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Abstracts

The Annual Scientific Meetings and Seminars of the Society of Cosmetic Chemists are important venues for informing the participants about the state of the art and recent technical advances in the field of Cosmetic Science. To provide broader dissemination of that information, the Publication Committee has decided to publish abstracts of the technical presentations made at these Meetings and Seminars in the *Journal.*—The Editor.

Society of Cosmetic Chemists ANNUAL MEETING

December 5–6, 1985
The Waldorf-Astoria, New York

Program arranged by the Society's Committee on Scientific Affairs
Jan Curry, Chairman, 1985

SESSION I
FRAGRANCE TECHNOLOGY

MAECIS: A computer program for the handling and analysis of flavor and fragrance molecules
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Chemical structure and information-handling present problems for flavor and fragrance companies because of the large number and structural diversity of molecules used by this industry for their product lines. This problem is compounded by the use of industry-specific, trivial names that contain no structural information. Examples are galaxolide and celestolide, names of two common, musk-like odorants. Our solution to this particular information-handling problem was the development of MAECIS, a user-friendly, interactive program written in FORTRAN for the DEC VAX 11-780 computer.

Applications of multivariate data analysis to fragrance material quality control
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Published gas chromatography data collected on lavender and lavandin oils have been analyzed by multivariate statistical methods. It will be shown that several techniques, including principal components, k-nearest neighbor, cluster, SIMCA, and discriminant analysis, can effect a machine classification of lavender from lavandin oils. The lavandin oils may be further classified as to Abrialis, Grosso, and Super hybrids. Application of these methods to several other materials of flavor fragrance interest will be discussed.

Segmenting fragrance preferences
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Consumer tests with both fine and functional fragrances reveal large differences among consumers in degree of liking, but substantial agreement in terms of sensory properties. Rather than considering the variability of preferences as an unavoidable "fact of life," it turns out that there are different segments of consumers in the population, showing well defined, homogeneous preferences. This paper shows how to uncover those segments, and find out what sensory characteristics consumers in each segment prefer. The paper also deals with the relation between sensory attribute level and acceptance for each segment (sensitivity and analysis), and the simultaneous scientific/commercial opportunities which present themselves upon discovering and isolating new consumer preference segments for fragrance.

Human odors and their effects on the menstrual cycle

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The possibility that human odors affect our reproductive biology has been discussed at some length in both the scientific and popular press; however, much of this discussion has centered on the possible existence of releaser pheromones or "sex attractant"-type effects. Our studies examined the thesis that human odors act in a primer pheromone fashion and alter the endocrinology of the menstrual cycle. Previous studies have shown that (a) menstrual cycle lengths of 29.5 + 3 days ("normal cycles") are more frequent in women who have weekly coital activity than in women who do not; and (b) women who spend time together are likely to show synchrony in the onset of their menstrual bleeding. To determine whether chemical substances from the axillae are involved in these phenomena, the menstrual cycle length of nulliparous women was evaluated following regular application of extract from either donor males or females. Female subjects who reported having a history of aberrant length cycles (26 days and 33 days) received extract from male donors, while those subjects who reported having normal cycle lengths received extract from female donors. Women receiving the male extracts for 13.5 + 1 weeks experienced more regular cycles compared to controls receiving only placebo applications; in addition, subjects receiving female extracts showed a significant shift towards menstrual synchrony with the donor females. These studies demonstrate that axillary constituents can shift the length and onset of the direct social contact. Both male and female extracts have also been examined by gas constituents. Secretions of both male and females contain a number of steroid constituents including the volatile steroids androstenone and androstenol. The concentrations of these components is being determined to see if there is menstrual or seasonal variation in female or male samples, respectively.

CONCURRENT SESSION ARRANGED BY CTFA MICROBIOLOGY COMMITTEE

Report of a cosmetic industry survey concerning correlation of preservative challenge and consumer use test results

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Results are presented of a cosmetic industry survey generated by the CTFA Microbiology Committee and distributed by CTFA. The survey requested information concerning correlation of preservative challenge and consumer use test results. The survey dealt with three product areas: water-based mascaras; solvent-based mascaras; and creams/lotions.

Validation of the microbiological integrity of cosmetic products through consumer use testing

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To ensure the development of microbiologically safe cosmetics, Avon Products, Inc. has developed an *in vitro* microbial challenge test which accurately predicts the preservative efficacy of a product after long-term consumer use. Over the past five years, 186 products which had met the *in vitro* challenge test criteria, were subjected to consumer testing. These products included mascaras, creams, lotions, liquid makeup, eyeshadows, eyeliners, and batch and hair preparations. Criteria for formula acceptability after use included: no recovery of *Pseudomonas sp., E. coli,* or *S. aureus,* and recovery of <100 cfu/g followed by no recovery of organisms upon a retest of the product. Over 99% of the products met these requirements. Only five out of approximately 4000 samples tested did not meet these test criteria, and were reformulated with increased preservative concentrations before release for sale. As a result of the failures, our *in vitro* challenge test was made more stringent by including a higher concentration of challenge organisms, a greater number of preservative-resistant product isolates, and more stringent inoculum reduction requirements. These procedures have resulted in an *in vitro* test which accurately predicts preservative efficacy of a cosmetic product after consumer use.

Correlation of *in vitro* challenge testing with in-use consumer testing for cosmetic products

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The cosmetic and drug industries use microbial challenge testing as an indicator of a product's ability to withstand microbial insults. The ability of a cosmetic product to withstand microbial insults experienced during consumer use is of particular interest to the regulatory agencies. The FDA, for example, has issued a contract to develop an *in vitro* test method that predicts whether or not a cosmetic will become contaminated during consumer use. This paper presents an *in vitro* challenge method for assessing the preservative efficacy of cosmetic products under typical consumer use conditions. Two products were used, an anionic shampoo and

a hand and body lotion. Three preservative conditions were investigated to give unpreserved, marginally preserved, and preserved products. The *in vitro* challenge test was based on the CTFA procedure but is modified to include product dilutions at four levels (30%, 50%, 70%, 100%). This modification aided in classifying the preservative efficacy of the formulae. The preserved formulae passed the challenge test at all product concentration levels including the most stringent 30% level (Pass 30%). The marginally preserved formulae passed the challenge test at only the 100% product concentration level (Pass 100%). The unpreserved formulae failed the challenge test. Data will be presented to show that the modified CTFA challenge procedure is predictive of the potential for product contamination after consumer use.

SESSION II
PLAQUE AND GINGIVITIS CLAIMS FOR ORAL HYGIENE PRODUCTS

Guidelines for the evaluation of products for the control of plaque and gingivitis

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The Council on Dental Therapeutics has reviewed laboratory and clinical studies on products for their safety and efficacy in the control of dental plaque and gingivitis. In its review of data from these studies the Council and its consultants concluded that there is considerable disagreement about the information necessary to conclusively demonstrate product efficacy. There is also disagreement regarding the design of studies to evaluate these products. In an attempt to resolve these issues, the Council developed, in consultation with more than 90 individuals and organizations, guidelines which will be used in reviewing these products in its acceptance program. Products which meet the criteria in these guidelines will be eligible to receive the Seal of Acceptance of the Council. The guidelines and the rationale for their development will be presented. Specific commercial products which have received the Seal of Acceptance and the studies which demonstrated their efficacy will be discussed.

FDA and the regulation of prescription drug advertising and promotion

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Disclosures before the Kefauver Subcommittee in 1960–61 led committee members to conclude that advertising to the medical profession had resulted in serious abuses and required new specific controls for the protection of the public. Congress had decided that reforms in prescription drug advertising practices were needed because usually favorable features about a drug were presented in advertising, but side effects, contraindications, warnings, and other limitations regarding usefulness of the drug, as well as other defects that needed regulatory consideration, were somehow forgotten or deemphasized. The Drug Amendments of 1962 corrected some of the prior deficiencies and later drug advertising regulations and administrative concepts provided further authority to overcome continued abuses. The 70's began a new era in advertising compliance activities and management. With the evolution of new methods to provide information to the health community, the FDA has entered the 80's with new priorities to examine in the field of promotion and advertising. It continues to exercise oversight in 1) the growing interest to promote products, concepts, and procedures well in advance of their approval, 2) the emerging technologies in electronic communications that have provided marketers with more outlets from which to promote their wares to health providers, and 3) the interest in promoting prescription products directly to consumers. Because of these and other current issues, the FDA is concerned about turmoil in the marketplace and whether further sanctions on current advertising practices will be necessary.

Influence of mechanical aspects of dentifrice and toothbrush in plaque control

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The toothbrush is the most popular mechanical device for cleaning teeth. The efficiency of toothbrushing is assessed in regard to varying brushing times, toothbrushing frequency, dentifrice load, and dentifrice abrasivity. Studies of the duration of toothbrushing time involving children and adults suggested that the average "scrub" time for children as well as adults is approximately 20 seconds. The wearout rate of toothbrushes is directly related to the number of filaments in a tuft and filament diameter, whereas cleansing features appear to have an inverse relationship to filament diameter: thicker filaments last longer but fail to clean as well as thinner filaments. Toothbrush configuration, shape, and size have not been clearly demonstrated to be dominant factors associated with toothbrush efficacy.

A system facilitating plaque removal via combination of chemical and mechanical procedures

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The development of a new modality for plaque removal is described—use of a plaque-loosening dental rinse prior to brushing. The functionality of such pre-rinses mandates formulations different from products intended for postbrushing or mouthfreshening uses. The pre-brushing rinse has a higher pH and contains surfactants and analgesic ingredients. Antimicrobial activity is secondary in terms of functionality of such pre-rinses. Significant efficacy of this dental rinse has been demonstrated in laboratory and clinical tests.

Chlorhexidine—a unique chemical for control of gingivitis

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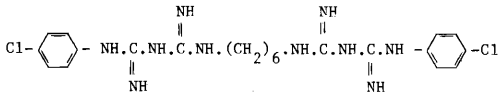
Chlorhexidine has been shown effective in controlling gingivitis for months and can be a lifesaving drug in the immunosuppressed. Chlorhexidine is a bisbiguanide of the following structure:



Chemistry, Toxicity, and Uses: It has the characteristics of a cationic surfactant. Chlorhexidine is relatively nontoxic. It is poorly absorbed in the gut, most passing through unchanged. The reported side effects from oral use include extrinsic staining of teeth and a slight transient desquamation, neither of which limits usefulness of the drug. It is used in surgical scrubs, disinfection of contact lenses, etc. It is available in some countries as a dental gel or as a mouthrinse.

Microbiology: Chlorhexidine is a broad spectrum antimicrobial agent which is effective against a number of oral microorganisms. After a single rinse with chlorhexidine, about 30% is retained in the oral cavity and this is slowly released into saliva, maintaining effective levels for several hours. This is perceived as contributing to the efficacy of chlorhexidine in the mouth. In humans, slight (about twofold) increases in resistance of oral bacteria to chlorhexidine have been observed during mouthrinsing. However, these increases dissipated or disappeared after cessation of use and did not limit efficacy of the drug.

In vivo studies: Studies in dogs have shown chlorhexidine effective in controlling gingivitis for up to seven years with no loss of alveolar bone. No meaningful increases in resistance of oral bacteria were observed. Under the severe challenge of the experimental gingivitis model in humans, no oral hygiene for three weeks, a chlorhexidine mouthrinse maintained gingivial health virtually unchanged from baseline. In clinical trials of longer duration, chlorhexidine mouthrinses have been shown to reduce gingivitis up to 80% in comparison with placebo' while establishing a level of gingival health similar to that of chlorhexidine in the experimental gingivitis model. Reductions in the number of bacteria in the oral cavity have been documented during rinsing with chlorhexidine. In immunosuppressed patients undergoing bone marrow transplants, a chlorhexidine mouthrinse has been shown to decrease candida and candida-associated morbidity and mortality. In this setting it may be considered a lifesaving drug.

Chlorhexidine today is the standard of comparison for any agent claiming antigingivitis efficacy. In clinical trial, chlorhexidine has produced reductions in gingivitis up to 80% while maintaining excellent gingival health for months. It can be a lifesaving drug in immunosuppressed patients.

Essential oils

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Essential oils, such as thymol, menthol, and eucalyptol, have been used in mouth rinses for over 100 years. These ingredients in mouth rinses have been documented to be antibacterial in laboratory tests. With the scientific association of microorganisms and plaque formation, and the suspected involvement of this process with carious lesions and gingivitis, the effect of essential oils on these processes have taken on new interests. For the past decade, products containing essential oils have been studied clinically for their role in oral health status. The studies have assessed short-term effects which occur within one or two weeks. Other studies have run for six months. Some studies have been conducted with no other oral hygiene than the mouth rinse alone, while others have allowed the use of the mouth rinses in an unsupervised setting of "usual home care." Almost uniformly, the results of the studies have been favorable to the products containing essential oils. In general, these products have retarded the development of plaque and have reduced the severity of gingivitis. The studies have also compared products containing essential oils to control groups using only a vehicle, or against plain water rinses. The results of these assessments have generally shown products containing essential oils to be more effective than the controls, thus pointing to the fact that these agents are active ingredients.

Sanguinaria/sanguinarine in the control of plaque and gingivitis

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In the past few years sanguinaria products have been

introduced into the marketplace for the control of dental plaque. Sanguinaria is a bontanical extract obtained from the plant *Sanguinaria canadensis*. Sanguinaria is composed of benzophenanthridine alkaloids and sanguinarine is the prominent alkaloid. Sanguinarine has a unique iminim ion chemistry that is responsible for its effectiveness against dental plaque formation. This presentation will include a review of clinical safety and efficacy studies. Both toothpaste and oral rinse clinical studies will be reviewed. Studies on the retention of sanguinarine in the oral cavity and its antimicrobial action against plaque-forming micro-organisms will be presented as a rational mechanism of action. Certain qualitative changes in plaque as a means of reducing gingivitis will also be considered. Sanguinarine represents an innovative new ingredient for use in the oral cavity with potential against plaque, gingivitis, and periodontal diseases.

SESSION III
IN VITRO SAFETY

In vitro approaches to toxicity testing: A status report

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Prompted by the partial successes of short-term cell culture tests for the evaluation of the potential mutagenicity and carcinogenicity of chemicals and the growing concern for the use of animals for toxicity testing, programs for the evaluation of target-specific chemicals are being developed. The strategies which may be employed to develop such tests and the difficulties and opportunities which they present will be described and analyzed. Ocular and neuronal *in vitro* test development will be emphasized.

Hydrophobicity of n-lauroyl amino acid as a parameter to determine primary skin and eye irritation

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Hydrophobicity of N-lauroyl (C_{12} fatty acid acyl) amino acids (LAA) were measured by reversed phase HPLC and TLC. The order of hydrophobicity of LAA, which corresponds to the character of side-chain residue of each amino acid, is found as follows: the Phe Ile Leu Val Trp Pro Ala Gyl Ser Glu. The primary skin and eye irritation for rabbits is tested by the Draize method and compared to the hydrophobicity. A good relationship is found between hydrophobicity and primary eye irritation, which is that lower hydrophobicity corresponds to lower irritation. A similar relationship is found for LAA between hydrophobicity and hemolysis for human red cells. In contrast, the primary skin irritation is inversely proportioned to the hydrophobicity, except for glutamic acid. As a result, it is assumed that hydrophobicity is a useful parameter to evaluate skin and eye irritation. Of the LAA's which have already been tested, N-lauroyl glutamic acid seems to be the mildest material.

Determination of surfactant irritancy from the swelling behavior of a collagen membrane

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Swelling of a collagen membrane by surfactants has been established as an *in vitro* method to evaluate anionic surfactant potential. The method was used to study the relationship of surfactant structure to swelling activity for alkyl sulfates and ethoxylated alcohol sulfates, in which the carbon chain number and ethylene oxide number were varied systematically. Results show that the C12 homologue induced the most swelling and that membrane swelling is inversely proportional to ethylene oxide content. Swelling response is dose-dependent. The assay was used to investigate surfactant interactions; additions of amphoteric surfactants to an anionic surfactant reduce the amount of swelling caused by the anionic alone. Results of this *in vitro* test correlate with findings from established *in vitro* and *in vivo* laboratory and clinical irritation assessments. These findings suggest a mechanism of skin irritation in which collagen is disrupted, leading to swelling of the skin.

SESSION IV
GENERAL PAPERS

Surfactant structure effects on stratum corneum swelling

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Surfactants in solution induce swelling of isolated stratum corneum (Robbins and Fernee; Putterman, *et al.*). The highest levels of swelling observed were for anionic surfactants, and very little swelling occurred with cationics and nonionics. For a homologous series of alkyl sulfates, swelling was maximal for the C12 homologue. We have now extended these studies to examine effects of structural variants of surfactants on swelling of stratum corneum. Swelling caused by surfactants increased with time, was dose dependent, and was saturable with increasing concentration. The extent of swelling was reduced with increased ethoxylation of dodecyl sulfate and depended upon the counterion. For homologous series of various anionic surfactants, max-

imal swelling occured between C12 and C14 carbon atoms. Surfactant interactions to reduce swelling were found; e.g., addition of ethoxylated alcohol sulfates and amphoterics to anionics produced less swelling than the anionics alone. The results suggest mechanisms of action of surfactants and a basis for *in vivo* irritation.

The use of magnitude estimation with parametric statistical methods in the subjective measurement of axillary odor

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A conventional axillary deodorant clinical study involves 3–6 trained odor judges providing numerical ratings of human axillary malodor intensities. A 0–5 or 0–10 rating scale is typically used. This paper discusses the use of the magnitude estimation rating scale method in these studies. In addition, clinical evaluation studies are presented. Advantages of the magnitude estimation method include scientific validity grounded in psychological literature, ratio scale properties supporting deodorant efficacy measurement in terms of "percent odor reduction," and statistical validity, flexibility, power, and convenience. A data analysis involving a total of 562 subject evaluations provides empirical justification for applying parametric statistical methods (t-tests, analysis of variance, regression, etc.) to the logarithm of the judge ratings. A simple method for analyzing data containing some zero ratings (whose logarithm is undefined) is presented. Subjects with higher initial odor levels are shown to yield greater percent odor reductions than those with lower initial odor levels. Study designs which control for this factor are recommended. The power to detect small product efficacy differences is shown to be diminished in studies which include other deodorants with large efficacy differences. Some considerations in the selection and training of judges are presented.

Stabilization of oil-in-water emulsions by gums

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Model emulsions containing 10% mineral oil, oleth 3, oleth 10, methylparaben, propylparaben, water, and several concentrations of selected gums were prepared. A two-step procedure, designed to prevent variations in initial particle size in emulsions containing the same emulsifier concentration, was employed. Median particle size, measured by an electronic sizing technique, was inversely related to emulsifier concentration. There was no change in particle size distribution of the emulsions after storage for 7 months. Viscosity values for emulsions containing xanthan gum did not change significantly during the storage period. In emulsions containing 0.25 to 1.0% emulsifier, addition of xanthan gum decreased the creaming rate to about the same extent. The logarithm of creaming rate was a linear function of gum concentration, making it possible to compare different gums quantitatively. The order of effectiveness in retarding creaming was xanthan gum carbosymethylcellulose, high viscosity methylcellulose, 4000 cp.

Thiol reduction of hair fibers in the presence of exogenous disulfides

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Reduction of keratin hair fibers with excess thiol proceeds in a two-step equilibrium reaction. Factors affecting this equilibrium were examined using amino acid analyses and fiber bundle tensile techniques. When hair fibers were treated with either ammonium thioglycolate or glycerly monothioglycolate, at a fixed pH and concentration, the rate and extent of reduction of these fibers were curtailed when exogenous disulfides were added to the reacting medium. Observations were made under various experimental conditions. Attempts were made to correlate loss of tensile properties of hair fiber bundles with percent keratin reduction in the presence of thiols containing exogenous disulfides. Loss of fiber bundle tensile properties were found to be related to the concentration of disulfide added to the thiol solution. Results of the experimental data obtained in these studies will be discussed.

Applications of matrix engineering in skin care

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Matrix engineering is a technology based on the naturally occurring polymers found in the intercellur matrix of all animal tissues. Based on the *in vivo* functions of connective tissue biopolymers, specialized properties of human tissues can be mimicked or enhanced. Derivatives and modifications of hyaluronic acid (HA) molecular networks have skin care applications arising from both their intrinsic properties and their ability to act as a cosmetic delivery system. Using such HA-based materials, efficacious cosmetic ingredients such as petrolatum can be delivered in formulations which mask their undesirable properties. Matrix engineering-based methods which bridge the gap between aesthetics and efficacy will be presented, and their impact on the classical differentiation of formulations into oils, lotions, and creams will be discussed.