subjects noted a "tightening" sensation, and coincidently, effacement of wrinkles was observed. The smoothing effect reaches a maximum within three to eight minutes. Under the stereoscopic skin microscope (Seitz) the finest wrinkles gradually become invisible, and moderate creases become shallower. All individuals respond, though to varying degrees. The largest furrows on the forehead and marked expression lines around the eyes and mouth are not markedly altered unless very large amounts are applied. When small amounts are used, the residue is essentially nonvisible even with magnification. Larger amounts than are required to reduce minor wrinkles may leave a rather fine transparent film which may later scale or flake. Repeated applications during the day may lead to a fine peeling which is the dried residue itself. The duration of the peak effect is two to six hours, depending on facial mobility. It is longest in the "poker-faced," inexpressive, passive person, whose face registers little emotion. On the other hand, energetic use of the facial muscles in speech and action is accompanied by more rapid reappearance of the wrinkles. If the face is violently contorted while the solution dries, the smoothing effect can be almost completely nullified. Moreover, if after maximal effect the subject repeatedly screws up the face in the pretense of creating a grotesque, horrendous appearance, the smaller wrinkles will reappear much sooner. Thus, facial inexpressiveness sustains the effect, while intense use of the facial muscles abbreviates it. When the effect begins to wane, re-moistening of the skin with a few drops of water will more or less reinstate what was lost. Even after eight hours, the wetting maneuver will palpably reduce the finer wrinkles, though usually not as completely as a fresh application. On the other hand, thorough washing of the face with soap and water at any time after drying will completely and instantly abolish the smoothening effect.

The antiwrinkling effect did not appear to be cumulative with repeated daily use. The cosmetic improvement was as great on the first as on the last day of use. Facial creams, applied after the solution dries, do not materially alter the effect. No adverse reactions have been encountered, and evidently, repeated use has not resulted in sensitization or irritation.

Effects On Cutaneous Structure and Function

Eight mm. punch biopsies were removed from the cheeks of ten subjects before the test. The solution was applied once daily for three months, and the skin re-biopsied in a nearby site. The sections were stained as follows: H & E, Hale-Orcein for acid mucopolysaccharides and elastic tissue, Mallory's trichrome for collagen, PAS for glycogen and basement membrane, and Masson's ammoniacal silver nitrate for melanin.

The pre-treatment specimens showed the changes expected for exposed areas, mainly marked elastotic degeneration of the cutis and variable cytologic abnormalities of the epidermis. The post-treatment biopsies were in no way different. No structural improvement could be observed; the applications had no discernible histologic or cytologic effect.

The treated and untreated sides of four subjects were compared as regards eccrine sweating, using Wada's starch-iodine method. The test was conducted one hour after a liberal amount of the solution had been applied to one side. Sweating was induced by placing the subject in a 130°F chamber for ten minutes. There were no apparent differences with respect to onset, number of functioning glands and volume of sweat.

The ability of albumin solution to impede cutaneous water loss was measured on isolated sheets of horny layer. Duplicate sheets of horny layer were obtained from the backs of two individuals by the cantharidin blister technique. One sheet was coated liberally with the albumin solution, and the other served as a control. These were sealed over water on diffusion chambers and the rate of water loss determined over a three-day period at 0% relative humidity at 37°C. The experiment was repeated three times with each sheet, applying an additional fresh amount at the end of each three-day period. The average values for the first subject were 0.86 and 0.83 mg./hr./cm.^{2} for treated and control specimens, respectively, and 0.63 and 0.70 for the second. The rate of diffusional water loss was not affected. The albumin residue does not form a water impermeable film.

Similar studies were conducted on four subjects as regards cutaneous permeability. The method consisted of determining the times required for 10% aqueous solutions of histamine dihydrochloride and Privine* to produce erythema and blanching (vasoconstriction), respectively.

* Product of Ciba Pharmaceutical Co., Summit, N. J.

Quantities of 0.02 ml. were carefully pipetted into a circular area 3.0 cm. in diameter and immediately covered with Saran Wrap* to prevent evaporation. It was found that the treated and untreated side did not appreciably or considerably differ as regards reaction times. The albumin residue neither aided nor retarded penetration.

Mode of Action

The above information reduces the number of explanations for the antiwrinkling effect. That there is any fundamental anatomic or physiologic change is ruled out by; (a) the rapidity of action, usually less than ten minutes; (b) prompt termination when the albumin is washed off by soap and water; (c) nullification by exaggerated facial movements; (d) lack of cumulative action upon repeated use; (e) unchanged permeability to water and drugs; and (f) absence of microscopic alterations after three months of daily use. Apparently, the effect is purely physical and not pharmacologic. Indeed, this would have been foretold by the impermeability of normal skin to proteins. It is highly improbable that significant amounts of albumin can enter the skin. Another possibility is a masking action, like filling up the wrinkles with putty. Stereoscopic visualization of the surface rules out such an effect. After drying, the physical presence of the material is scarcely apparent. It certainly does not accumulate in the furrows. A physical film is seen only when the amount is excessive, and even then there is no piling up in the wrinkles. Some additional simple studies led to a satisfactory explanation.

When thinly coated with the solution, a circular sheet of isolated stratum corneum will soon contract greatly, resulting in marked puckering and folding. This suggests the presence of a fine continuous film which shrinks as it dries and is also adherent enough to contract the underlying tissue. The "tightening" sensation is the direct manifestation of this contractile force. This observation presented a new problem in that contraction should aggravate, not relieve, wrinkles, as witness the formation of folds if the skin is drawn together between the fingers. To test this point, circles 1.5 cm. in diameter were marked out on various wrinkled areas of the face with red dye. Two right angle diameters were obtained and the area calculated as a circle. The solution was liberally applied and the area redetermined thirty minutes

* Product of The Dow Chemical Co., Midland, Mich.

later. Although such measurements are rather crude, the areas had not appreciably decreased, unlike the behavior of horny sheets. On the face, the circular test areas are of course moored to the surrounding skin, and the tension produced is not sufficient too vercome the peripheral resistance. A force is exerted, but it is not able to express itself as a contraction.

It was decided to test the antiwrinkling effect of other substances which are known to form films upon drying, such as glues and mucilages. The following substances were applied to wrinkled skin: (a) Craftman's* All Purpose White Glue, (b) Duco† Cement, (c) Mucilage, (d) Egg albumin and (e) Carter's‡ Paste. Each of these after drying palpably reduced the wrinkles but with varying degrees of effectiveness. Egg albumin and mucilage were inferior to the albumin solution under test. The glue and paste were comparable, and Duco Cement, unless applied very thinly, aggravated the wrinkles. The contractile force of dried Duco Cement is evidently so great that the tissue is pulled in from the periphery, accentuating the existing wrinkles. It was clear that all these materials behave like albumin and exerted purely physical effects. The more effective ones, however, are cosmetically objectionable, forming obvious films or cellophane-like "skins," which may be peeled off as intact sheets. After a while they crack and scale, worsening the appearance. Egg albumin is free of this defect but is considerably less effective. The latter is an ancient remedy, formerly in the repertoire of aristocratic ladies experienced in the cosmetic art. Modern women, depending entirely on commercially formulated cosmetics, have neglected the discoveries of their ingenious forebears, disdaining such practices as folklore. The newer beef albumin solutions represent a technical improvement on the home artistry of the ancients, who used what was easily at hand. Centuries had to intervene before this particular cosmetic skill was rediscovered!

Discussion

The value of albumin has been recognized and ignored, even in modern times. One patent (1) concerns an alcoholic solution of filtered egg albumin which purports to make the skin smooth and youthful. Another patent (2) was assigned for the cosmetic use of albumin derived from swine ovaries and placentas. In a concentration of 5% in various

* Product of Sears Roebuck & Co.

† Product of E. I. du Pont de Nemours & Co.

‡ Product of Carter's, Inc., Co.

vehicles it is said to tighten the skin surface, causing a distinct reduction in the skin folds and wrinkles.

A review of the above observations leads to the following hypothesis concerning the mechanism of the antiwrinkling effect. Any solution which forms a contracting film as it dries will promptly and temporarily efface wrinkles. Senile facial skin is loose and flabby and can be easily extended or stretched by a minor force which would have lesser effects on young skin. This laxness reflects the degeneration of the underlying connective tissue. The normal feltwork of elastic and collagen fibers is markedly altered. The elastic tissue is greatly increased, while collagen fibers, the main dermal component, are physically degraded and reduced. As the solution dries, the contractile tension will tend to pull on the surrounding skin which, however, yields little. Instead, the force generated on the lax skin lifts up the furrows to the normal surface, thereby obliterating them. The action is simply one of elevating the wrinkles to the level of the surrounding skin. The same effect can be obtained temporarily by ballooning the skin by injecting water, or rather permanently, by injecting inert silicone fillers. The force of the albumin solution is not great enough to elevate the deep and wide wrinkles of the forehead, although these become narrower. The stronger films produced by generous amounts of glues and cements can partially accomplish this. Indeed, the latter may undesirably pucker the skin into artificial folds. An upper limit to the degree of contraction desired is clearly imposed. The particular merit of albumin is that it blends more or less imperceptibly with the skin and does not form a visible, detachable plastic sheet. The glues and cements are disqualified on this account; their physical presence is detectable, and they ultimately crack and peel.

Summary

Purified solutions of beef albumin promptly and temporarily efface the finer wrinkles of aged facial skin. The effect is purely physical and is simply a remodeling of surface topography.

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References

(1) Goncarova, V., *U. S. Patent* 2,043,657 (1936).
(2) Keck, J., and Tronnier, H., *U. S. Patent* 3,041,245 (1962).

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Aqueous Topical Adhesives
I. Film Forming Base

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Presented December 2, 1964, New York City

Synopsis—A considerable amount of interest has recently arisen with regard to the preparation of protective and medicated films for cosmetic and dermatological uses. The majority of these widely accepted preparations are aerosols containing plain or medicated resin dressings; however, they have shortcomings due to the need for an organic solvent. Thus, the development of a preparation containing a water-washable resin as the main film-forming component was considered desirable.

Polyvinyl alcohol was chosen as the soluble synthetic resin because of its apparent lack of toxicity and the relative stability of its films. Water-washable and easily peeled film-forming liquid preparations were formulated by blending various emulsions or dispersions with polyvinyl alcohol. The preparations showed good stability and could contain water-soluble medicaments.

Introduction

Men have used many materials and devices in the treatment and protection of injured skin. Treatment usually involved the application of a medicament, while protection was gained by covering the afflicted area with cloth or some other suitable material. In earlier times readily available materials such as various oils, lard, and other vegetable or animal fats were used either alone or as the base for various skin remedies. They were gradually replaced by more stable materials. Today, many medicinal agents in many different forms are used in the treatment of skin disorders and as protectants against skin irritants. Still, a protective covering is usually required. The removal of both

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the protective covering and the medicament from the injured area of the skin is often difficult, and materials suitable as protective coverings are not always easily available.

Many plastic materials have appeared on the American market since the introduction of vinyl acetate by Staudinger in 1927. Many of these plastics can deposit a tough, continuous film on the skin. It is theoretically possible to incorporate one or more of these plastic materials into a dermatological preparation, which on drying would leave such a film on the skin. This preparation would eliminate the need for a bandage; and if medicinal agents were included in the formula, it would serve both as a treatment and protective covering. A preparation of this type containing a water-soluble plastic would be readily removable by being washed with water or by being peeled. Sperandio and co-workers have prepared an ointment base (1) and a film-forming base (2, 3) of this type with polyvinyl alcohol as the water-soluble plastic.

It was the purpose of this investigation to formulate a liquid film-forming base that could be applied with a roll-ball type of application or with a brush. This would eliminate the "unsanitary" aspect of ointment application.

The emulsifying, binding, thickening, and to some extent film-forming properties of polyvinyl alcohol have found use in cosmetic preparations. Cleansing creams, shaving creams, and some other cosmetic preparations containing polyvinyl alcohol have been prepared. Polyvinyl alcohol is not a primary skin irritant and does not produce skin sensitization (2, 3). There is no evidence that it is taken up directly by epithelial tissue. From the point of view of chemical effects no toxicity has been demonstrated.

Thus, on the basis of its water solubility, its film-forming power, its apparent lack of toxicity, and the relative stability of its films and solutions, polyvinyl alcohol was chosen as the water-soluble synthetic resin to be used as the major film-forming component in the preparation of a water-washable film-forming dermatological base.

Such a base would be useful as a skin protective and after incorporation of the proper chemicals as an antiseptic, antipruritic, or anesthetic bandage for small areas of the skin.

The base should exhibit the following characteristics:

1. It should be a viscous liquid capable of even application to the skin by means of a brush or a roll-ball type of applicator.

2. It should dry rapidly, depositing a continuous film on the skin.
3. It should be nonirritating.
4. It should be stable under normal conditions.

The film produced by this preparation after drying should:

1. Be sufficiently elastic to withstand normal stresses and abuses.
2. Adhere to the skin for a reasonable time without cracking or lifting.
3. Be flexible enough to prevent cracking by joint movements.
4. Be easily removable by being washed with water or being peeled.

Experimental

Aqueous or hydroalcoholic solutions of polyvinyl alcohol cannot be efficiently used as dermatological film-forming preparations without modifications because the solutions of high viscosity are tacky and difficult to spread. Solutions of low viscosity are too mobile and have low water resistance. Thus, modifications of polyvinyl alcohol solutions will be considered.

Dispersions of Various Solids in Polyvinyl Alcohol Solutions

It was felt that dispersions of solid oil-soluble materials such as cetyl alcohol, stearyl alcohol, paraffin, beeswax, and stearic acid (either alone or in combination) in polyvinyl alcohol solutions would overcome these difficulties. The formulas for two of these dispersions are given in Table I (formulas 1 and 2).

The formulations were prepared as follows: A slurry was formed by sifting the polyvinyl alcohol slowly into the vortex created by a high speed stirrer immersed in the preserved water or in a mixture of the preserved water and glycerin. The stirring apparatus consisted of an electric stirrer fitted with a four-bladed plastic propeller shaft. The slurry was heated on a water bath for 30 minutes or until the polyvinyl alcohol had completely dissolved. The solid material or materials to be dispersed and the surface active agents were heated on a water bath to 77°C. The polyvinyl alcohol solution, cooled to 72°C, was added slowly in small portions to the melted mixture with constant stirring, which was continued until the temperature of the preparation dropped to about 40°C. This method of preparation will hereafter be designated as the "Vortex Method."

The nonionic surface active agents were included in the formulations as auxiliary dispersing agents and as plasticizers for the polyvinyl

alcohol. The quantities of nonionic surface active agents used were calculated to yield a product that would be hydrophilic. Glycerol was included in several of the formulations for its emollient and humectant properties. Preserved water, containing a 0.04% mixture (65:35) of methyl and propyl paraben, rather than distilled water was used be-

TABLE I

Dispersions of Various Solids in Polyvinyl Alcohol Solutions

Ingredients	Formulations					
	1	2	3	4	5	6
Paraffin	5.0 g.	5.0 g.	...	...	...	...
Stearic acid	3.0 g.	2.5 g.	...	8.0 g.	...	...
Cetyl alcohol	...	10.0 g.	6.0 g.	...	4.0 g.	4.0 g.
White wax	15.5 g.	...	...	...	...	...
Resin latex WC-130®[a]	...	...	...	...	12.0 g.	15.0 g.
Elvanol 51-05®[b]	10.0 g.	...	15.0 g.	15.0 g.	10.0 g.	10.0 g.
Elvanol 72-60®[b]	...	7.0 g.	...	...	3.0 g.	3.0 g.
Tween 60®[c]	1.9 g.	3.0 g.	2.5 g.	2.5 g.	3.0 g.	3.0 g.
Arlacel 80®[c]	1.1 g.	...	0.5 g.	0.5 g.	...	...
Glycerol	...	5.0 ml.	5.0 ml.	5.0 ml.	...	...
Propylene glycol	...	...	...	...	5.0 ml.	5.0 ml.
Ethanol	...	...	10.0 ml.	10.0 ml.	10.0 ml.	10.0 ml.
Preserved water[d]	63.5 ml.	67.5 ml.	61.0 ml.	59.0 ml.	53.0 ml.	50.0 ml.

[a] Product of Union Carbide Chemicals Company, New York, N. Y.

[b] Product of the E. I. du Pont de Nemours and Company, Wilmington, Del.

[c] Product of Atlas Chemical Industries, Inc., Wilmington, Del.

[d] Preserved water contains 0.04% of a mixture (65:35) of methyl paraben and propyl paraben.

cause of the susceptibility of polyvinyl alcohol solutions to mold growth. The consistency, film-forming ability, and ease of peeling evaluations are given in Table III.

Most of the formulations were unctuous in consistency and spread easily on the skin. They all deposited films on the skin after drying, but more than 20 minutes was required. The films produced were moderately adhesive but were of low tensile strength and remained somewhat sticky.

A second series (formulas 3 and 4, Table I) was prepared in an attempt to improve the nature of the films and to reduce the drying time. Cetyl alcohol or stearic acid were the only solids used while ethanol was added in an attempt to shorten the drying time.

The formulations were prepared by the Vortex Method, with a slight modification for the incorporation of the ethanol. The ethanol was

diluted with an equal volume of the preserved water and added slowly with constant stirring to the otherwise completed preparation (cooled to 40°C). The consistency, film-forming ability, and ease of peeling evaluations are given in Table III.

Although all of the formulations in this series deposited a film on the skin, the drying time was not greatly reduced. All of the films had low tensile strength, moderate water resistance, and moderate flexibility. The films were difficultly peelable.

*Dispersions of Resin Latex WC-130[a] * in Polyvinyl Alcohol Solutions*

It was felt that stronger, more flexible, less water sensitive films would result if another water-soluble or water dispersible film-forming plastic

TABLE II

Castor Oil Emulsions Containing Polyvinyl Alcohol

Ingredients	Formulations		
	7	8	9
Castor oil	6.0 g.	6.0 g.	6.0 g.
Arlacel 80	3.5 g.	3.5 g.	3.5 g.
Tween 60	1.5 g.	1.5 g.	1.5 g.
Elvanol 51-05	12.0 g.	15.0 g.	15.0 g.
Elvanol 72-60	1.0 g.	0.5 g.	0.5 g.
Rhoplex B-15[a]	12.0 ml.	...	...
Resin latex WC-130	...	...	15.0 ml.
Sorbitol solution USP	5.0 ml.	5.0 ml.	5.0 ml.
Ethanol	5.0 ml.	4.0 ml.	4.0 ml.
Preserved water[b]	54.0 ml.	53.5 ml.	50.5 ml.

[a] A product of the Rohm and Haas Company, Philadelphia, Pa.

[b] Preserved water contains 0.04% of a mixture (65:35) of methyl paraben and propyl paraben.

were included in the formulations. Formulas are given in Table I (formulas 5 and 6). Resin Latex WC-130 is a stable dispersion of an unmodified vinyl acetate polymer capable of producing continuous flexible films on various surfaces. It is stable over a wide range of pH, is stable to the addition of a wide variety of inorganic salts, and may be used in preparations containing nonionic surface-active agents.

The formulations were prepared by the Vortex Method with the Resin Latex being added to the hot mixture just prior to cooling. The films produced by these formulations were somewhat stronger and more flexible than those produced by previous formulations, but their water resistance, adhesiveness, and time of formation improved only slightly.

* A product of Union Carbide Chemicals Company, New York, N. Y.

TABLE III

Evaluation of Formulations

	Formulation								
	1	2	3	4	5	6	7	8	9
Consistency	VL	SS	VL	VL	L	SS	VL	VL	VL
Film formation	1	1	2	2	1	1	3	4	4
Ease of peeling	1	1	1	1	1	1	2	3	3

Key:

Consistency

VL = Viscous liquid.

SS = Semi-solid.

L = Liquid.

Film formation

1. Film formed, required more than twenty minutes.
2. Film formed, required from ten to twenty minutes.
3. Film formed, required from five to ten minutes.
4. Film formed, required less than five minutes.

Ease of peeling

1. Peeled with difficulty.
2. Good.
3. Excellent.

Their consistency, film-forming ability, and ease of peeling evaluations are given in Table III.

Dispersions of Rhoplex Emulsions in Polyvinyl Alcohol Solutions

Rhoplex AC-33® * and B-15® * are aqueous emulsions of acrylic polymers. They readily deposit films from solution at normal temperatures without the addition of plasticizers and show excellent adhesion on a variety of surfaces. Thus, they were substituted for the Resin Latex polymer in the same proportions.

All of the formulations containing the Rhoplex emulsions deposited a film on the skin. The properties of the films were very similar to those of the vinyl acetate films except that they lost their adhesiveness and cracked whenever they were subjected to stretching (movable parts of the body, i.e, joints).

Castor Oil Emulsions Containing Polyvinyl Alcohols

A final series of castor oil emulsions containing both water-soluble (Elvanols) and water-insoluble (Rhoplex B-15) plastic materials was prepared. Representative formulations are shown in Table II. They were prepared in the following manner:

* Products of the Rohm and Haas Company, Philadelphia, Pa.

The castor oil and one or more emulsifiers were heated on a water bath to 75°C. A solution of the Elvanol or Elvanols was prepared in a mixture of preserved water and sorbitol solution U.S.P. or propylene glycol as described under the Vortex Method. The Elvanol solution was then added slowly to the castor oil phase with constant stirring. When the resulting emulsion had cooled to about 45°C, the Rhoplex B-15 and finally the alcohol (if included in the formulation) were added slowly in small portions. Stirring was continued for a minimum of 5 minutes thereafter.

It was hoped that by replacing the cetyl alcohol with a fixed oil a film-forming preparation possessing all the desired attributes could be prepared. Castor oil was chosen because it was known to increase the flexibility and adhesiveness of other films.

All the emulsifiers yielded oil in water emulsions as desired. The most efficient emulsifier was found to be the Arlacel 80-Tween 60 mixture in the proportion of 3.5:1.5 by weight. Propylene glycol was replaced by the sorbitol solution in order to make the product spread more easily. All of the formulations in this series yielded products that were white viscous emulsions; the films were all soft, flexible, smooth, and rubbery.

Formulation number 8 in Table II possessed all the desired characteristics listed in the introduction. Formulation number 9 in Table II, in which Resin Latex WC-130 replaces the Rhoplex B-15, gave a product identical with number 8 with respect to its consistency and film characteristics. Thus, formulations number 8 and 9 yielded the best film-forming liquid preparations from among the more than fifty formulations prepared.

Stability and Compatibility

Bulk quantities of formulations number 8 and 9 were prepared and stored at room temperature. After 18 months, there was no evidence of separation, mold growth, or other deterioration, and no significant change in the pH or viscosity of either product.

Formulation number 9 was found to be compatible with 0.5% neomycin sulfate, 0.1% benzalkonium chloride, 0.1% phenylmercuric nitrate, and 1.0% dibucaine hydrochloride. Formulation number 8 however, was compatible only with the phenylmercuric nitrate.

Summary

Two plastic-containing liquid preparations which form a flexible, continuous film on the skin have been formulated. Both preparations

are stable at room temperature. It was also found that water-washable and easily peeled film-forming preparations can be prepared by blending emulsions or dispersions of water-insoluble plastic materials with emulsions or dispersions of water-soluble plastic materials. Formulations containing Elvanol 51–05, Elvanol 72–60, and either Resin Latex WC-130 or Rhoplex B-15 were found to produce the best film-forming liquid preparations.

Modification of these basic formulations to make them useful in aerosols will be discussed in Part II of this series.

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References

(1) Haberle, J. E., and Sperandio, G. J., *J. Am. Pharm. Assoc.*, NS1, 306 (1961).
(2) Ward, J. B., and Sperandio, G. J., *Am. Perfumer and Cosmetics*, **79**, 53 (1964).
(3) *Idem*, *J. Soc. Cosmetic Chemists*, **15**, 327 (1964).

J. Soc. Cosmetic Chemists, 16, 571-587(1965)

An Evaluation of the Potentials of Neutron Activation Analysis in Cosmetic Chemistry

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Synopsis—The basic principles of activation analysis are presented. The neutron reactions used, the availability of neutron sources, and the mathematics describing the production of radioactivity during an activation and the subsequent decay of the radioactivity are discussed. The instrumental and radiochemical techniques used to complete an analysis are also described. In addition, a number of examples are cited to illustrate how cosmetic chemists might use this unique method in applications to such analytical problems as the determination of the elemental constituents in raw materials, product specifications, or the toxicity of cosmetics and related materials.

The Principles of Activation Analysis

The many rapid technological advances experienced during the last decade in the pharmaceutical and allied industries have brought with them a need for very accurate analytical methods. The purity of a product, control of its production, and evaluations of the process used to manufacture the product require sensitive and specific analytical techniques. As a result, an analyst must become highly specialized in those techniques and instruments capable of detecting traces of impurities or additives. He also must use those methods of sample preparation capable of minimizing contamination, and he must provide

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that kind of technology which may shorten the time required for analyses and interpretation of the results.

The recent developments in activation analysis techniques now offer the prospect of rapid, reliable analyses for many elements in concentrations as small as parts per million or parts per billion. In general, there is no need to prepare the sample in any way; thus the risk of contamination and subsequently a change in impurity levels during the assay is eliminated. In many instances, the samples need only weigh a few milligrams. Sampling can be automatic, and the assays can be completed by the use of batch-wise or continuous operations.

Activation analysis is a method of elemental analysis using techniques of nuclear transmutation. When an isotope of a stable element is irradiated by the nuclear particles produced in a nuclear reactor, a particle accelerator, or some other source, some of the atoms of the isotope interact with the bombarding particles and are converted into a radioactive isotope of the same element. Depending on the nature of the bombarding particles, the atoms can be converted into different radioisotopes of the same element or into isotopes of different elements. Each radioelement may be uniquely identified by its emission spectrum. For example, a gamma-ray scintillation spectrometer measurement of a radioactive sample can be plotted as count rate *versus* energy of radiation. The photopeaks in the spectrum indicate the presence of particular radioelements, and the amount of radioactivity they contain may be used to measure the amount of the radioelement present.

Nuclear Reactions

As has already been stated, activation analysis methodology is based on the interaction between fundamental nuclear particles and the stable nuclei of the elements. Bohr (1) describes a nuclear interaction as the union of a nuclear particle with the stable nucleus to form a new "compound" nucleus. In this nuclear transformation, the new nucleus is unstable because the kinetic energy of the nuclear particle and the additional binding energy are rapidly distributed among all of the particles of the new nucleus, and it will break up and change into a more stable state.

Nuclear reactions are analogous to ordinary chemical reactions (2). They exhibit a mass change (heat of reaction) and an energy of activation, and they occur at various reaction rates depending upon the experimental conditions. Bringing the reactants together initiates a nuclear

reaction. In a typical nuclear reaction, such as the reaction

$$Cl^{37} + {}_0n^1 \rightarrow Cl^{38} + \gamma, \quad (1)$$

Cl^{37}, a stable isotope of chlorine, is the target nucleus; n, a source of neutrons, or the reacting nuclear particles; Cl^{38} is the artificially produced radioisotope; and γ, an emitted particle of residual energy. Cl^{37} is 24.6% abundant; Cl^{38} decays with a half-life of 37.3 min. and in its decay emits both beta and gamma radiations.

The analogy between nuclear and chemical reactions can be elaborated upon by a consideration of the following equations:

$$2Mn(NO_3)_2 + 5NaBiO_3 + 16HNO_3 \rightarrow 2HMnO_4 + 5NaNO_3 + 5Bi(NO_3)_3 + 7H_2O. \quad (2)$$

$$Mn^{55} + n \rightarrow Mn^{56} + \gamma \quad (3)$$

$$Mn^{56} \xrightarrow[2.58h]{\beta^-,\gamma} Fe^{56} \text{ (stable)} \quad (4)$$

In the chemical reaction (eq. 2), the amount of Mn^{+2} can be determined by titrating the permanganate ions (MnO_4^-) formed with ferrous sulfate, whereas in the nuclear reaction (eq. 3) the amount of Mn^{55} can be determined by measuring either the β or γ radiations emitted by Mn^{56} as it decays to stable Fe^{56} (eq. 4). In each instance, an end product must be obtained before the analysis can be completed. Chemical agents, such as the bismuthate and the nitric acid, achieved this in the chemical reaction. The neutrons from a bombarding source become the agents to produce radioactive Mn^{56}.

The probability that a nuclear reaction will occur as the reactants are brought together can be represented by the "cross section" concept of kinetic theory. In describing the method of producing radioelements, Broda (3) explains that the probability of an induced nuclear reaction is expressed in terms of a "reaction cross section," σ, i.e., the nuclei being bombarded by a source of nuclear particles are ascribed effective target areas which must be hit for the reaction to occur. In a nuclear reaction, cross sections are often of the order of 10^{-24} cm.^{2}/nucleus. This unit of the target area has become known as a "barn." The cross sections of the individual reactions are often determined by assaying the radioactivity induced into the sample by a nuclear particle beam, or source, of known intensity. This "activation method" distinguishes not only between different reactions of the same nucleus but also between the contribution of different kinds of nuclei, including individual stable isotopes of the same element, to the nuclear process.

TABLE I

Examples of Nuclear Reactions

Type Reaction	Particle Source	Typical Reaction Equation	Half-Life of Radionuclide	Approximate Number of Reactions of This Type Known
n, γ	Reactors, cyclotrons, Van de Graaff, accelerators, low-intensity neutron sources	$Na^{23} + n \rightarrow Na^{24} + \gamma$	15 hr.	132
n, p	Reactors, cyclotrons, Van de Graaff, accelerators, low-intensity neutron sources	$Mg^{24} + n \rightarrow Na^{24} + p$	15 hr.	78
n, α	Reactors, cyclotrons, Van de Graaff, accelerators, low-intensity neutron sources	$Al^{27} + n \rightarrow Na^{24} + \alpha$	15 hr.	54
$n, 2n$	Reactors, cyclotrons, Van de Graaff, accelerators, low-intensity neutron sources	$Na^{23} + n \rightarrow Na^{22} + 2n$	2.58 yr.	90
n, f	Reactors, cyclotrons, Van de Graaff, accelerators, low intensity neutron sources	$U^{235} + n \rightarrow$ Fission products	Varied	108
p, n	Cyclotrons, accelerators	$Sc^{80} + p \rightarrow Br^{80} + n$	17.6 min.	95
p, γ	Cyclotrons, accelerators	$C^{12} + p \rightarrow N^{13} + \gamma$	10.05 min.	30
d, p	Cyclotrons, accelerators	$P^{31} + d \rightarrow P^{32} + p$	14.3 days	122
d, n	Cyclotrons, accelerators	$C^{12} + d \rightarrow N^{13} + n$	10.05 min.	87
d, α	Cyclotrons, accelerators	$Mg^{24} + d \rightarrow Na^{22} + \alpha$	2.58 yr.	50
$d, 2n$	Cyclotrons, accelerators	$Cr^{52} + d \rightarrow Mn^{52} + n$	5.69 days	30
α, n	Cyclotrons, accelerators, radioactive sources	$S^{32} + \alpha \rightarrow Cl^{34} + n$	1.53 sec.	63
		$Mg^{25} + \alpha \rightarrow Al^{28} + p$	2.3 min.	30
γ, n	Betatrons, radioactive sources	$O^{16} + \gamma \rightarrow O^{15} + n$	2.07 min.	40

Since the discovery of artificial radioactivity in 1934 by Curie and Joliot (4), several hundred artificial radioactive isotopes have been prepared by at least five types of nuclear particle bombardments, i.e., neutrons, protons, deuterons, α particles, and γ rays. Table I gives examples of typical nuclear reactions used in activation analysis, the particle sources, and the approximate number of reactions that have been observed for each type of nuclear bombardment. Neutron reactions of the (n,n') type have also been observed. Other proton reactions that are known include (p,α) and (p,p) types, whereas α reactions of the types (α,α), $(\alpha,2n)$, $(\alpha,3n)$ and (α,d) can also produce radioactive elements.

The half-lives of artificially produced radioactive elements can range from the order of a few microseconds to many years. This characteristic, as well as the type of radiations they emit as they decay, govern the practical use of particular radioisotopes in activation analysis.

The Activation Analysis Equations

In activation analysis, the sample material to be analyzed is placed in a source of nuclear particles for a period of time long enough to induce a measurable amount of radioactivity into a stable isotope of the element being determined. The rate of growth (or production) of radioactive atoms, N^*, with time may be calculated by

$$\frac{dN^*}{dt} = f\sigma_{ac}N - \lambda N^* \tag{5}$$

Equation 5, on integration over the period of irradiation, becomes

$$N^* = \frac{f\sigma_{ac}N(1 - e^{-\lambda t})}{\lambda} \tag{6}$$

where:

f = the number of particles (flux) bombarding the nuclei in the sample, as particles/cm.^{2}·sec.;

σ_{ac} = the "activation" cross-section for the nuclear reaction, *barns*, or 10^{-24} cm.^{2} per target atom;

N = the number of target atoms;

$(1 - e^{-\lambda t})$ = the ratio of the amount of radioactivity produced in time, t, to that produced in infinite time. May be expressed as a "saturation factor," S;

λ = the radioactivity decay constant for the radionuclide formed, based upon the relationship $\lambda = 0.693/t_{1/2}$, where $t_{1/2}$ is the half-life;

N^* = number of radioactive atoms produced.

The amount of radioactivity, A, in disintegrations per second exhibited by the radioactive atoms, N^*, produced in an irradiation time, t, is given by the equation

$$A = \lambda N^* = f\sigma_{ac} N(1 - e^{-0.693t/t_{1/2}}) \quad (7)$$

where t and $t_{1/2}$ are expressed in seconds.

In activation analysis the element being determined is either monoisotopic or multi-isotopic; so equation 7 can be expressed as

$$A = \frac{6.02 \times 10^{23} f\sigma_{ac}\theta W(1 - e^{-0.693t/t_{1/2}})}{M} \quad (8)$$

where W is the weight of an element in grams of atomic weight M, and θ is the abundance of the isotope of the element being irradiated.

At the end of the irradiation, the induced radioactivity will immediately decay with its own characteristic half-life, so that at some time d after the end of the irradiation the radioactivity is equal to

$$A = \frac{6.02 \times 10^{23} f\sigma_{ac}\theta W\ (1 - e^{-0.693t/t_{1/2}})\ (e^{-0.693d/t_{1/2}})}{M} \quad (9)$$

where $e^{-0.693d/t_{1/2}}$ is the decay factor, D, for the radionuclide.

Equation 9 can be rearranged to give an equation for the determination of the concentration of the element being analyzed by activation analysis:

$$W = \frac{AM}{(6.02 \times 10^{23})(f)\ (\sigma_{ac})\ (\theta)\ (S)\ (D)} \quad (10)$$

From these equations, it can be seen that the amount of radioactivity produced (and, therefore, the sensitivity) is influenced by those factors which are fixed for any one element, and those which may be varied by the analyst. The activation cross section is an important nonvariable factor; for any type of nuclear particle reaction, it is fixed for the particular isotope of the element undergoing the reaction. For instance, the activation cross sections for the n,γ reactions can range from the order of millibarns to several hundred barns. Hence the sensitivity with which an element can be detected is dependent upon cross section, in that those elements having larger activation cross sections will have greater sensitivity.

Of similar importance, the supply (or flux) of the bombarding nuclear particles reflects upon the sensitivity obtainable by activation

analysis. For instance, irradiations made at a flux of 10^{13} particles/cm.^{2}·sec. will make an activation analysis at least 100 times more sensitive than an irradiation in a flux of 10^{11} particles/cm.^{2}·sec. Neutron fluxes ranging from 10^5 to $10^{14}n$/cm.^{2}·sec. have been used in neutron activation analysis applications.

The saturation factor S, or the ratio of the amount of radioactivity produced during an irradiation, may vary from 0 to 1. The maximum sensitivity occurs when $S = 1$. However, it is not necessary in many cases, nor is it practical in most, to irradiate to saturation. For example, if a radioisotope has a half-life of 30 days, then in a 30-day irradiation period 50% of the maximum amount of radioactivity that could be produced would be obtained; in another 30 days, it would build up to 75% of maximum. To reach maximum radioactivity production, it would be necessary to irradiate for 300 days. Thus, an additional 270 days are required to produce only twice as much radioactivity as can be obtained in 30-day irradiation. Saturation for elements having short half-lives, i.e., minutes, hours, or even a few days, can be reached in a reasonable time. Even though the time necessary to reach saturation is dependent upon the half-life of the radioisotope, the optimum irradiation time is best chosen by the analyst in order to fit the operational schedule of the nuclear particle source being used e.g., a reactor or cyclotron.

The half-life of the induced radionuclide does not control the inherent sensitivity of the method. However, it can become a limitation, if the half-life of the radioelement is short or if it requires a long time to measure its radioactivity. In almost all activation analyses, it is desirable that the time between the end of the irradiation and the actual measurement of the radioactivity be short. If the sample weight is increased, then so is the sensitivity, as one would predict from equation 10.

The nature of the radiations emitted by the radionuclide formed can also affect the sensitivity of the method. The radioactivity A of a radionuclide produced in a given period of irradiation is constant for a given weight of element, and the amount of radioactivity emitted by the radionuclide as it decays is expressed in *disintegrations/second*. However, no routine counting method is 100% efficient; that is, it does not detect every one of the disintegrations being emitted. If the emitted radiations are soft X-rays or very weak β particles, the actual efficiency for measuring these particles may be 1% or less. Thus, the more efficiently the radioactivity of a radionuclide is measured the greater is the

sensitivity. Price (4) discusses the over-all efficiency of detection devices for the various kinds of rays and particles emitted by radionuclides.

An activation analysis can be completed in one of two ways: either by an *absolute* method, or by a *comparator* method. In the absolute method, it is necessary that the nuclear particle flux be measured during the bombardment, that the cross section for the reaction and the radioelement's half-life be known accurately, and that the radioactivity be measured absolutely. The uncertainty in measuring the intensity of the nuclear particles sometimes can be large. The literature cross section and half-life tabulations shown some discrepancies, and the error in absolute measurements can be very large, because it is extremely difficult to measure small amounts of radioactivity absolutely.

The comparator method is most frequently used. In this method, a known amount of the element to be determined is irradiated simultaneously with the unknown sample and processed after the irradiation in the same manner as the unknown sample. Since all of the terms in equation 10, except those for W and A, are the same for both the comparator and unknown samples, a simplified equation results:

$$\frac{W \text{ in unknown}}{W \text{ in comparator}} = \frac{A \text{ in unknown}}{A \text{ in comparator}} \qquad (11)$$

Corrections for chemical yield (if a radiochemical separation is made), radioactive decay, and sample weights must be considered in equation 11.

Activation Analysis Methods

All types of nuclear particles, i.e., neutrons, protons, deuterons, alpha, and gammas, can interact with the nuclei of elements. Sources of all of these particles have been used in activation analysis. However, it is significant to note that the use of protons, deuterons, alphas, and gammas in activation analysis has been limited. Several reasons can be cited for explaining this lack of usage. For example, the heat dissipated within the chamber of an accelerator, as well as the small area of the charged particle beam available for activation, have minimized the use of such devices in activation analysis. Another difficulty with the use of charged particle accelerators is that many different nuclear reactions can occur simultaneously during an irradiation so that competitive reactions greatly

influence the ease with which an element can be determined. The most important factor in favor of neutron activation analysis is that, after 1950, nuclear reactor facilities became more readily available to most researchers and that the rigid requirements of sample type and sample sizes that could be irradiated were relaxed. In addition, newer reactors have provided much more intense neutron sources. Likewise, the development of techniques for inserting neutron-producing targets into Van de Graaff accelerators have contributed to the increased use of neutron activation analysis (5).

General Procedure of Analysis

Most activation analyses follow a procedure similar to that outlined in Fig. 1:

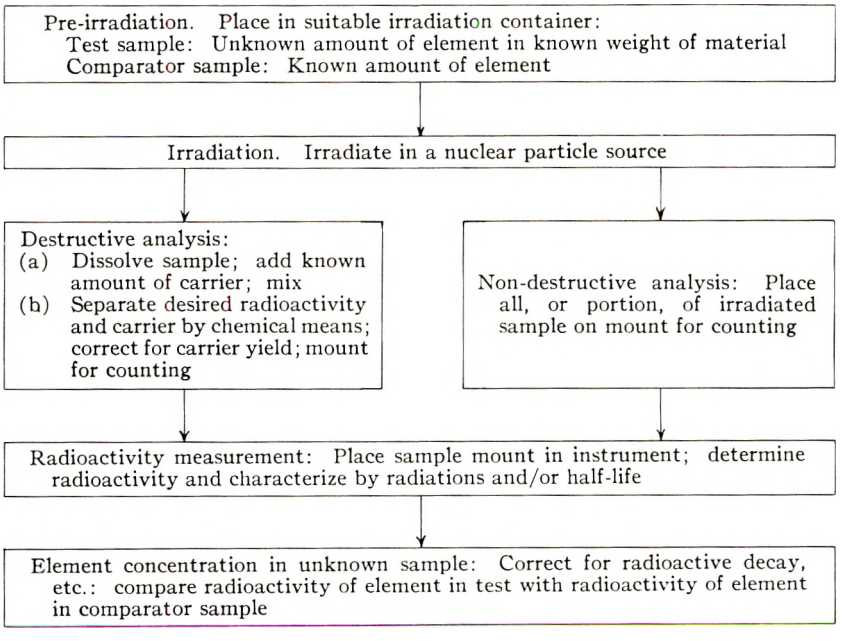

Figure 1. A typical procedure for radioactivation analysis

Preparation of Samples

Sample preparation is quite simple. Unless it contains an appreciable amount of material having a high neutron capture cross section, no

preliminary separations have to be made. Thus, the opportunities for accidental contamination of the sample with any of the elements sought are almost negligible. In practice, the test samples are placed directly in small quartz or plastic tubes, which are then sealed and placed in aluminum or plastic irradiation containers. Because of the extreme sensitivity of the method, the sample size can be quite small. Individual comparator samples are prepared for each of the elements sought and irradiated under identical conditions with the sample.

Irradiation of Samples

The period of irradiation used during an activation analysis is usually determined by the half-life of the radionuclide being used in the analysis. In most laboratories, the duration of the irradiation interval is controlled by the analyst.

Post-Irradiation Processing of Irradiated Samples

After the irradiation, the samples may be processed by one of the following general methods:

(a) *Radiochemical Separation:* This classical method involves the use of chemical separations and is usually the method of choice for samples of unknown composition or where the radiation spectrum from the activated components is known to be complex. In this method, the sample is dissolved, and known quantities of inert elemental carriers are added as "carriers" for each of the radionuclides sought. Then a series of chemical separations are performed to isolate in a radioactively pure form these various species. These separations need not be quantitative since corrections for chemical yield can be made for the amount of the added inactive carrier finally recovered. After the elemental separation, the radioactivity of the test sample is measured with a β or γ counter (4) and compared with the radioactivity induced in the comparator sample which has been processed in the same manner as the test sample.

Radiochemical separation methods are based upon techniques involving precipitation, ion exchange, solvent extraction, electrolysis, etc. Typical precipitation-type methods of radiochemical analysis used in determining the constituents of aluminum-base alloys have been re-

ported by Brooksbank *et al.* (6). Another report (7) outlines an analytical scheme based upon precipitation that is used routinely in activation analysis. Ion exchange techniques, such as those used by Kraus *et al.* (8) and Hicks *et al.* (9), have also been used in activation analysis applications.

(b) *Nondestructive Analyses:* The second general method of treating an irradiated sample is an instrumental technique which eliminates the necessity for wet chemical separations. However, it lacks some of the sensitivity that can be obtained with radiochemical separations, but it has a considerable advantage in the routine analysis of multicomponent systems. The method is based upon the use of γ-ray scintillation spectrometry for separating and identifying quantitatively the various gamma radiations in an irradiated sample (4, 10). Typical data obtained by this method are given in several of the references cited in this report (6, 11–14).

A γ-ray scintillation spectrometer comprises a detection element, usually a sodium iodide crystal, which has a high efficiency for converting γ radiations into visible light pulses of amplitude proportional to the energy of the incident radiation, and an electronic system for amplifying these pulses and sorting them into discrete energy channels. A plot of the data will give an energy spectrum of the radiation from a particular sample. In such spectra, each γ-ray energy will be displayed as a well-defined photopeak at that energy. The position of the peak in the spectrum constitutes an identification of the radioactive component, and the area under the peak is a measure of the amount of stable element present in the sample. Figure 2 is a typical γ-ray spectrum. In this particular one, a method has been used to unscramble the components of the original spectrum by a "complement-subtraction" method. The details of this method have been described elsewhere (15). A computer-integrated system for γ spectrometry is already being used to analyze large numbers of activation analysis samples routinely (16). Connally and Leboeuf (17) have estimated that γ-ray intensities as measured by γ-ray scintillation spectrometry can be better than $\pm 2\%$.

Applications of Activation Analysis

Activation analysis has been applied to the determination of at least 70 elements. Solid, liquid, and gaseous samples can be analyzed in an almost routine manner. Macroanalysis applications are also reported,

TABLE II

Neutron Activation Analysis

Element	Typical Detection Limits,[a] Micrograms	Element	Typical Detection Limits,[a] Micrograms
Sodium	0.02	Indium	0.00002
Magnesium	0.06	Tin	0.07
Aluminum	0.0009	Antimony	0.007
Silicon	0.5	Tellurium	0.02
Phosphorus	4	Iodine	0.0004
Sulfur	20	Cesium	0.03
Chlorine	0.004	Barium	0.02
Potassium	0.2	Lanthanum	0.002
Calcium	0.2	Cerium	0.9
Scandium	0.0003	Praseodymium	0.005
Titanium	0.05	Neodymium	0.03
Vanadium	0.00008	Samarium	0.004
Chromium	1	Europium	0.00004
Manganese	0.0002	Gadolinium	0.006
Iron	400	Terbium	0.01
Cobalt	0.00003	Dysprosium	0.000005
Nickel	0.2	Holmium	0.002
Copper	0.005	Erbium	0.003
Zinc	0.006	Thulium	0.08
Gallium	0.01	Ytterbium	0.01
Germanium	0.03	Lutetium	0.0004
Arsenic	0.008	Hafnium	0.03
Selenium	0.0003	Tantalum	0.06
Bromine	0.0002	Tungsten	0.009
Rubidium	0.02	Rhenium	0.002
Strontium	0.08	Osmium	0.2
Yttrium	0.09	Iridium	0.000006
Zirconium	2	Platinum	0.009
Niobium	0.0006	Gold	0.002
Molybdenum	0.04	Mercury	0.05
Ruthenium	0.08	Thallium	0.02
Rhodium	0.000005	Lead	60
Palladium	0.01	Bismuth	30
Silver	0.00003	Thorium	0.0004
Cadmium	0.2	Uranium	0.002

[a] Based on calculations involving the production and measurement of 40 disintegrations per second of radioactivity when a 1 g. test sample is irradiated in UCCND's 5-Megawatt Research Reactor for 30 min. at a neutron flux of 3×10^{13} neutrons/cm.^{2}·sec.

and the use of neutron activation analysis as a complementary method to other analysis techniques, such as particle-size distribution analysis, is also known.

The elements that can be determined and their limits of measurement for a given set of analytical conditions are arranged in order of increasing atomic number in Table II. Neutron activation analysis has already been used to determine most of these elements in both inorganic and organic materials, such as biological tissues and fluids, chemicals, metals and alloys, ores and minerals, plastics and resinous materials, petrochemicals, soils, vegetation, and waters.

The specific examples of activation analysis that follow were selected to illustrate its potential usefulness to the cosmetic chemist. It should

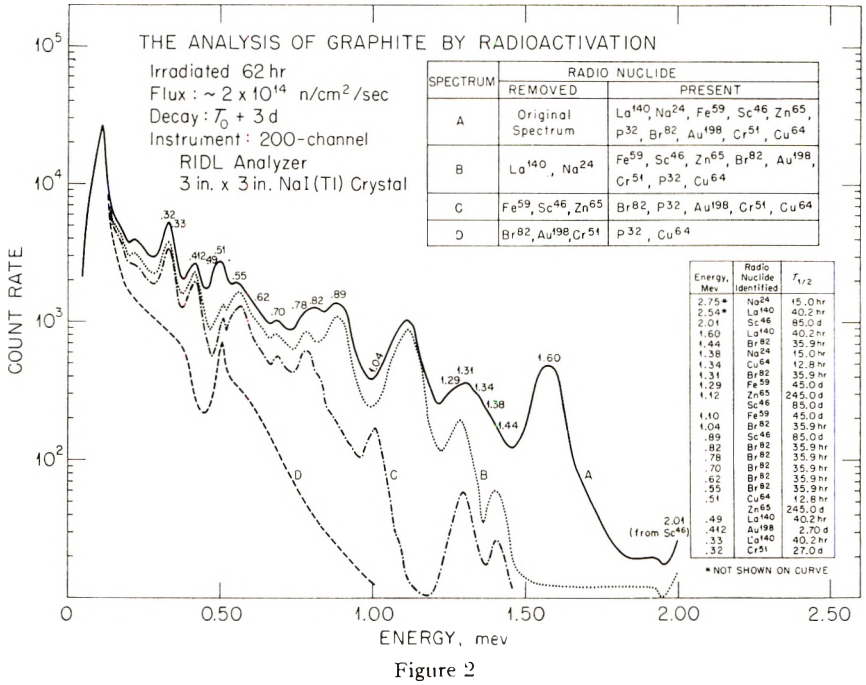

Figure 2

prove to be a convenient method to solve many problems in cosmetic research and product development as well as a practical technique for production and process control problems.

For example, Kaiser and Meinke (18) have used activation analysis as a rapid method to determine microgram amounts of cobalt from vitamin B_{12}. Rat kidney tissue and vitamin preparations have been analyzed by a

15-min radiochemical separation procedure coupled with γ-ray scintillation spectrometry. The 10.5 min. Co^{60m} radionuclide was used in these analyses. Savachuck (18) used activation analysis to determine microgram amounts of strontium in rat bones in order to show that a small amount of strontium in the diet of growing animals increases the fracture resistance of the bone during growth.

Dewar and Lenihan (19) studied a case of chronic arsenical poisoning, resulting from a daily intake of a dose of an arsenic and potassium bromide mixture by the subject, by analyzing hair, nails, and skin. The data obtained in this work are as follows:

Head hair (initial tests)	65 p.p.m.
Fingernail (initial tests)	11 p.p.m.
Skin (initial tests)	7 p.p.m.
Beard hair (initial test)	8 p.p.m.
Beard hair (8 days later)	2 p.p.m.
Hair (18 months later)	0.9 p.p.m.
Nail (18 months later)	0.5 p.p.m.
Skin (18 months later)	0.3 p.p.m.

Fergusson *et al.* (20) applied the method in an investigation of 106 patients who were suffering from various diseases of the skin already noted as being morphologically similar to those produced by actual arsenic poisoning. They report in studies on several cases of exfoliative psoriasis and dermatitis that the arsenic content of hair, nail, and skin was normal, i.e. 0.3–0.4, 0.2–0.3, and 0.1–0.2 p.p.m., respectively. They concluded that, although arsenic had not been found in abnormal amounts, activation analysis had an assured place among the diagnostic techniques available for demonstrating the etiological factors which may be considered in the production of pigmentation, exfoliative states, and malignancies.

Perkons and Jervis (21) reported on the value of activation analysis in toxicology studies concerned with higher-than-normal concentrations of arsenic, selenium, and mercury in hair, skin, and nails. For example, they report that the mean value of arsenic in human hair is 0.7 p.p.m. for men and 0.36 p.p.m. for women. In a study on hair taken from different individuals, they showed that the selenium content could range from 0.3 to 4.0 p.p.m., while the mercury content ranged from 1 to 12 p.p.m. They reported that variations exist in the "normal" contents of other

elements in human hair. Typical data obtained in the analysis of hairs from six different individuals were as follows:

	Elemental Concentrations (p.p.m.)						
Sample	Ge	Cu	Na	Br	Au	Zn	Mn
1	15	169	503	1.1	2.9	322	...
2	29	398	600	0.3	5.6	523	...
3	126	22	22	6.9	0.2	1270	22
4	49	182	68	6.4	3.4	212	...
5	36	32	422	0.6	0.6	834	0.4
6	109	304	145	0.2	4.9	244	2

Poey and Leddicotte (22) have used neutron activation analysis in a preliminary, comparative assessment of the discoloration that sometimes occurs in sterilizing drug solutions by heating or as a result of storing the solutions for long periods of time. Most of these discolorations are due to oxidation effects promoted or accelerated by the presence of some heavy metals acting as catalysts. Mn, Cu, and Na in concentrations as small as 0.0005, 0.002, and 0.004 p.p.m., respectively, were determined in distilled water and in polyethylene bottles used as storage containers. In the same investigation, stored samples of adrenalin and Vitamin C were analyzed for Mn, Cu, and Na. The presence of As, Sc, and Au in these materials was also noted, and their concentrations were determined. The results were as follows:

	Elements Concentration (p.p.m.)					
Drug	Mn	Cu	Na	As	Sc	Au
Adrenaline	1.9	0.5	3.8	1.4	0.7	0.03
Vitamin C	0.07	0.06	1.1	<0.05	<0.1	<0.01

The results of this investigation suggest that more specific tests for such elements need to be incorporated into the "U. S. Pharmacopoeia" requirements on sensitive drugs.

Tuckerman *et al.* (23) used neutron activation analysis in a preliminary survey of the kinds and amounts of trace elements present in drugs prepared according to good manufacturing practice. Samples of various lots of each drug as obtained from the manufacturers, irradiated, and assayed nondestructively by γ scintillation spectrometry. At least 35 different materials used in drug manufacturing were analyzed. Elements usually found were sodium, bromine, and manganese; occasionally copper, arsenic, and antimony; and in a few samples, mercury

scandium, thorium and gallium. The data presented below give the range of concentration observed:

Element	Concentration Range (p.p.m.)
Na	0.6–1280
Br	0.02–800
Mn	0.004–19
Cu	0.1–12
As	0.01–1.0
Sb	0.03–0.9
Hg	0.01–0.6
Ga	0.68–1.2
Sc	0.002–0.5
Th	0.01–0.08
Al	8–10

This preliminary survey shows that there is a need to extend such work so that legal standards for drugs, as recommended by the "U. S. Pharmacopoeia" and the "National Formulary," can be established to insure good manufacturing practices and to exclude toxic quantities of metals.

Conclusion

Activation analysis, whether completed by instrumental or radiochemical separations, should have an important place in the analytical requirements of cosmetic science. The examples of activation analysis cited above show that it can be used in applications in diverse problem areas. Accurate and precise analyses can be carried out to complete such metabolic studies as those concerned with the rate and degree of penetration of ingredients from cosmetic formulations through the skin and the identification and measurement of minute amounts of residues and metabolites. Also, tests on the ingredients present in most materials and the purity of a finished product can be readily made with activation analysis techniques. Experience will determine the area of interest, and it is evident that activation analysis can satisfy the need of the cosmetic industry by providing a precise and sensitive method for elemental analyses.

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References

(1) Bohr, N., *Nature*, **137**, 344 (1936).
(2) Kamen, M. D., *Radioactive Tracers in Biology, An Introduction to Tracer Methodology*, Academic Press, New York, 1951, p. 21.

(3) Broda, E., *Advances in Radiochemistry and in the Methods of Producing Radioelements by Neutron Irradiation*, Cambridge Press, 1950.
(4) Price, W. J., *Nuclear Radiation Detection*, McGraw-Hill, New York, 1958, pp. 162–211.
(5) Burrill, E. A., and Gale, A. J., "Activation Analysis with Van de Graaff Neutron Sources," High Voltage Engineering Corp., Cambridge, Mass. (1954).
(6) Brooksbank, W. A., Leddicotte, G. W., and Dean, J. A., *Anal. Chem.*, **30**, 1785 (1958).
(7) Moeller, D. W., Leddicotte, G. W., and Reynolds, S. A., *J. Sanit. Eng. Div., Am. Soc. Civil Engrs.*, SA2, 11 (1959).
(8) Kraus, K. A., and Nelson, F., Vol. VII, *Proceedings of 1955 Geneva Conference*, United Nations, New York, 1956, pp. 113–35.
(9) Hicks, H. G., Gilbert, R. S., Stevenson, P. L., and Hutchin, W. H., Livermore Report No. LRL-65 (Dec. 1953).
(10) Morrison, G. H., and Costrove, J. F., *Anal. Chem.*, **27**, 810 (1955).
(11) Sayre, E. V., Murrenhoff, A., and Weick, C. F., Brookhaven National Laboratory Report BNL-508 (T-122) (April 1, 1958).
(12) Borg, D. C., Paper 841, *2nd Intern. Conf. on the Peaceful Uses of Atomic Energy*, Geneva, Switzerland (Sept. 1958).
(13) Brooksbank, W. A., Leddicotte, G. W., and Reynolds, S. A., *Anal. Chem.*, **28**, 1033 (1956).
(14) De, A. K., Meinke, W. W., *Ibid.*, **30**, 1474 (1958).
(15) Bate, L. C., Emery, J. F., and Leddicotte, G. W., "The Quantitative Analysis of Complex Radionuclide Mixtures by Gamma-Ray Spectrometry," Oak Ridge National Laboratory, Oak Ridge, Tenn., Report ORNL-2917 (1959).
(16) Nostrand, J. W., and Kramer, H. H., Preprint No. 2.4-2-64, 19th Annual ISA Conf. Oct. 12, 1964, New York.
(17) Connally, R. E., and Leboeuf, M. B., *Anal. Chem.*, **25**, 1095 (1953).
(18) Savachuck, W. B., *J. Dental Res.*, **38**, 49 (1959).
(19) Dewar, W. A., and Lenihan, J. M. A., *Scot. Med. J.*, **1**, 236 (1956).
(20) Fergusson, A. G., Dewar, A. W., and Smith, H., *Arch. Dermatol.*, **81**, 931 (1960).
(21) Perkons, A. K., and Jervis, R. E., *J. Forensic Sci.*, **7**, 449 (1962).
(22) Poey, B. S., and Leddicotte, G. W., unpublished data.
(23) Tuckerman, M. M., Bate, L. C., and Leddicotte, G. W., unpublished data.

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Book Reviews

NEW HOPE FOR YOUR SKIN. By Irwin I. Lubowe, E. P. Dutton & Co., Inc., New York, 1963. 299 pages. Price $4.95.

The major purpose of this book, as stated in the author's preface, is to acquaint the intelligent layman with recent developments in better skin care. In this reviewer's opinion the author has failed to achieve his purpose.

This is a personal book based on the experiences of the author. It is readily apparent that the author's approach reflects his own preferences, as developed in his own practice, for various aspects of skin care, rather than recent developments in better skin care as they would be (and are partially through quotations in this volume) reported by experts in the specific areas. This is not to deny that a given regimen in the hands of a specific practitioner can be effective.

There is only one use for this publication that occurs to this reviewer. It is a suitable historical record that can be buried in some time capsule for recovery in some future millennium to provide a record of dermatology as it was practiced during the second quarter of the twentieth century.—JOSEPH B. JEROME—American Medical Association.

CHEMICAL CARCINOGENESIS AND CANCERS by W. C. Hueper and W. D. Conway, Charles C Thomas Publishers, Springfield, Ill., 1964. 744 pages, indexed. Price $20.

This is a rather frightening book because the authors forcefully point out that the modern industrial environment exposes the human body to a variety of carcinogens—known, suspected, and unknown. A large portion of the book is, of course, devoted to the discussion of carcinogenic hydrocarbons and aromatic amines, the danger of which has been known for years. At the same time, some rather innocuous materials have been included in the author's discussion of carcinogens, thereby weakening their justifiable warning. In addition, the inclusion of essentially safe chemicals (which are only suspect carcinogens or are carcinogens only under unusual testing conditions) provides grist for the mills of medical and nutritional quacks and faddists.

The authors, in fact, indict industry-at-large for exposing the

general public to environmental carcinogens and strongly advocate more thorough and careful testing of raw materials. Many raw materials used in the cosmetic industry are included in this volume, and this reviewer has taken time to delve into the background of CMC, which is classified by the authors as a carcinogen. The authors base the carcinogenicity of CMC on publications by Lusky and Nelson [*Fed. Proc.*, 16, 318 (1957)] and by Gardner [*Cancer Res.*, 19, 170 (1959)]. A review of these two publications suggests that the inclusion of CMC amongst carcinogens is not fully justified. Lusky and Nelson produced fibrosarcomas after 73 weekly subcutaneous injections of 1 cc. of 2% carboxymethylcellulose in rats at the site of the injection. These tumors are classified as having "moderate histological malignancy." On the other hand, Gardner administered a solid mixture of 97.3% urea, 0.6% adipic acid, and 2.1% carboxymethylcellulose acids intravaginally into mice. After prolonged repeat administrations, a high incidence of cancerous lesions occurred in the test animals. The book's authors state, "Among the ingredients of this carcinogenic mixture, carboxymethylcellulose is the only substance possessing known carcinogenic properties." In fact, Gardner states, "Experiments extending over 1 year, in which the three ingredients listed were given separately, have so far yielded no vaginal carcinomas."

This reviewer will be the first to recognize that the picture concerning CMC is not entirely clear. There are many grades of CMC manufactured by reliable companies. CMC is widely used as a thickener in topical preparations and in foodstuffs. It is also the active constituent of a number of proprietary pharmaceuticals and has a long and apparently safe history under these conditions. The classification of CMC as a carcinogen under these circumstances in a scientific volume is questionable and perforce throws doubt on the possible dangerous properties of other chemicals listed in this volume. Thus the inclusion of CMC seriously weakens the authors' basic argument.

At times, the authors make points which are almost ludicrous; for example, on page 638 they imply that advertisements for resort areas having a very sunny climate should contain a warning as to the possible and actual cancer hazards to the skin connected with excessive and indiscriminate exposure to sunshine.

Despite its many faults, this is a most provocative book and one that should be read by public health officials, product development people, and chemical manufacturers. Even though the book presents some questionable conclusions, it is an unmistakable danger signal that must not be ignored by responsible people.—M. M. RIEGER, Warner-Lambert Research Institute.

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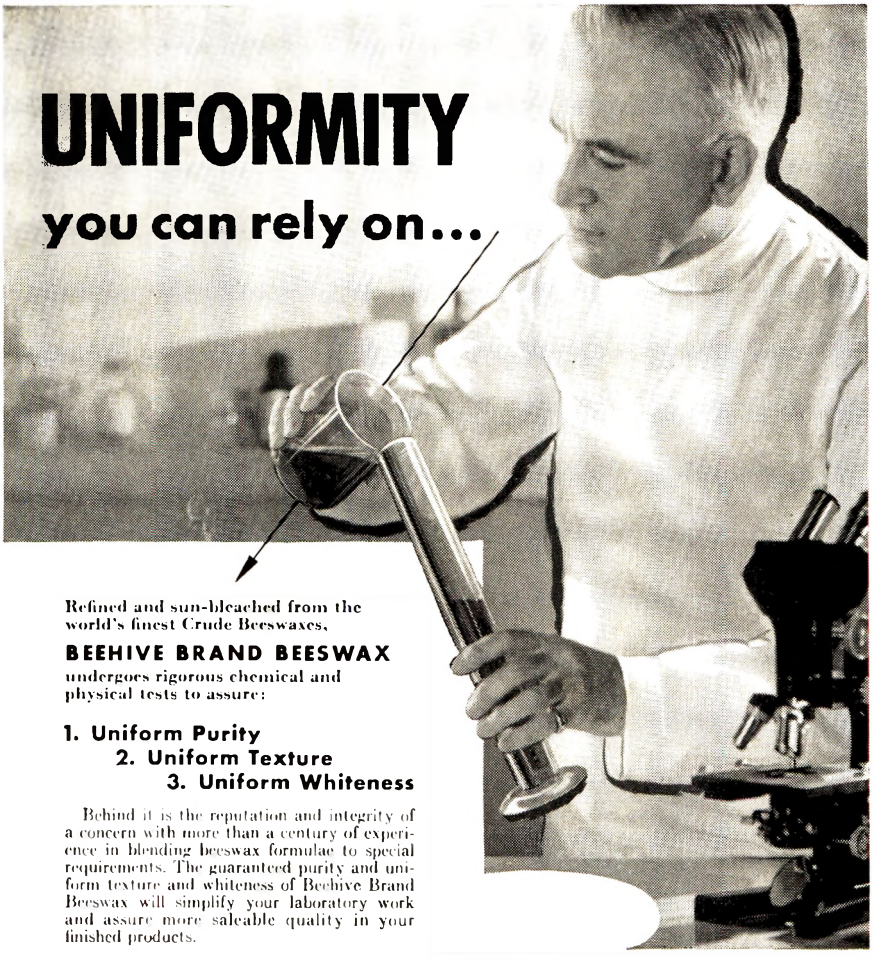

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