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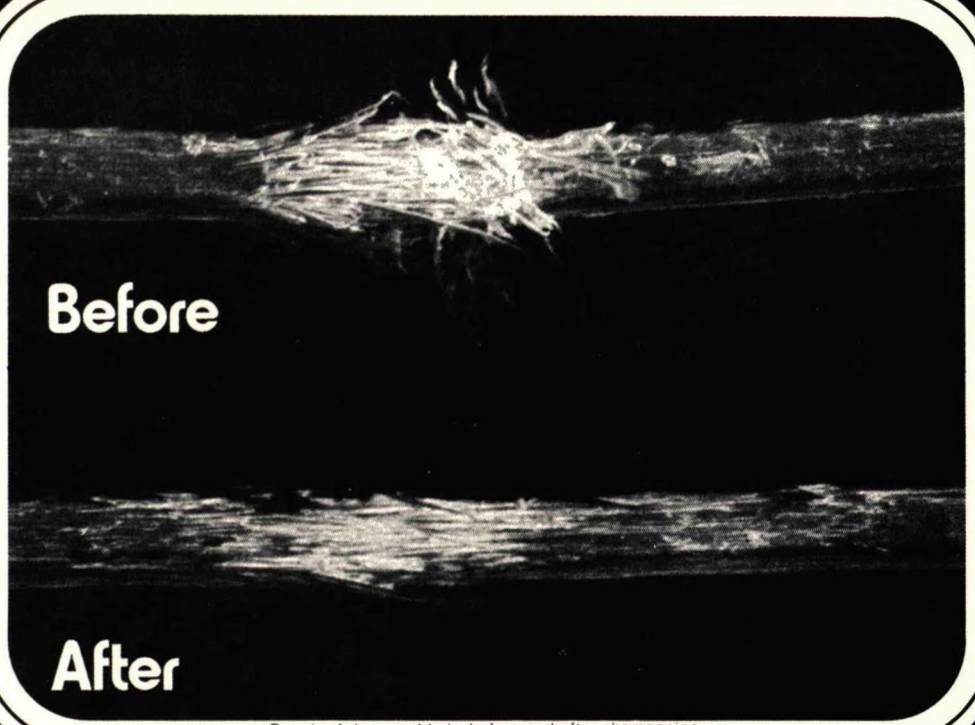

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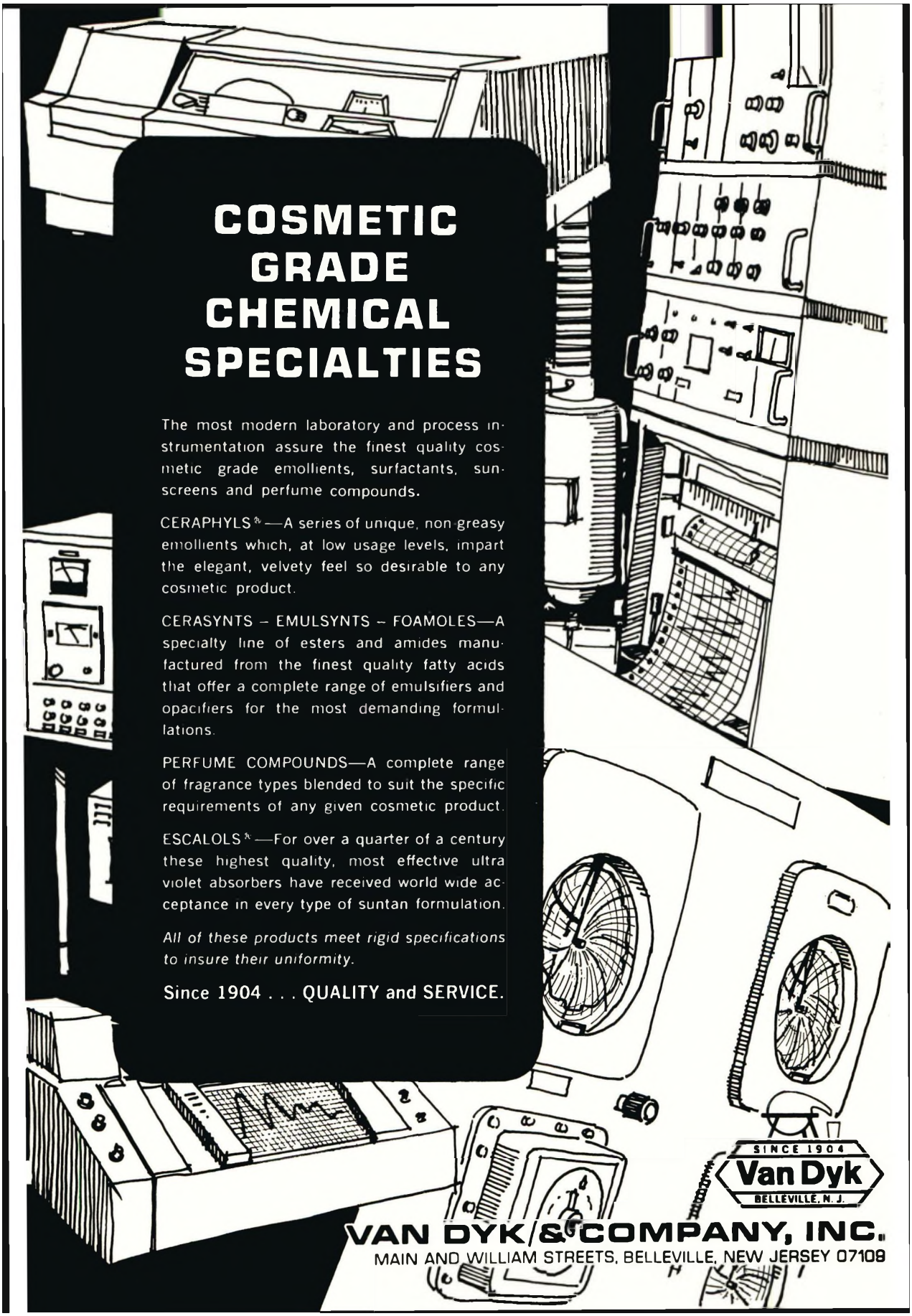

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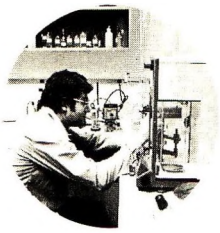

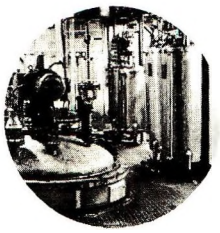

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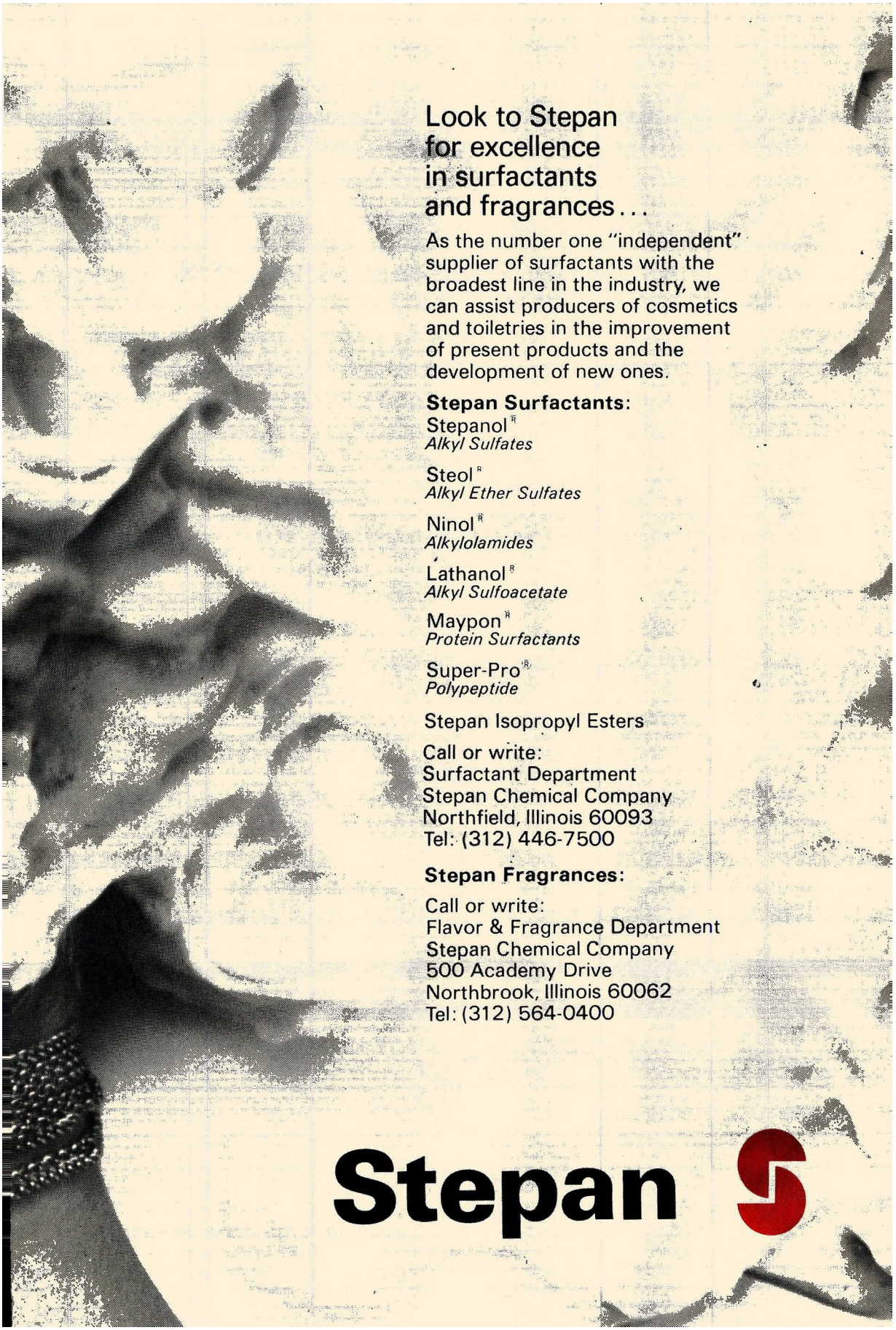

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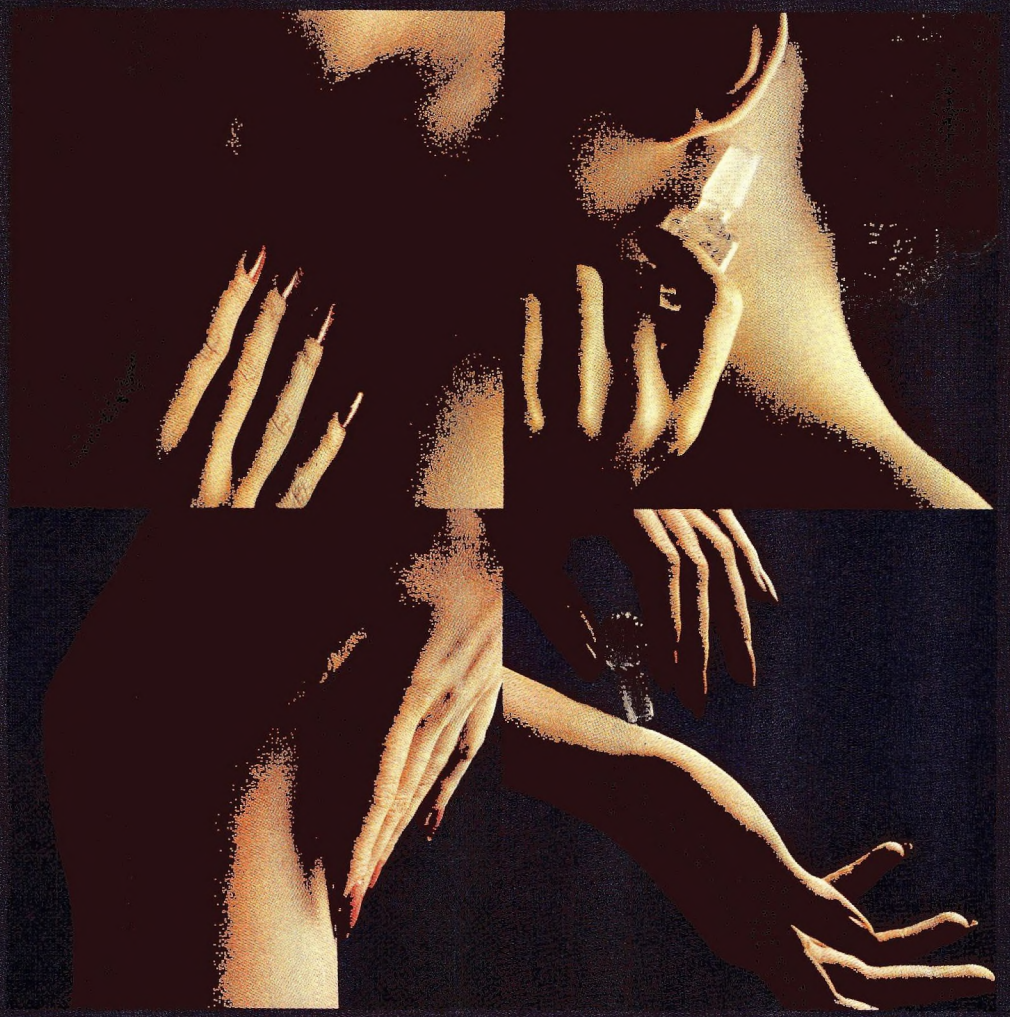

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SYNOPSES FOR CARD INDEXES

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

Pheromones (olfactory communication): Stanley K. Freeman. *Journal of the Society of Cosmetic Chemists.* 29, 47 (February 1978)

Synopsis—In view of the intimate relationship between the olfactory and limbic systems, olfactory communication could be involved in various aspects of reproductive physiology in man. The pheromone concept implies that learning and/or prior experience with odorants do not play an essential role in its effect. Recent evidence suggests that associative learning rather than a pheromone phenomenon should be seriously considered in the interpretation of certain features of primate behavior mediated by the sense of smell.

Application of lower titanium oxide in cosmetics: Fukuji Suzuki, Shoji Fukushima, Takeo Mitsui and Saburo Ohta. *Journal of the Society of Cosmetic Chemists* 29, 59 (February 1978)

Synopsis—Carbon black and iron black Fe_3O_4 are black pigments commonly used in the cosmetic industry. Due to its hydrophobic character, carbon black has poor dispersibility in water, and iron black, due to its ferro-magnetic character, is not readily dispersible in any liquid. In order to solve these problems the authors investigated the possibility of synthesizing lower titanium oxide and using them as a black pigment in cosmetics. The general formula of the lower titanium oxide is Ti_nO_{2n-1} in which n can be any positive integer. When n is small, the resultant compound is bluish-black. As n increases, the compound becomes gray.

The lower titanium oxide most suitable for cosmetics was obtained by calcining a mixture of a titanium dioxide pigment and a metallic titanium powder in a vacuum electric furnace. While it has a tinting strength corresponding to that of carbon black and iron oxide black, it is superior in many other respects when used in cosmetics.

Evaluation of hair fixatives—a new technic utilizing torsional measurements: Stuart H. Ganslaw and F. Theodore Koehler. *Journal of the Society of Cosmetic Chemists* 29, 65 (February 1978)

Synopsis—A new laboratory test, twist retention analysis (TRA), utilizing a torsional braid analyzer, is described as a tool for evaluating hair fixative set holding ability under humid conditions. Excellent statistical correlation to traditional laboratory Curl Retention testing is demonstrated. Twist Retention Analysis is shown to give more precise measurements than earlier evaluation techniques and allows the use of smaller sample populations. This new test is shown to give statistical correlation (90 to 100 min), to long-term (5 to 21 hr) Curl Retention testing, allowing rapid evaluation of fixative performance. Conclusions about fixative differences can be made at a faster rate. Statistical differences between fixatives are determined that could not be established by Curl Retention testing.

Topical moisturizers: quantification of their effect on superficial facial lines: Elias W. Packman and Eugene H. Gans. *Journal of the Society of Cosmetic Chemists* 29, 79 (February 1978)

Synopsis—This single-blind study was designed to test a new method of quantitative evaluation as used by trained judges to visually assess changes in superficial facial lines (SFL's) following the application of topical moisturizers. The method consists of a system for reproducible scoring of these lines, based on ratings for their frequency times their depth, by component area of the face. Controlled half-face comparisons in five test series involving no treatment, water, and four moisturizers revealed that:

1. The method provided good reproducibility of baseline SFL values, and of changes in these values through time upon repetition of the same treatment in different series.
2. The method also provided values for the distribution of SFL's by facial area, and values indicating a differing response of facial areas to applications of moisturizers. The greatest per cent reductions were noted for SFL's around the eyes, followed by lines around the cheek and mouth. Lines on the forehead and chin changed noticeably less.
3. With quantitative evaluation, trained judges can produce a reliable rank ordering of more effective treatments, less effective ones, and control treatments such as water or no treatment.

The panel study as a scientifically controlled investigation: moisturizers and superficial facial lines: Elias W. Packman and Eugene H. Gans. *Journal of the Society of Cosmetic Chemists* 29, 91 (February 1978)

Synopsis—Characteristic features of the controlled study (randomized treatment, comparison agent, blinded evaluation) were incorporated into a panel investigation of the objective effects of five topical moisturizers, water, or no treatment on superficial facial lines, as perceived by a 12-member untrained consumer evaluation panel, assessing the skin of a separate group of subjects who used the test materials. The method proved sufficiently sensitive in almost 900 single-blind, half-face comparative evaluations to demonstrate that:

1. Under the conditions of the scientific investigation, a consumer panel composed of normal users who have not been trained as professional evaluators can detect and visually evaluate the effect of moisturizers on other consumers, thereby providing an important estimate of consumer relevance to cosmetic performance.
2. The technique is sensitive enough to detect the differing degrees of performance that existed among the various treatments.
3. Three of the five moisturizers studied were significantly superior to water, which in turn was assessed more favorably than no treatment.
4. The extent of effectiveness existing for a particular cosmetic tended to prevail throughout the study group and was not concentrated in particular subjects.

J. Soc. Cosmet. Chem., 29, 47–58 (February 1978)

Pheromones (olfactory communication)

STANLEY K. FREEMAN* *International Flavors & Fragrances (R&D) Union Beach, NJ 07735*

Received February 25, 1977. Presented at Annual Meeting, Society of Cosmetic Chemists, December 7, 1976, New York, New York.

Synopsis

In view of the intimate relationship between the olfactory and limbic systems, OLFACTORY COMMUNICATION could be involved in various aspects of reproductive physiology in man. The PHEROMONE CONCEPT implies that learning and/or prior experience with odorants do not play an essential role in its effect. Recent evidence suggests that associative learning rather than a pheromone phenomenon should be seriously considered in the interpretation of certain features of primate behavior mediated by the sense of smell.

1. INTRODUCTION

Pheromones, substances used in communication between members of the same species, probably originated about two billion years ago when the first simple cells externally secreted chemical signals for the purpose of aggregation. It is not unreasonable to assume that this mode of communication was continued a billion years later with the emergence of the first eucaryotes or nucleus-containing cells(1). Chemical communication in single cell organisms is believed to be a necessary prelude to the evolution of multicellular organisms. Haldane (2) speculated that communication among single cell organisms was the direct lineal ancestor of intercellular communication, *i.e.*, hormone function. On the other hand, it has been suggested recently (3) that chemocommunication among aquatic animals could have originated in a transition from hormones to pheromones. Only minor evolutionary changes are required compared to the major modifications necessary to enable an olfactory system to function in air. In the latter case, odorants must be altered to become volatile, suitable organs must be developed for odorant production, etc. Observations of both marine and terrestrial animal behavior indicate that chemical communication occurs in most animal phyla. The term pheromone emerged from the diligent and ingenious investigation of Karlson and Butenandt (4) in 1959 on the sex attractant of the silkworm moth, and referred to chemicals liberated by an insect that induce immediate behavioral responses in another insect of the same species. Insect physiologists call these

*Deceased March 10, 1978.

substances *releaser* pheromones. Because this designation is too restrictive for the considerably more complex mammalian systems, the concept of *primer* pheromones was introduced. These substances produce endocrine changes, *e.g.*, the release of reproductive hormones into the bloodstream, causing physiological changes in the recipient animal. Striking examples of behavioral effects brought about by this mode of chemical communication may be seen in female mice: 1. Pregnancy block frequently occurs when a recently impregnated mouse is exposed to the odor of a male of a strain different from that of the stud male, while exposure to males of the same strain as the stud male does not prevent implantation [Bruce Effect (5)]; 2. A decrease of reproductive capacity of the animal occurs when the odor of other mice increases its corticosteroid production [Ropartz Effect (6)]; 3. Estrus is suppressed and pseudopregnancies develop when four or more female mice are grouped together in the absence of a male [Lee-Boot Effect (7)]; and 4. The estrous cycle is induced and accelerated in grouped females by exposure to an odorant present in the urine of male mice [Whitten Effect(8)].

Although pheromones may be classified as olfactory or oral according to their site of reception, the overwhelming majority found in the world of insects and mammals are volatile and airborne compounds that are olfactorily sensed. More than two hundred chemicals have been characterized from insects that mediate overt sexual behavior and modify mating behavior (9). In contrast, relatively few mammalian pheromones have been isolated and identified, although many are known to exist. Pheromones have been identified in those species with specialized scent glands, *e.g.*, Marmoset monkey, Mongolian gerbil, European rabbit, blacktail deer, and pronghorn antelope (10). A sex attractant was reported to be present in the female rhesus monkey (11–16), but a recent study (17,18) did not support this claim. Pheromones in fish may play a role in territorial defense, attraction and recognition of the other sex, parents or off-spring, and guidance of fish migrating upstream to their spawning sites. However, the only pheromones known with certainty are the alarm substance which elicits a fright reaction (19), and substances which induce exploratory feeding behavior (20).

The following discussion basically will pursue two approaches in the multifaceted aspects of olfactory communication in primates. First, it will be shown in Section 2 that anatomical and clinical evidence suggests that pheromones could be involved in the mediation of behavior. Second, in Section 3 a brief will be presented for the role of learning and/or prior experience as an alternative to the pheromone concept.

2. OLFACTORY PATHWAYS

2.1 OLFACTORY EPITHELIUM AND OLFACTORY BULB

Lucretius wrote (21), "You may readily infer that such substances as agreeably titillate the sense (of smell) are composed of smooth round atoms. Those that seem bitter and harsh are more tightly compacted of hooked particles and accordingly tear their way into our senses and rend our bodies by their inroads." Many and diverse odor theories have since been proposed, crossing a spectrum from reasoned conjecture to implausible speculation. Actually, we have no more than a limited understanding of the mechanism underlying olfaction. It is generally accepted that the olfactory and taste systems in all vertebrates, including man, conform to the same basic plan. In contrast with the cells of the taste mucosa, which are highly specialized cells related to skin

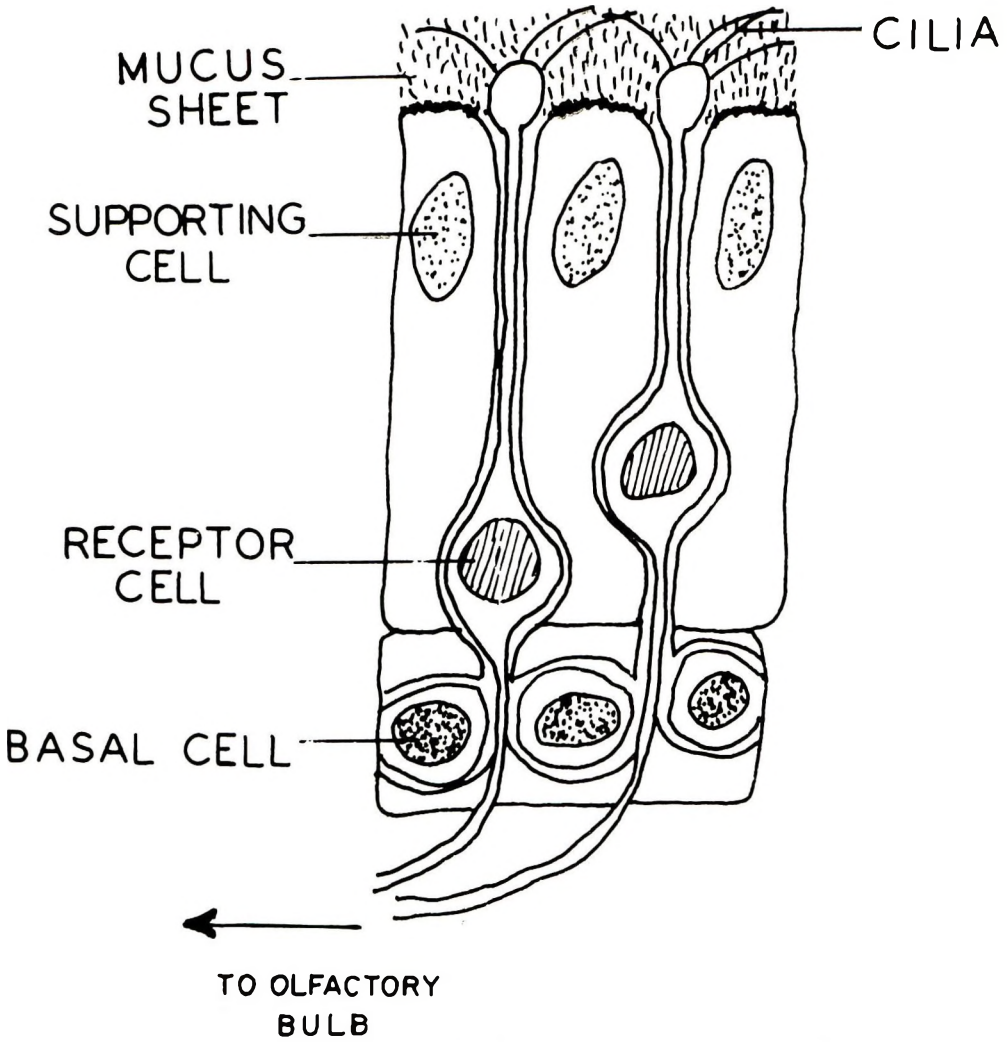

Figure 1. Schematic illustrating the salient features of the olfactory epithelium

cells, the olfactory epithelium contains primary sense cells or true neurons. The olfactory system of terrestrial animals consists of four basic elements (Figures 1,2): 1. The receptor membrane where the information is received; 2. The nerve over which it is transported; 3. The olfactory bulb in which it is presumbly processed; and 4. The pathways over which the processed information is delivered to the higher centers of the brain where the information is translated into patterns of recognition, association, etc. In a broad sense, the olfactory process probably begins with a reversible physical interaction between odorant molecule and receptor sites of the epithelium. The molecular structure of the odorant appears to be the only source of chemoreceptory discrimination, that is, the ability of the higher centers to distinguish between different sets of patterns arising from interaction of odorant molecules and peripheral systems (22). Interaction is presumed to be followed by a summation of the resulting energy effects in the receptor cells, which, similar to all other cells of the body, are bounded by

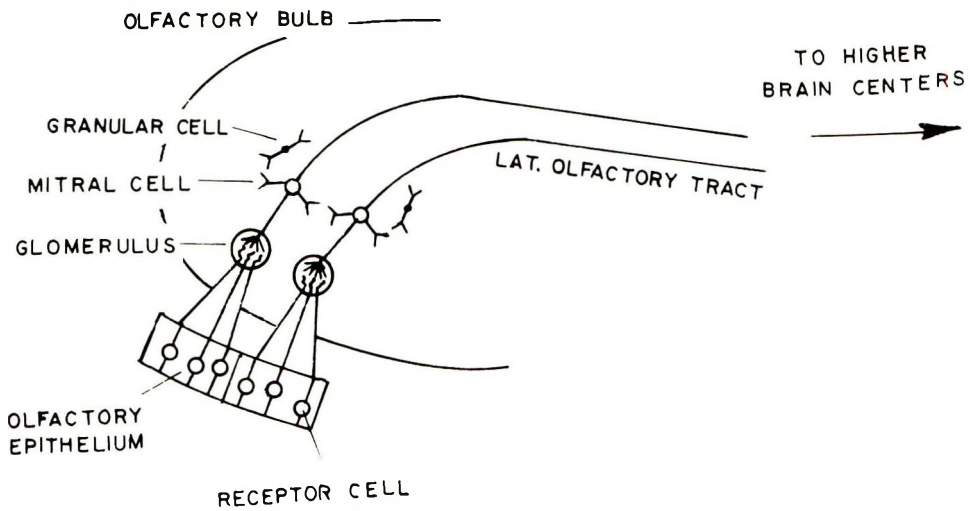

Figure 2. Schematic illustrating the basic anatomical elements of the olfactory system

plasma membranes. Resembling other cellular transduction systems, notably those of audition and vision, an important feature of the transduction events in chemoreceptors is that they are membrane phenomena (23). Delicate bundles of fine unmyelinated fibers, collectively called the olfactory nerve, pass from the receptor cells, enter at the olfactory bulb surface and terminate in the glomeruli level. The individuality of the olfactory information generated in a single receptor cell probably is retained up to the level of the glomeruli. A redistribution is believed to occur between the two levels of the glomeruli and the mitral cells, suggesting that the bulb processes the original information before delivering it to the higher centers. At a deeper level within the bulb, the mitral and granule cell synapses are concerned both with olfactory processing and with integration of feedback information passing from the higher centers of the brain through the granule cells. It should be noted at this point that the human olfactory capability generally rivals that of vision and audition. For example, in man there are circa 10^7 olfactory receptors, each of which can conduct up to ten impulses per second (24). Thus, the peak information capacity of the receptor membrane is approximately 10^8 bits per second, a figure quite close to the visual and hearing systems.

2.2 THE OLFACTORY CORTEX AND THE LIMBIC SYSTEM

Whereas releaser pheromones exert their effect by rapid "recognition and association," primer pheromones somehow must affect the endocrine system. In this regard, let us examine the olfactory cortex, which is defined as the sites that receive direct synaptic outputs from mitral cells in the olfactory bulb. Despite overgrowth from the cerebral cortex, the phylogenetically primitive olfactory cortex mediates social and sexual behavior of most mammalian species studied. Several areas of this primordial cortex receive direct projections from the mitral cells of the olfactory bulb via the lateral olfactory tract. The olfactory cortex serves as a powerful relay, since the outgoing information channels are approximately 100 times more numerous than the incoming mitral fibers.

The relationship between olfactory and limbic parts of the brain are simplistically di-

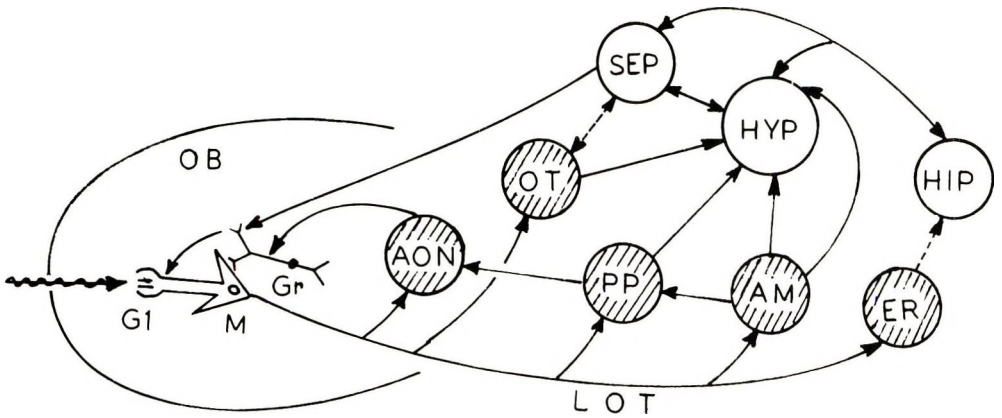

Figure 3. Schematic relationship between olfactory and limbic systems (ref. 25). Olfactory Cortical Structures (shaded circles), Limbic System (open circles), Olfactory Bulb (OB), Mitral Cell (M), Granular Cell (Gr), Glomerulus (Gl), Anterior Olfactory Nucleus (AON), Prepyriform Cortex (PP), Amygdala (AM), Entorhinal Cortex (ER), Olfactory Tubercle (OT), Septum (SEP), Hypothalamus (HYP), Hippocampus (HIP), Lateral Olfactory Tract (LOT)

picted in Figure 3 (25). These areas are interconnected in highly complex ways and only in the past few years has a number of new methods been acquired for studying them. Hence, it can be expected that a more sophisticated diagram will replace Figure 3 in the near future. It is fair to state that at this time a unanimity of opinion does not exist pertaining to the intricate relationships among the various parts of the olfactory and limbic systems. The limbic system is believed to be concerned with visceral and behavioral mechanisms, particularly those associated with the expression of emotional states and with sensory and sexual functions. The anterior olfactory nucleus is thought to serve as part of a negative feedback loop that affects mitral cell output. Fibers from the olfactory tubercle (a rudimentary structure in man) passing to the septal area appear to be principally non-olfactory. In fact, recent observations (26) suggest that the olfactory bulb has certain general modulatory functions in addition to its sensory role as a processor of olfactory information. One of the main inputs to the hippocampus comes from the entorhinal cortex, which in turn receives direct connections from the olfactory bulb. The hippocampus is well developed in such animals as the dolphin which lacks olfactory bulbs, but evidence indicates that the hippocampus receives inputs from the olfactory bulb, when present. The hippocampus may play a role in odor memory (27). Interestingly, olfactory memories are unique in that specific odors can be retained significantly longer than can visual or auditory memories (28). It is not uncommon for people to be vividly reminded of particular events, over long periods of time, which were associated with certain odors. The largest site in the olfactory cortex is the prepyriform cortex, or anterior pyriform cortex, generally regarded as the primary cortex in the olfactory pathway. Axons that leave this area distribute, *inter alia*, to the surrounding olfactory regions and parts of the hypothalamus. Consequently, the prepyriform cortex is strategically located to affect central brain structures that are crucially involved in many types of behavior. Recently it has been demonstrated that fibers project from the prepyriform cortex to the thalamus, one of the key relay centers of the brain to the frontal cortex (29). Such a thalamic connection to neocortex raises the possibility of greater sophistication and association with other stimulus events than

older anatomical evidence would have implied. Among the connections leading into the amygdaloid complex, only olfactory fibers are well defined anatomatically; nearly all parts receive either direct or indirect connections (30). The hypothalamus, the most important part of the limbic system as far as behavior is concerned, receives connections from the amygdaloid complex. Hypothalamic activity regulates the secretion of the gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), from the anterior pituitary. In man, the amygdala has been shown to activate olfactory hallucinations and also is implicated in differentiating and identifying odors (31). Electric stimulation of the amygdala and the pyriform cortex of human subjects has been reported to be followed by immediate and excessive incretion of adrenocorticotropic hormone (ACTH) together with a rise of plasma cortisol (32). Of even greater interest, significant increases were observed in plasma cortisol arising from electrical stimulation of the olfactory mucosa (33). No change in plasma cortisol occurred in individuals with post-operative anosmia. The phenomenon was interpreted as demonstrating that intact olfactory pathways allow the electric stimulus to reach hypothalamic structures, which in turn permit the release of ACTH-releasing factor and rise in cortisol level. This interpretation suggests that a specific odorant(s) can cause the same type of effect as observed with electrical stimulation.

From the foregoing anatomical and clinical considerations, albeit sketchy, it is evident that an intimate relationship exists between the olfactory and limbic systems in humans. Consequently, pheromonal effects could be involved in various aspects of reproductive physiology in man, similar to those known to occur in non-human animals.

2.3 THE PREOPTIC AREA AND OLFACTORY SENSITIVITY

Pfaff (34) compared responses of the normal male rat to urine and non-urine odors by measuring signals from the olfactory bulb and preoptic area, which is an anterior extension of the hypothalamus. A high proportion of preoptic region units responded differently to estrous female rat urine odor than to ovariectomized female urine, while only a low proportion of olfactory bulb units did so. A reversal was evident for non-urine odors. Approximately 75 per cent of all units, in both the olfactory bulb and the preoptic area, responded differently to urine odors than to non-urine odors. These data suggest that it is theoretically possible for receptor site information, coded by the olfactory bulb, to be "decoded" solely in the preoptic area. Therefore, a volatile chemical, not necessarily detected as an "odorant," might be physiologically active by virtue of the olfactory-preoptic-hypothalamic-pituitary relationship. Also, if the olfactory efficiency of the cells in the preoptic area is greater than those in the brain regions responsible for other aspects of odor perception, it is possible that certain odorants, *i.e.*, pheromones, in sub-threshold concentrations for regions in the brain other than the preoptic area, can bring about a response in the preoptic area of mammals.

3. ENDOCRINE FUNCTION AND OLFACTORY SENSITIVITY IN WOMEN

Biosynthesis of pheromones and scent gland secretion in mammals usually are influenced by the hormonal states of the body. Pheromones associated with reproduction in lower animals display their effectiveness at or near estrus, the period of ovulation and maximum sexual receptivity in the female. Fluctuations in odor detection

performance changes with amounts of circulating estrogen and progesterone in the rat (35). Peak olfactory acuity occurs around the ovulatory period and the fluctuations are not evident in ovariectomized rats. A similar behavior is manifested in women. LeMagnen (36) found that the ability of women to detect the odor of a musk (Pentadecanolide) reached a maximum near or on the day of ovulation. Many materials of both animal and vegetable origin display a musk odor (37) and it has been often stated, with little substantiation, that musk odorants are of biological significance to man. Although the considerable variation in olfactory acuity with regard to Pentadecanolide was reported to be specific for this chemical (36), subsequent investigators (38,42) demonstrated increased sensitivity for at least eight different odorants in the time near ovulation. This cyclic variation correlates with alterations in hormonal levels occurring during the ovarian cycle. Men and ovariectomized women show no variation of olfactory acuity with time. Women with decreased gonadal secretion who were not receiving estrogen often displayed poor odor sensitivity. Estrogen treatment significantly enhanced, but testosterone lowered, their acuity to odorants. Since menstruation is triggered by a decrease in estrogen levels, it is not unexpected that odor thresholds in women reach a maximum during the period of menstrual flow. The prepiriform cortex and preoptic area have particularly high uptake of estradiol, an estrogenic hormone, in the female rat (43). It is tempting to speculate that the increased estrogen liberated during woman's ovulatory phase of the menstrual cycle is accompanied by the hormone's increase in these regions of the olfactory pathway, thereby causing a heightened olfactory sensitivity to odorants. Despite our ignorance of the precise manner by which gonadal hormones influence odor sensitivity, a consistent finding in most studies is the well defined correlation between circulating level and type of hormone with the performance of the sense of smell in the female.

In higher animals, the mechanism to ensure mating involves more than one sensory modality and often may require a complex interaction of diverse influence mediated by all the sensory processes. For example, women possess lower thresholds, *i.e.*, greater sensitivities, to visual (44) and auditory (45) stimuli at approximately the time of ovulation. From the viewpoint of evolution, such peak attuning to sensory signals would increase the probability of coitus and result in an increased probability of conception. In man's dim past, increased sensitivity to an olfactory signal (acting as an aphrodisiac pheromone) continually emanating from the male might have been perceived by women near the time of ovulation only. Odor quality also may play a role in the olfactory behavioral response. The perceived quality of certain odors changes on dilution. Consequently, even if a biologically important odor is detectable throughout the menstrual cycle, the perceived odor quality may change with perceived intensity fluctuations.

Until recently, anecdotal and indirect observations have indicated that social grouping of the human female can cause synchronization of menstrual timing. Such an effect is not unlike that seen in rodents (7). McClintock (46) conducted a study with young women living in the same college dormitory and demonstrated that menstrual synchrony indeed occurred. In addition, the data indicated a parallel with the Whitten effect (8) in mice in which the suppression of estrus in groups of female mice is released by the introduction of a male pheromone. The suppression of the ovulatory cycle in some of the women was released when they were exposed to men. Odor may be implicated in these phenomena, but further studies must be conducted in order to determine the basis of the intriguing effects.

4. LEARNED VERSUS INATE RESPONSES TO ODORS

From Aristotle's proposal (47) that the various categories of animals might be arranged on a graded scale of complexity or perfection with man at the top, came the general acceptance that all animals could be ranked on a single continuous dimension known as the *scala naturae*. However, such a "phylogenetic scale" is inconsistent with contemporary views of animal evolution. Hodos and Campbell (48) commented, "Comparative psychologists have failed to distinguish between data obtained from living representatives of a common evolutionary lineage and data from animals which represent divergent lineages. Only the former can provide a foundation for inferences about the phylogenetic development of behavior patterns." Primates evolved as a special branch of the insectivore line, *e.g.*, shrews, moles and hedgehogs, dating back more than 60 million years. Over this period of time, carnivores and rodents have followed independent and different courses of development from the primate line and from each other. Consequently, from the aspect of the evolution of primate characteristics, comparisons such as rat-cat-man are meaningless. The rodent olfactory system can be compared to man's because they are basically similar despite the fact that there is no phylogenetic relationship. A clue to patterns of evolution in the human lineage could be gained from a comparison among living insectivores, prosimians, Old World monkeys and man. It was for this reason that special importance was accorded to recent work (11–16) pertaining to the influence of vaginal odors of female rhesus monkeys on the sexual behavior of the male rhesus. The proposed existence of a primate pheromone sparked interest in the search for human pheromones. Before discussing the putative rhesus monkey pheromone and its implication for hominids, let us briefly review some recent knowledge and thoughts relevant to learned responses to odor.

The pheromone concept implies that learning and/or prior experience with odorants do not play an essential role in its effect. However, it is now generally recognized that the original definition of pheromone is misleading, even for insects. The olfactory stimulus is not always simple (49) and insect behavior may be more plastic or modifiable by previous experience than heretofore suspected (50). In other words, an insect's response to pheromones is not necessarily programmed by genetics. Since mammalian behavior is infinitely more complex and more flexible, responses to pheromones are intricate, variable and often experience-oriented (51). Because of the strong dependence on experience, Bronson (51) has proposed the term *signalling* rather than *releasing* for those odors yielding an immediate effect on mammalian behavior. Mammalian responses to sex pheromones are far more easily modified by early associations than has been supposed (52,53). Similar to avian imprinting, there often appears to be a sensitive period for olfactory imprinting (54). Early experiences with artificial odorants, ranging from cage shavings to arbitrarily selected perfumes, have modified sexual behavioral preferences, eating, aggression, exploration, etc., in lower animals (53). For example, weanling rat pups showed a preference for citral subsequent to injecting their lactating mothers with this chemical. Not unexpectedly, there is a paucity of information pertaining to the sense of smell in human neonates. Newborn infants respond to sensory stimuli and their suckling behavior changes on presentation of various odorants (55). Suckling ceased or decreased in frequency on exposure to iodoform, anise or peppermint oils in approximately the same percentage of children as was observed in rabbits, kittens and puppies. Russell (56) reported the existence of olfactory maternal attraction in a recent study on human neonates. Sleeping infants were presented with breast pads previously worn by breast-feeding mothers. Two-day

old subjects showed essentially no response. At two weeks they exhibited general arousal with little attendant discrimination between their mother's pad and those of strange mothers. At six weeks of age, six of the ten infants tested could identify the maternal odor from that of a stranger. In an earlier and independent investigation (57), a differential response was shown six days after birth. The source of these odors is not known with certainty. The response may be due to a true maternal odor or, as demonstrated in other primates (58), originate in odors placed on the mother by the neonate. In either instance, olfactory cues generate behavioral responses in infants. The ontogenetic implications are fascinating. For example, would the putative maternal odor or similar odor "imprinted" between one and six weeks give rise to a behavioral response later in the adult? Regarding the effects of odor on developing Homo sapiens, Bieber (59) stated, "The sense of smell is the primary sensory modality in the heterosexual development of heterosexual responsivity." Furthermore, it has been suggested (60) that olfaction may play a crucial role in the establishment of sexual identity.

An interesting study (61) has demonstrated that adult male hamsters undergo a dramatic change toward the female's vaginal secretion when its presentation was followed by lithium chloride poisoning. The secretion, which is sniffed and ingested by the male, contains a substance that specifically affects sexual motivation which does not depend on previous experience. Surprisingly, hamsters form aversions to the vaginal secretion when it has been followed by a single experience with poisoning. The experiments suggest that adult mammals' responses to sex pheromones are much more easily modified by experience than has been supposed. The olfactory system, in consort with limbic structures, served to free animal behavior from the rigidity of inborn reflex mechanisms mediated by the hypothalamus, *e.g.*, temperature regulation and the autonomic control of cardiovascular and digestive systems. As a result, not only are specific, genetically programmed pheromonal effects made possible, but also those associated with past life experiences.

The sexual behaviour of the male rhesus monkey to an odorant emitted by the female tended to support the belief held by some scientists and laymen (62-64) that specific, naturally occurring body odors ("pheromones") may have previously unsuspected influences on social and sexual behaviors of man. Michael and Keverne (11–14) reported that male rhesus monkeys are strongly attracted to and copulated with estrogen-treated females, presumably on the basis of olfactory cues. A series of low molecular weight aliphatic acids, *i.e.*, acetic, propionic, isobutyric, butyric and isovaleric, were proposed to be the active components of the vaginal secretions (15). The acid mixture, when substituted for the vaginal secretions, was said to have similar stimulatory effects on the males. In view of the basic importance of these findings to a general theory of primate behavior, Goldfoot and co-workers (17,18) performed additional evaluations of the effects of vaginal material on the male rhesus sexual behavior. Their detailed study failed to support the conclusions drawn from previously published work, that is, vaginal secretions and aliphatic acids essentially were without effect on the males. The significant procedural differences between the two groups of investigators lie in Michael *et al's* practice of prior selection of males and on specific experiences provided them which, in effect, trained the males to respond to the odor cues (18). Although a clearer picture will emerge after further experimentation, the effect of associative learning in the rhesus monkey rather than a pheromonic phenomenon appears to best explain the evidence accumulated to date.

Failure of an animal to subsequently respond to an arbitrarily selected odorant used in a learning experiment does not necessarily signify the lack of capability for olfactory communication. Seligman and Hager (65) have shown that learning has its biological boundaries. They make a most persuasive case for the "preparedness" (66–68) hypothesis in behavior studies in contrast to that of "equipotentiality" (69,70). In the latter, it is assumed that all perceptible stimuli are equivalent. Implicit in the preparedness hypothesis is the premise that learning is continuous with instinct. Lockhard (71) wrote, " . . . . natural selection has produced special learning abilities such that some ecologically relevant task is learned at a much faster rate than an arbitrary task, or natural stimuli are much more effective than artificial stimuli." It follows that the chances of a successful associative learning experiment would be increased when a biologically significant odor cue is used. Although there have been conjectures (62,63) concerning apocrine gland, skin and vaginal secretions serving as olfactory communicants, little is known of the effects of these odors on man. Behavioral responses elicited by olfactory messengers probably are strongly influenced by the context within which odorants are presented. Also, human volatile secretions may vary with emotional state. More than 70 years ago Ellis (72) wrote, "Women, like men, frequently give out an odor during coitus or strong sexual excitement. This odor may be entirely different from that normally emanating from the woman." Another comment of this prescient psychologist, and one that should be heeded by present-day investigators, also pertains to odor and the emotional state (72): "If a certain degree of tumescence is required before a personal odor can exert an attractive influence, a powerful personal odor, strong enough to be perceived before any degree of tumescence is attained, will tend to cause repulsion."

Despite the difficulties involved in gaining answers to the question of olfactory communication in primates, the quickening pace of research soon should enable us to form conclusions about learned odor associations. In the writer's opinion, the associative learning premise is potentially far more intriguing than the pheromonal model for human behavior. Although emotional responses of man are dominated by vision and hearing, olfaction certainly has not abdicated its function in shaping motivated behavior.

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Application of lower titanium oxide in cosmetics

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Synopsis

Carbon black and iron black (Fe_3O_4) are black pigments commonly used in the cosmetic industry. Due to its hydrophobic character, carbon black has poor dispersibility in water, and iron black, due to its ferro-magnetic character, is not readily dispersible in any liquid. In order to solve these problems the authors investigated the possibility of synthesizing LOWER TITANIUM OXIDES and using them as a black pigment IN COSMETICS. The general formula of the lower titanium oxide is Ti_nO_{2n-1} in which n can be any positive integer. When n is small, the resultant compound is bluish-black. As n increases, the compound becomes gray.

The lower titanium oxide most suitable for cosmetics was obtained by calcining a mixture of a titanium dioxide pigment and a metallic titanium powder in a vacuum electric furnace. While it has a tinting strength corresponding to that of carbon black and iron oxide black, it is superior in many other respects when used in cosmetics.

INTRODUCTION

Black pigments, commonly used in the cosmetic industry at the present time, are two in number: namely, carbon black and iron oxide black (Fe_3O_4). However, both are pigments not easily formulated into make-up cosmetics of the dispersion type. Carbon black has a hydrophobic surface and its surface area is extremely large (about ten times that of titanium dioxide pigment). Iron oxide black, though considered to have a hydrophilic surface, tends to strongly coagulate in any medium due to its ferromagnetic character. This gives rise to poor dispersibility with considerable viscosity changes when the formulation calls for producing different shades of cosmetics and, furthermore, color separation occurs on the surface of the cosmetics when this material is used along with other pigments such as titanium dioxide.

In order to solve these problems, we explored many black pigments showing greater dispersibility and most obviously with a high safety factor when used in cosmetics. In the lower titanium oxides, we noted several pigments with great possibilities.

It is well known that there are the three crystal forms of titanium dioxide: anatase, rutile and brookite. In the cosmetic or paint industry, pigments of the former two types are used. Titanium dioxide is a very stable compound. On the other hand, titanium can

make various oxides which are expressed as Ti_nO_{2n-1} in which n can be any positive integer. They are generally called lower titanium oxides (1-4). Ehrlich describes two methods for their synthesis. The first involves the reduction of titanium dioxide (Ti_2O_3 or Ti_3O_5 is synthesized as a result of the loss of oxygen when TiO_2 is heated in a hydrogen stream at temperatures of 1200 to 1500°C). The second occurs as a phase reaction by heating a mixture of titanium dioxide and metallic titanium (in appropriate ratio) in a vacuum. Ehrlich referred to the fact that the lower titanium oxide has a dark shade. We investigated the lower titanium oxides in detail and found that, as expected, some of them had superior qualities compared to the above two black pigments.

EXPERIMENTAL

MATERIALS

A metallic titanium and three kinds of titanium dioxide pigments were used. The titanium powder was an analytical grade reagent (above 99 per cent) from Kishida Chemical Co. Ltd., of which the specific BET surface area (S_{N2}) was 0.24 m^2/g. The titanium dioxides (TiO_2) were all commercially available powders for pigment use of which S_{N2} was 8.5 (#328, NL Industries), 25.0 (P-110, Degussa) and 54.0 m^2/g (P-25, Degussa), respectively. All the materials used in the experiment were free of any heavy metals which are prohibited from use in cosmetics.

METHOD OF PREPARATION

The titanium and titanium dioxide were mixed in predetermined ratios using a ball-mill or a portable Henshel mixer. About 70 g of the mixture was heated in a vacuum electric furnace at 600, 800, and 1000°C at a vacuum of below 10^{-2} torr for 1, 2, 4, 8, and 20 hr. Figure 1 illustrates the arrangement of the equipment used for the calcination process. After heating, the furnace was allowed to cool to below 200°C by turning off the electric current while still maintaining the vacuum; then the product was taken out. Above this temperature, the lower titanium oxide is apt to oxidize and become white. The product was pulverized in a mortar since it aggregated slightly by sintering.

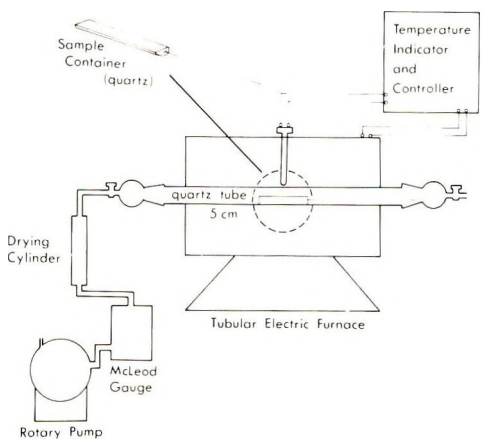

Figure 1. Arrangement of equipment used in the calcination

METHODS FOR TEST

The following procedures were carried out in order to characterize the synthesized materials:

a) *X-Ray diffraction:* Crystallographic assessment of the products was carried out using a Rigaku Denki X-ray diffractometer (RU-3) by Cu-Kα radiation.

b) *Color measurement:* A CC-1 Color Computer (Tokyo Shibaura Electrics), a visible light absorption spectrometer equipped with a minicomputer, measured the color of the products and that of 10 per cent mixtures in TiO_2 #328. The latter is for assessing the tinting strength of the products. The L-value in the Hunter's equation, which expresses lightness, will be used for referring to the blackness and tinting strength of the products. Other chromatic values such as hue (= b/a) and saturation [= $(a^2 + b^2)^{1/2}$] were of no use since the products were achromatic.

c) *Viscosity and superficial appearance of a slurry:* Products were mixed with TiO_2 #328 at the ratios 0/100, 15/85, 25/75, 50/50, 75/25, and 100/0 using an Emide mixer. The mixture (70 g) was dispersed into a tetradecane-sorbitan monooleate 34/4 v/v solution, which was passed through a three-roller mill. Viscosity of the slurries was measured with a Ferranti-Shirley cone-plate viscometer under the condition to give a maximum shear rate of 1720 sec^{-1} with a 10 sec sweep time. Apparent viscosity was obtained from the shear stress at the maximum shear rate. Attention was paid to the appearance of the slurry surface throughout this experiment.

RESULTS AND DISCUSSION

OPTIMUM CONDITION FOR SYNTHESIS

In order to determine the shortest time required for the calcination reaction to be completed, the existence of unreacted starting materials such as TiO_2 and Ti in the product was examined by X-ray diffraction. Figure 2 shows an example of the results in which one can note the progress of the reaction. With time, the diffraction peaks of the starting materials decreased in intensity and the intensity of the end product increased. Figure 2 indicated that the reaction had been completed after 4 hr. Table I summarizes the time required for the completion of the reaction at different temperatures. Table I

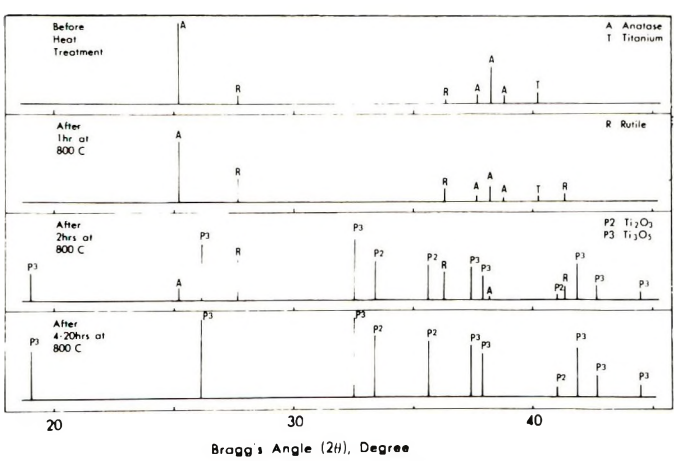

Figure 2. An example of the change in X-ray diffraction patterns with time for a Ti - TiO_2 mixture

Table 1.
Time required for the reaction to come to completion at each temperature.

Raw materials	Temperature (°C)	Time (hr)
TiO_2 (54.0 m^2/g)	600	4
	800	1
	1000	1
TiO_2 (25.0 m^2/g)	600	> 20
	800	4
	1000	1
TiO_2 (8.5 m^2/g)	600	> 20
	800	>20
	1000	20

also shows that the time for the reaction to come to completion becomes longer with decreasing S_{N2} of the TiO_2 used. This is understandable based on the consideration that the reaction rate becomes faster as the particle size of the starting material decreases, since the decrease in particle size causes the lowering of the melting point or of the lattice defects of crystals. This was noted by Kelvin and Herring (5,6). The reaction time did not change with the mixing ratio of Ti and TiO_2.

As well known, the reaction can be made faster by raising the calcination temperature, but the latter causes the aggregation of particles by sintering. Since higher temperature causes stronger aggregation, the reaction should be conducted at the lowest temperature possible within the conditions of the time stipulated. Thus, it is reasonable that each of the TiO_2 of P-25, P-110, or #328 grades can be calcined at 600°C for 4 hr, 800°C for 4 hr or 1000°C for 20 hr, respectively.

TESTS FOR PIGMENTS

For application as a black pigment in cosmetics, the degree of blackness and tinting strength of the pigment should first be examined. These conditions were studied so as

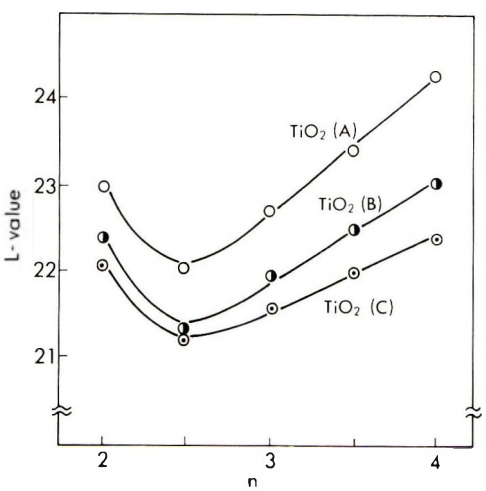

Figure 3. Change of L-value as a function of n for the synthesized Ti_nO_{2n-1}

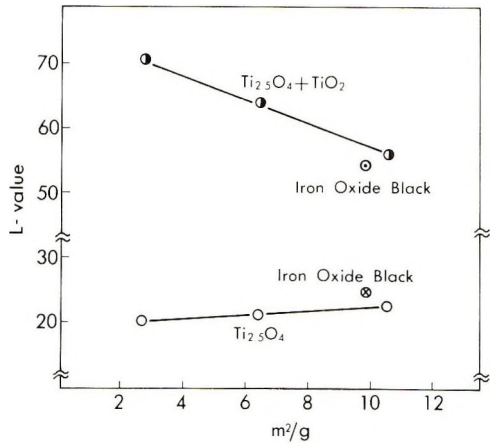

Figure 4. Change of L-value as a function of the S_{N2} of synthesized $Ti_{2.5}O_4$ for the 10 per cent mixture of $Ti_{2.5}O_4$ and TiO_2

to obtain the most useful lower titanium oxide. These results are shown in Fig. 3–4. These data suggest that the blackest pigment is obtained at n = 2.5 regardless of the type of TiO_2 used and when n is fixed the pigment having the largest S_{N2} shows the highest in tinting strength. Thus, a pigment having a higher tinting strength can be synthesized using a TiO_2 having the smaller particle size. Use of TiO_2 P-25 as a starting material is advantageous because of the ease of synthesis. Crystallographically, $Ti_{2.5}O_4$ is a mixture of Ti_2O_3 and Ti_3O_5.

VISCOSITY OF A SLURRY IN WHICH THE PIGMENT WAS DISPERSED

Figure 5 shows the plots of viscosity of the slurry in which the obtained pigment was dispersed versus the ratio of the pigment/TiO_2. In the figure, Fe_3O_4 is also plotted for the convenience of comparison. Clearly, the influence of the new black pigments on the viscosity was smaller than that of Fe_3O_4. This fact is important when formulating different shades of cosmetics in a given product line. Should the viscosity change with

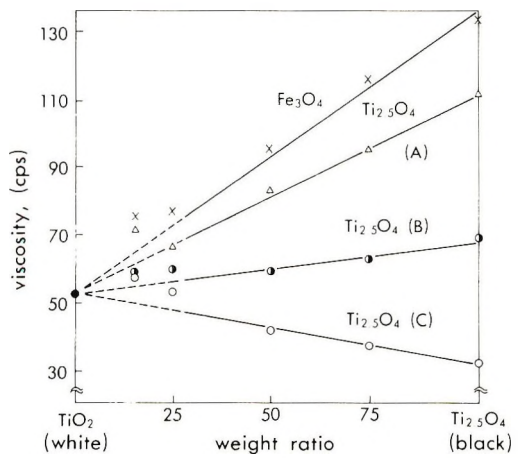

Figure 5. Change of viscosity as a function of mixing ratio of $Ti_{2.5}O_2$ and TiO_2 for the slurry

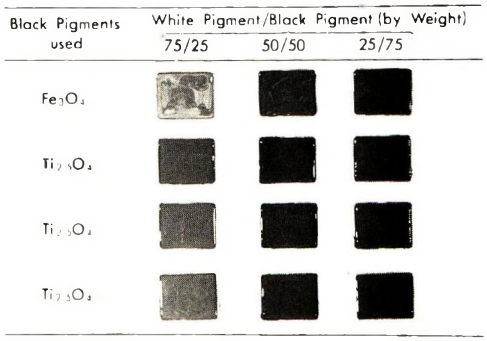

Figure 6. Photographs of slurries including different black pigments

the difference in shade, then modification of each individual formulation for each shade of the cosmetic is necessary.

HOMOGENEITY OF A DISPERSION

As to the homogeneity of the dispersion, the Fe_3O_4 slurries gave some striped patterns on the surface but the new pigments gave none. These phenomena are shown in Fig. 6. This characteristic is of considerable importance since it is a measure of homogeneity and has great impact on the commercial value of the final products. In terms of the safety problem, titanium dioxide has long been used in the cosmetic industry and is a proven, safe ingredient. In the test, carried out in this laboratory, the synthesized materials were of course confirmed to be safe.

SUMMARY

1. The authors obtained a new black pigment by calcining a mixture of TiO_2 and Ti powders in vacuum.
2. This new product was noted to have better dispersibility than Fe_3O_4 or carbon black pigments and can be considered a good replacement for these materials in cosmetics.

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Evaluation of hair fixatives—a new technic utilizing torsional measurements

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Synopsis

A new laboratory test, TWIST RETENTION ANALYSIS (TRA), utilizing a TORSIONAL BRAID ANALYZER, is described as a tool for EVALUATING HAIR FIXATIVE set holding ability under humid conditions. Excellent statistical correlation to traditional laboratory Curl Retention testing is demonstrated. Twist Retention Analysis is shown to give more precise measurements than earlier evaluation techniques and allows the use of smaller sample populations. This new test is shown to give statistical correlation (90 to 100 min), to long-term (5 to 21 hr) Curl Retention testing, allowing rapid evaluation of fixative performance. Conclusions about fixative differences can be made at a faster rate. Statistical differences between fixatives are determined that could not be established by Curl Retention testing.

INTRODUCTION

Laboratory measurements of fixative curl holding ability under humid conditions have been described in the literature (1–4) over the past decade. These techniques employ visual observations of vertically positioned hair swatches and measure percent drop as a function of time. These test procedures require multiple samples, usually 7 to 15, to give statistically significant measurements. Due mainly to physical handling of curls during preparation and reliance upon visual measurements to record results, substantial error factors can be introduced.

Bogaty (5) has suggested that hair frequently assumes a helical coil configuration in the course of its being combed into style. Curl holding, previously described, has generally not taken these torsional configurations into consideration in analysis of test results. This paper will present a new performance test, Twist Retention Analysis (TRA), for evaluating hair fixatives, utilizing torsional measurements of hair/resin composites under humid conditions. Evaluation is automated with the use of a Torsional Braid Analyzer.

It will be demonstrated that Twist Retention Analysis is a precise measurement of the set holding capacity of hair fixatives, permitting the use of a small sample size in order to obtain statistically significant conclusions.

Statistical analysis is presented that compares conventional Curl Retention with Twist Retention measurements. A high degree of correlation between the two tests is observed. Differences between hair fixatives will be shown to develop at a faster rate with TRA, giving correlation after short time intervals, to long-term Curl Retention analysis.

Parameters of Twist Retention testing are discussed, including swatch size, degree of twist of swatch, air flow rate, fixative pickup, and effect of shampooing upon performance.

A strain gauge apparatus is used for precisely determining the amount of fixative on the sample swatch.

EXPERIMENTAL

FIXATIVE FORMULATIONS

Eight hair fixative formulations (Table I) were prepared from 0.50 to 4.00 per cent by weight in andydrous ethanol. Neutralization was carried out, if needed, to the manufacturer's recommended level with 2-amino 2-methyl 1-propanol (AMP).

Three of the formulations (D1, E1, E2) were resins in conjunction with typical plasticizers at a level of 15 per cent on the resin solids.

TORSIONAL BRAID ANALYZER

A Torsional Braid Analyzer (6), Model 100B1[1] was utilized for measurement of Twist Retention (Fig. 1). The sample is suspended in the center of an enclosed vertical cylindrical chamber, fixed in place at the top and free to rotate at the bottom. A schematic

TABLE I

FIXATIVE FORMULATIONS

RESIN A -	poly-vinyl pyrrolidone *(molecular weight 40,000)*
RESIN B -	vinyl acetate (70)/vinyl pyrrolidone (30) *copolymer*
RESIN C -	*(vinyl acetate/crotonic acid/vinyl neodecanoate terpolymer) neutralized 80% of its available acidity with 2-amino 2-methyl 1-propanol (AMP)*
RESIN D -	*(butyl half ester of methyl vinyl ether/ maleic anhydride copolymer) neutralized 7% of its available acidity with AMP*
RESIN E -	*octylacrylamide/acrylates/butyl amino ethyl methacrylate polymer neutralized 90% of its available acidity with AMP*
FORMULATION - D1 -	*Resin D plus 15% on the resin weight, of poly-propylene glycol (26) oleate*
FORMULATION - E1 -	*Resin E plus 15% on the resin weight, of poly-propylene glycol (26) oleate*
FORMULATION - E2 -	*Resin E plus 15% on the resin weight, of poly-ethylene oxide (molecular weight 1000)*

[1]Chemical Instruments Corp., P.O. Box 399, Woodbury, NJ 08096.

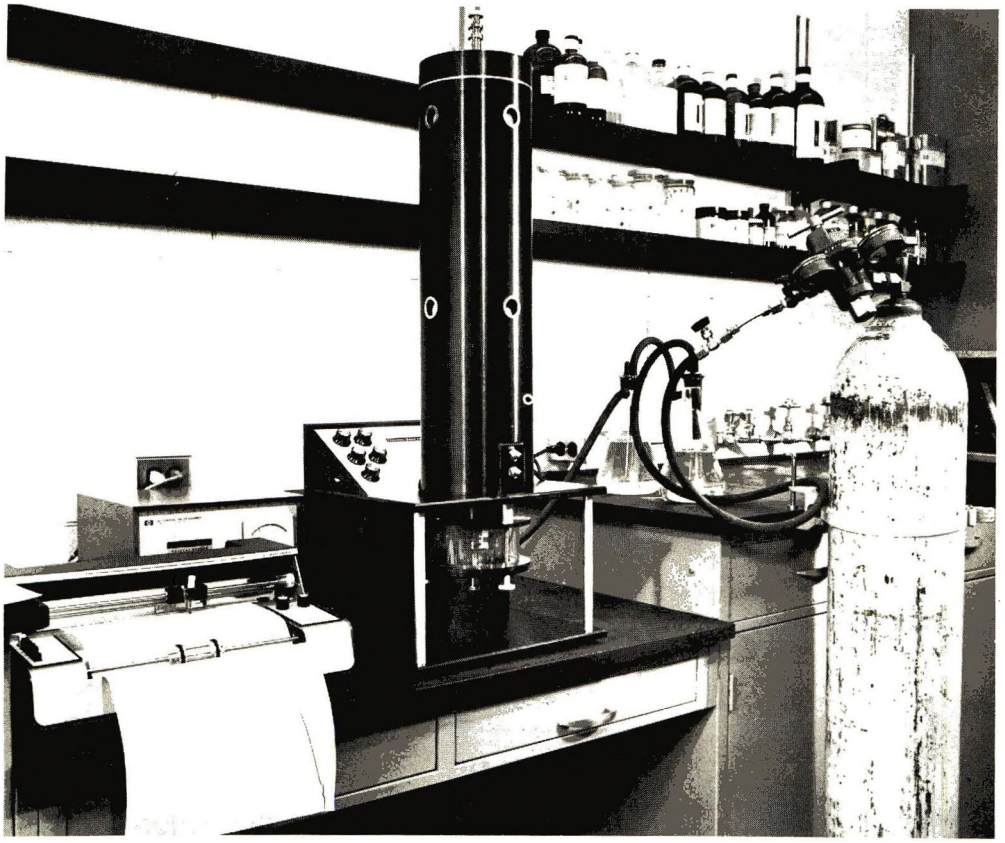

Figure 1. Torsional Braid Analyzer

cross-sectional diagram of this apparatus (Fig. 2) shows the sample chamber isolated from the outside environment. Any desired atmosphere of gas may be passed through the chamber, entering at the top.

A linear-with-angle optical transmission disc (transducer) converts the torsional motion of the sample into a convenient electrical readout. An optical system is used in which a

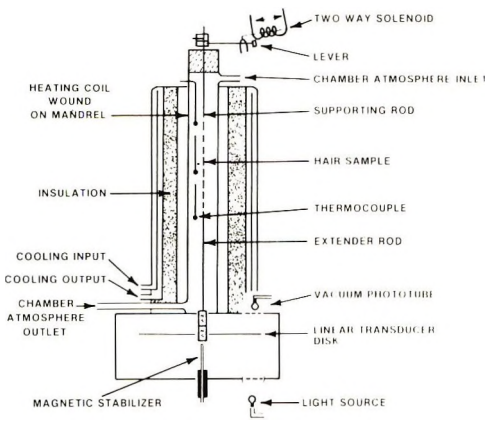

Figure 2. Schematic diagram of the Torsional Braid Analyzer

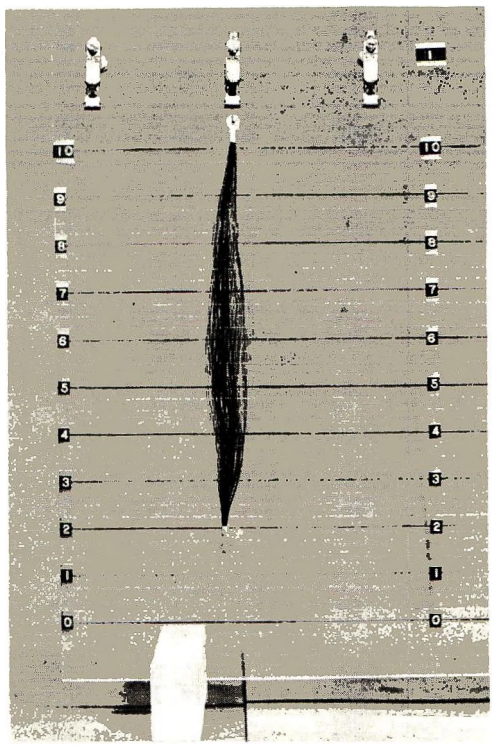

Figure 3. Twist Retention hair swatch

constant light source is attenuated by the transducer and relayed to a linear-response photocell. Voltage readings were recorded on an Omniscribe® 5110-2[2] recorder.

Humid air was introduced into the sample chamber by passing purified compressed air through water, using glass dispersion tubes (Ace Glass[3] #7202 porosity C) to insure adequate moisture saturation (Fig. 1). Air flow rate was accurately controlled within a working range of 15 to 200 ml/min. Relative humidity of the test environmental air was determined to be 90 to 93 per cent R.H. Temperature was controlled at 21 to 25°C.

TWIST RETENTION TESTING

Approximately 0.25 g of 25 cm long Remi Blue String, European, brown hair[4] was saturated with water and combed into a swatch free of twists. The swatch was then carefully bound at both ends with copper ring lugs (size 4) placed 203 mm apart. The hair swatch was allowed to dry at room temperature for 1 hr after which an adhesive was applied at the ring lug/hair junctions to permanently affix the hair to the ring lugs. The swatch was conditioned for 16 hr at 50 per cent relative humidity before adjusting (by trimming) to a net hair weight of 0.20 to 0.21 g (Fig. 3).

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[2]Houston Instruments, 1 Houston Square, Austin, Texas 78753.
[3]Ace Glass Inc., Vineland, New Jersey 08360.
[4]DeMeo Brothers, New York, New York.

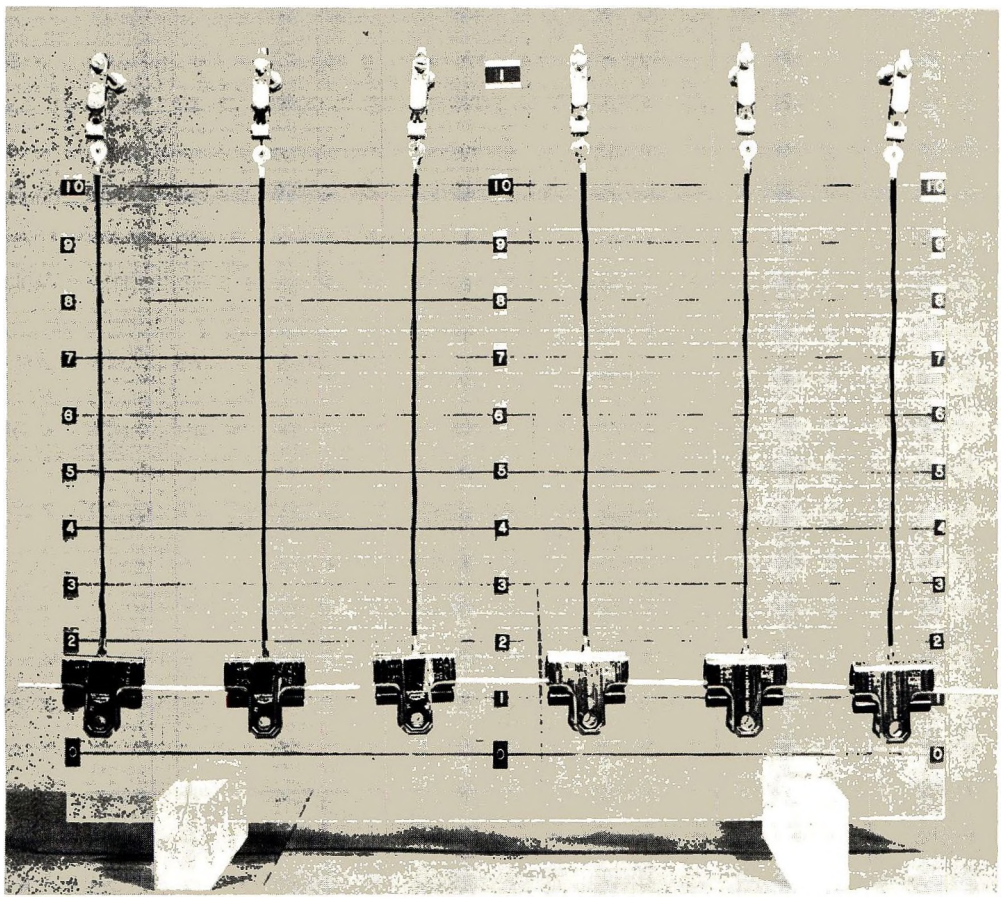

Figure 4. Twisted, fixative-saturated hair swatches on a retention panel

The swatch was conditioned at 50 per cent R.H. and 22°C for 16 hr in a Tenny Environmental Chamber, Model TH-10[5], and then secured to a vertical Lucite®[6] retention panel. Copper wire was placed through the hole in the upper ring lug and attached to an alligator clip on the retention panel. The swatch was then rotated until the lower ring lug was parallel to the retention panel. A clamp (approximately 12.5 g) was attached to the lower ring lug, twisted clockwise 720 degrees, and secured in place to prevent untwisting (Fig. 4). Sufficient fixative solution was applied from an eyedropper at the upper ring lug to saturate the swatch (approximately 2 ml). Excess resin solution was allowed to drip off the swatch. It was then allowed to dry and condition (16 hr at 50 per cent R.H., 22°C) on the retention panel.

The torsional chamber was equilibrated at 90 to 93 per cent R.H. A fixative-saturated swatch was removed from the retention panel and mounted in the Torsional Braid Apparatus taking care not to disturb bonding. The swatch was then allowed to untwist freely and the rate of untwisting recorded as a function of time for a total of 120 min.

[5]Tenny Engineering Inc., Union, New Jersey.

[6]Lucite is a registered trademark of E.I. DuPont de Nemours & Co., Inc., Wilmington, Delaware.

Per cent twist retention was calculated using the following formula:

$$\text{Twist Retention } (\%) = \frac{D_t}{D_0} \times 100 \qquad \text{(I)}$$

D_0 = initial twist (degrees)
D_t = twist (degrees) remaining at time (t)

CURL RETENTION TESTING

Approximately 2 g of 30 cm long Remi Blue String, European, brown hair was tied into a swatch by binding the hair one inch from the root end. After washing with a commercial shampoo and thoroughly rinsing, it was cut to a length of 18 cm from the bound root end.

Excess water was removed from the swatch and it was combed through to remove snarls or tangles. The wet swatch was wrapped into a helical configuration along a 1.25 cm diameter Teflon mandrel, secured in place, and allowed to dry for 16 hr at 50 per cent relative humidity and 22°C. It was then removed from the Teflon mandrel and suspended from the root end on a retention panel. With a manually activated Camar SS 10 pump[7], and from a distance of 25 cm, 0.6 g of a fixative formulation (2 per cent solids in anhydrous ethanol) was applied to the swatch. The sample was removed from the retention panel and allowed to dry in a horizontal position for 2 hr at 50 per cent relative humidity and 22°C.

The conditioned curl was placed on a retention panel and an initial reading of length recorded. The panel was then placed into humidity chamber maintained at 90 ± 2 per cent relative humidity and 22°C. Curl extention length was determined at various time intervals.

Per cent curl retention was calculated using the following formula:

$$\text{Curl Retention } (\%) = \frac{L - L_t}{L - L_0} \times 100 \qquad \text{(II)}$$

L = Length of hair fully extended
L_0 = Length of hair before exposure
L_t = Length of hair after exposure time (t)

FIXATIVE PICKUP MEASUREMENTS

Pickup (weight per cent fixative) was determined for the TRA sample swatch with a nulled pressure transducer or strain gauge apparatus described by Micchelli and Koehler (2). (This instrument precisely converts weight into a measurable electrical output.)

A TRA test swatch was suspended from the strain gauge and approximately 2 ml of a fixative solution was applied at the upper ring lug. Excess fixative solution drained off the swatch. Weight (milligrams) was recorded as a function of time (Fig. 5). Assuming

[7]Diamond International Corp., Calmar Div., City of Industry, CA 91749.

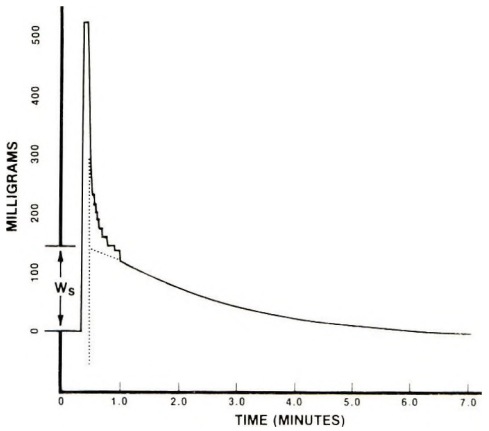

Figure 5. Pickup measurements by strain gauge apparatus. Fixative solution deposited on hair swatch (milligrams) *vs.* time

the solvent evaporation rate was constant over the first part of the drying curve, extrapolation of the curve yielded a wet solution pickup weight (W_s). Resin pickup was determined by the following formula:

$$\text{Resin Pickup}\,(\%) = \frac{W_s\,S}{W_h} \times 100 \qquad \text{(III)}$$

W_s = weight (grams) of solution picked up
S = per cent fixative solids (by weight) in the test solution
W_h = weight (grams) of swatch

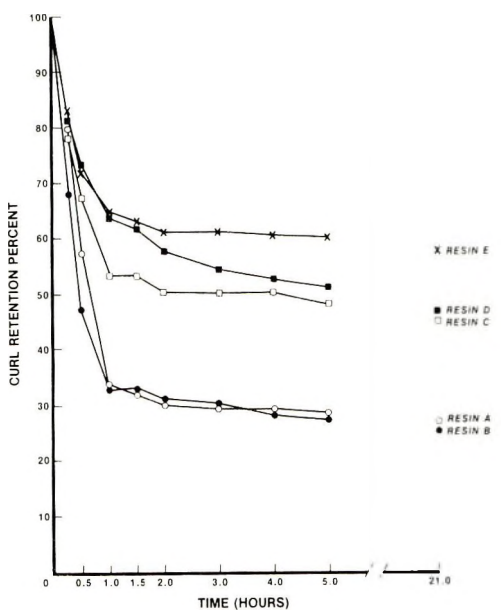

Figure 6. Curl Retention Analysis—Set I—Average curl retention (per cent) as a function of time (hours) for 2 per cent solutions of Resin A, B, C, D and E at 90 percent R.H., 22°C

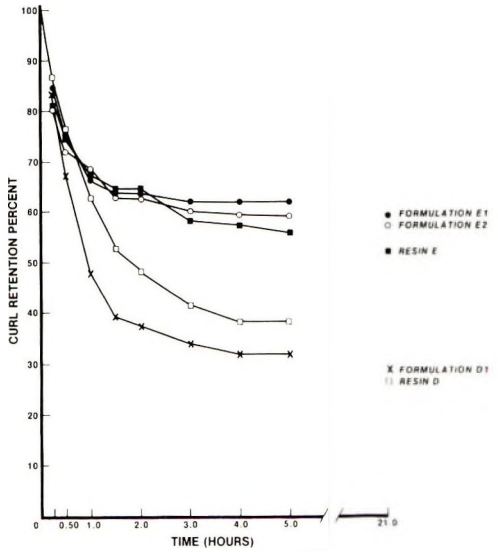

Figure 7. Curl Retention Analysis—Set II—Average curl retention (per cent) as a function of time (hours) for 2 per cent solutions of Resins D, E and Formulations D1, E1, E2 at 90 per cent R.H., 22°C

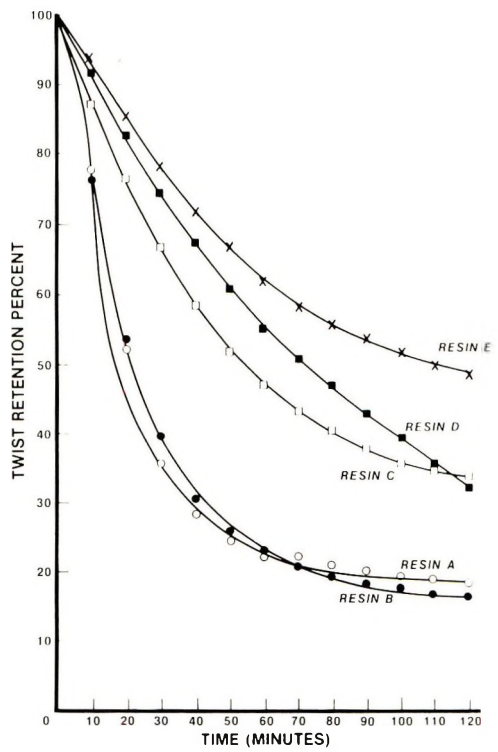

Figure 8. Twist Retention Analysis—Set I—Average Twist Retention as a function of time (minutes) for Resin A, B, C, D, and E at 90 to 93 per cent R.H., 21 to 25°C, and 2 per cent fixative solids (0.19 per cent pickup)

CURL RETENTION ANALYSIS—SET I

Resins A through E were evaluated by Curl Retention for 21 hr. Fourteen replicates were used to insure maximum statistical significance. Plots of average curl retention (per cent) versus time are shown in Figure 6.

CURL RETENTION ANALYSIS—SET II

Resin D, E and Formulation D1, E1, E2 were evaluated by Curl Retention for 21 hr using 7 duplicate samples. Plots of average curl retention (per cent) versus time are shown in Figure 7.

TWIST RETENTION ANALYSIS—SET I

Resins A through E were evaluated by TRA using 2 per cent resin solutions. The results from 5 replicates were averaged and plotted against time (Fig. 8).

TWIST RETENTION ANALYSIS—SET II

Resins D, E and Formulations D1, E1 and E2 were evaluated by TRA using 2 per cent resin solution. The results from 2 replicates were averaged and plotted against time (Fig. 9).

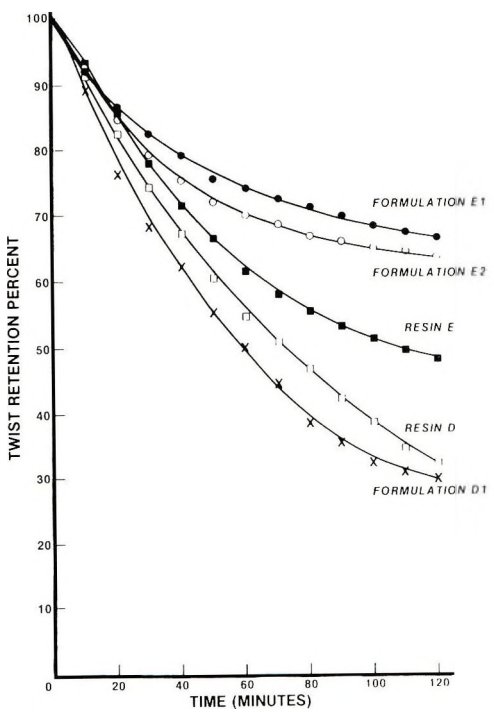

Figure 9. Twist Retention Analysis—Set II—Average Twist Retention as a function of time for Resins D, E and Formulations D1, E1, E2 at 90 to 93 per cent R.H., 21 to 25°C and 2 per cent fixative solids (0.19 per cent pickup)

RESULTS AND DISCUSSIONS

TWIST RETENTION ANALYSIS—TEST VARIABLES

During the study of Twist Retention Analysis, a number of variables were investigated, *i.e.*, the weight of hair per swatch, amount of applied twist, air flow rate, and swatch reuse characteristics after shampooing.

It was found that at a fixed degree of twist, as the number of hair fibers (weight) per swatch was increased, the Twist Retention increased. This was reasonable since, as the number of hair fibers in the sample is increased, the number of cross-over points per unit length was also increased. This resulted in an increased number of hair-to-hair bonding sites. To eliminate hair weight as a test variable, a constant weight of 0.20 to 0.21 g per swatch was selected.

The amount of applied twist was varied and studied between 180 and 900 degrees in 180 degree increments. Five replicate samples were evaluated at each twist increment and statistically compared. As the twist was increased, the coefficient of variation (Formula IV) decreased (increased precision) and was minimized above 540 degrees. An applied twist of 720 degrees was selected as optimum.

Air flow rate was varied between 15 and 200 ml/min. Flow rates below 40 ml/min gave rise to non-reproducible results, while the flow rates above 55 ml/min gave constant Twist Retention/time relationships. Sample-to-sample reproducibility at 40 ml/min or below was poor, while at or above 55 ml/min it was significantly (acceptably) improved. Under low flow rate conditions it is suspected that the hair/fixative composite partially dehydrates the air, giving a non-reproducible Twist Retention response.

Swatches were tested after 20 fixative application/shampoo cycles to study the effect of possible swatch deterioration. No significant differences were observed between the first and the last shampoo cycle. Swatches were, however, discarded after 20 shampoo cycles.

STATISTICAL ANALYSIS

Resins A through E, evaluated by both Curl and Twist Retention Analysis—Set I, were compared using standard statistical techniques. Coefficient of variation, correlation coefficients, and confidence of difference between resins were calculatd as a function of time.

TABLE II

COEFFICIENT of VARIATION

RESIN	TWIST RETENTION SET I *AVERAGE OVERALL TIME INTERVALS*	CURL RETENTION SET I *AVERAGE OVERALL TIME INTERVALS*
A	9.2	17.1
B	10.7	20.5
C	9.1	24.2
D	7.9	20.0
E	4.7	11.9

TABLE III

CORRELATION COEFFICIENT [a]

TWIST RETENTION ANALYSIS - SET I

VS.

CURL RETENTION ANALYSIS - SET I

CURL RETENTION TIME (HOURS)	TWIST RETENTION TIME (MINUTES)											
	10	20	30	40	50	60	70	80	90	100	110	120
0.25	261	335	357	338	317	303	289	282	276	282	294	305
0.50	43	62	76	70	68	68	69	75	90	111	140	165
1.00	38	6	4	5	6	7	10	15	29	47	72	95
1.50	4	2	3	2	3	6	9	15	29	46	70	42
2.00	4	3	3	1	0	1	3	6	16	29	48	66
3.00	7	6	6	4	2	1	2	3	9	17	31	46
4.00	10	11	11	8	5	3	3	2	5	11	23	35
5.00	11	14	14	11	6	4	3	2	3	8	19	30
21.00	22	30	30	25	17	12	9	6	2	2	7	15

a - VALUES REPORTED AS $=(1-r) \times 10^3 = C_{xy}$

Coefficient of variation (Formula IV) was computed as a function of time for each resin (the higher the coefficient of variation the less reproducible the test procedure).

$$\text{Coefficient of variation } (\%) = \frac{S_t}{X_t} \times 100 \qquad \text{(IV)}$$

S_t = Standard deviation at time (t)
X_t = Average Twist or Curl Retention per cent at time (t)

Coefficients of variation for Twist Retention Analysis and Curl Retention Analysis are shown in Table II. TRA coefficients of variation for each fixative are approximately one-half of those for Curl Retention Analysis, indicating significantly less variability.

Table III shows corrected correlation coefficients (C_{xy}) (Formula V) at various time comparisons between the tests.

$$C_{xy} = (1 - r_{xy}) \times 100 \qquad \text{(V)}$$

C_{xy} = corrected correlation coefficient between Twist Retention at time (x) and Curl Retention at time (y)
r_{xy} = correlation coefficient between Twist Retention at time (x) and Curl Retention at time (y)

The region of best fit between the two methods of analysis is shaded in Table III. Corrected correlation coefficients of five or less are shaded. (These are correlation coefficients of 0.995 or greater.) TRA after short times was observed to correlate best

TABLE IV

CONFIDENCE of DIFFERENCE BETWEEN RESIN PAIRS

TWIST RETENTION - SET I vs. CURL RETENTION - SET I

(MINIMUM TIME TO OBTAIN 95% and 99% CONFIDENCE)

	TWIST RETENTION ANALYSIS		CURL RETENTION ANALYSIS	
	MINIMUM TIME (MINUTES)		*MINIMUM TIME (MINUTES)*	
RESIN PAIR	**95%**	**99%**	**95%**	**99%**
A-B	>120	>120	>1260	>1260
A-C	10	10	30	60
A-D	10	10	30	30
A-E	10	10	30	30
B-C	10	10	15	15
B-D	10	10	15	15
B-E	10	10	15	15
C-D	>10 <70	>10 <20	>60 <90	>1260
C-E	10	10	60	180
D-E	60	80	240	1260

to Curl Retention Analysis after extended times. As an example, Twist Retention Analysis after 90 to 100 min correlates to Curl Retention Analysis after 21 hr.

Confidence of difference between Resin pairs (probability that one fixative has improved performance over another) was calculated as a function of time. The time required for one fixative to show improved performance over another at 95 per cent and 99 per cent confidence was recorded for each Retention test as shown in Table IV. (Confidence intervals of 95 per cent and 99 per cent are commonly chosen to relate to significant and highly significant differences respectively.) For each Resin pair, where differences were observed, Twist Retention required a shorter time than Curl Retention to reach 95 per cent and 99 per cent confidence. As an example, Resin pair D-E required only 80 min with TRA to achieve 99 per cent, while Curl Retention Analysis required 1260 min.

RESIN PICKUP MEASUREMENTS

Average fixative pickup values for Resins A through E and Formulations D1, E1 and E2 were determined. Pickup values of 0.04 per cent, 0.09 per cent, 0.19 per cent and 0.43 per cent correspond to 0.50 per cent, 1.0 per cent, 2.0 per cent and 4.0 per cent fixative solution concentrations. These pickup values at a given solution concentration were found to be independent of resin type in the fixative composition.

TWIST RETENTION VERSUS FIXATIVE PICKUP

Resin E was tested by Twist Retention Analysis at average pickups of 0.04 per cent, 0.09 per cent and 0.43 per cent (Fig. 10). Decreasing pickup showed significantly faster

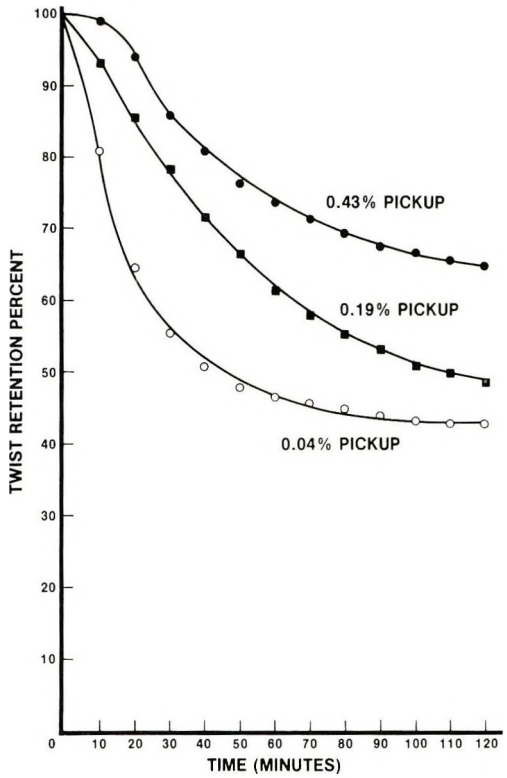

Figure 10. Twist Retention per cent *vs.* time for Resin E at 0.04 per cent, 0.19 per cent, 0.43 per cent pickup (weight) on hair

rates of untwisting as a function of time, indicating the necessity for maintaining constant pickup when making fixative comparisons.

FIXATIVE FORMULATION WITH PLASTICIZER

Resins D and E, formulated with 15 per cent plasticizer (by weight) were evaluated by both Twist and Curl Retention Analysis (Figs. 7, 9). Statistical comparisons (correlation coefficient) showed excellent agreement between the two tests.

Twist Retention Analysis, employing only two replicate samples per fixative, was able to determine differences between fixative pairs E–E1 and E–E2 at a 99 per cent confidence interval after 80 min. Curl Retention Analysis, employing seven replicate samples per fixative, was not able to distinguish a significant difference at the 95 per cent confidence level, even after 21 hr.

CONCLUSIONS AND SUMMARY

A new laboratory test, Twist Retention Analysis (TRA) was described as a tool to evaluate fixative performance on hair with the use of a Torsional Braid Analyzer. Statistical correlation between TRA and classical Curl Retention Analysis was shown to be excellent (correlation coefficients of 0.995 or greater). Curl Retention Analysis re-

quired a large sample population (*i.e.*, 7 to 15 replicates) while TRA sample population could be as small as two replicates.

It is suggested that sources of error in Curl Retention Analysis are primarily a result of physical handling of curls during test preparation and the use of visual observations to record results. The technique of swatch preparation in the TRA procedure is felt to provide a sample with greater uniformity. Additionally, the TRA method maintains precise control of air flow and an automated output of sample response.

Twist Retention method of analysis was shown to give statistical correlation (after 90 to 100 min) to long-term (5 to 21 hr) Curl Retention testing. Use of this new test significantly decreases the testing time required to evaluate fixative performance on hair. Valid conclusions of fixative differences (to 95 per cent and 99 per cent confidence) were made much faster by Twist Retention Analysis.

Twist Retention Analysis was able to distinguish statistical differences between fixatives (*i.e.*, Formulations E1 and E2 compared to Resin E) where Curl Retention Analysis could not. It is felt that fixative differences that heretofore might have been overlooked can now be determined.

This paper confirms Bogaty's (5) findings that torsional forces are important in the setting of hair on the head. The statistical correlation of the new test, which induces solely torsional-stresses to a hair swatch, to the performance of curled hair swatches seems to imply, in fact, that torsional stress is one of the most important factors determining the performance of set hair.

Modern day life-styles have required curl holding performance of hair fixatives to function over extended periods of time. More and more consumers are requiring a hair fixative to hold a set with one application or less per day. Until the development of the described test it could take up to 24 hr to evaluate hair fixative performance under humid conditions. With the TRA method, meaningful results can be obtained in less than 2 hr.

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Topical moisturizers: quantification of their effect on superficial facial lines

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Synopsis

This single-blind study was designed to test a new method of QUANTITATIVE EVALUATION as used by trained judges to visually assess changes in SUPERFICIAL FACIAL LINES (SFL's) following the application of topical MOISTURIZERS. The method consists of a system for reproducible scoring of these lines, based on ratings for their frequency times their depth, by component area of the face. Controlled half-face comparisons in five test series involving no treatment, water, and four moisturizers revealed that:

1. The method provided good reproducibility of baseline SFL values, and of changes in these values through time upon repetition of the same treatment in different series.
2. The method also provided values for the distribution of SFL's by facial area, and values indicating a differing response of facial areas to applications of moisturizers. The greatest per cent reductions were noted for SFL's around the eyes, followed by lines around the cheek and mouth. Lines on the forehead and chin changed noticeably less.
3. With quantitative evaluation, trained judges can produce a reliable rank ordering of more effective treatments, less effective ones, and control treatments such as water or no treatment.

INTRODUCTION

Recent articles (1,2) attest to the growing importance of regulatory and consumer interest in regard to cosmetic products. Current focus primarily pertains to the substantiation of safety. However, it is plausible to expect that a requirement such as declaration of ingredients will cause the consumer to be more conscious than previously of these ingredients' contribution to performance. Thus, demonstrated proof of performance may well come to play a greater role in product differentiation. In that interplay between the market shaping the product and the product shaping its market,

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one can readily imagine that increased consumer awareness of cosmetic effectiveness will result in greater emphasis on it by those firms able to demonstrate the action of their products.

For that, it will be necessary to have available a range of scientifically valid, controlled investigatory procedures for cosmetics, as well as toiletries, comparable in its way to that range of procedures developed previously for drug products. For cosmetics and toiletries, the problem is complicated by the fact that we usually are dealing with short-term actions, meaningful to the extent that they are perceived by the user, and yet subject to the user's expectations.

Among the approaches developed to define these actions are evaluation of changes in skin condition by an expert observer (3,4) and by use of instrumental means (5–7) after the application of lotions or moisturizers. In a concurrent article (8), we describe utilization of consumers who have not been trained as cosmetic evaluators to assess perceived overall effect of topical facial moisturizers on a separate group of subjects, and to do so within the format of the controlled study.

In this article, we describe a controlled trial of a different technique by which two trained judges under the supervision of a clinical researcher (by visual assessment) can quantify in detail the effect of topical moisturizers on superficial facial lines (SFL's).

EXPERIMENTAL

TECHNIQUE

The method was developed as a reproducible scoring system for the assessment of visually perceived changes in the kind of lines (superficial facial lines) that temporarily respond to treatment with effective topical moisturizers, as contrasted to the deeper lines and more pronounced wrinkles that do not respond. Each half of the face was divided into its four component areas (forehead, beside and under the eyes, cheek and mouth, chin—see Fig. 1) to increase the accuracy of scoring and to define responses by individual area.

To determine the SFL score in each area, two judges were trained as noted below. Each judge, working separately, assigns a descriptive rating (very shallow, shallow, and deeper) for each SFL in an area, groups the SFL's by descriptive rating, and then multiplies, according to the numerical scales below, the frequency rating times the depth rating for each type of SFL. The values for all SFL's in an area are then summed.

SFL score per area = *Frequency Rating*	times	*Depth Rating*
0 (no SFL's)		1 (very shallow)
1 (1 or 2 SFL's)		
2 (3 or 4 SFL's)		2 (shallow)
3 (5 or 6 SFL's)		
4 (more than 6 SFL's)		3 (deeper)

Use of this five-point (0–4) frequency rating scale prevents changes in a large number of very trivial lines from producing a skewed positive effect.

For example, if a component area had 4 very shallow, 2 shallow, and 1 deeper SFL's, the SFL score for that area would be:

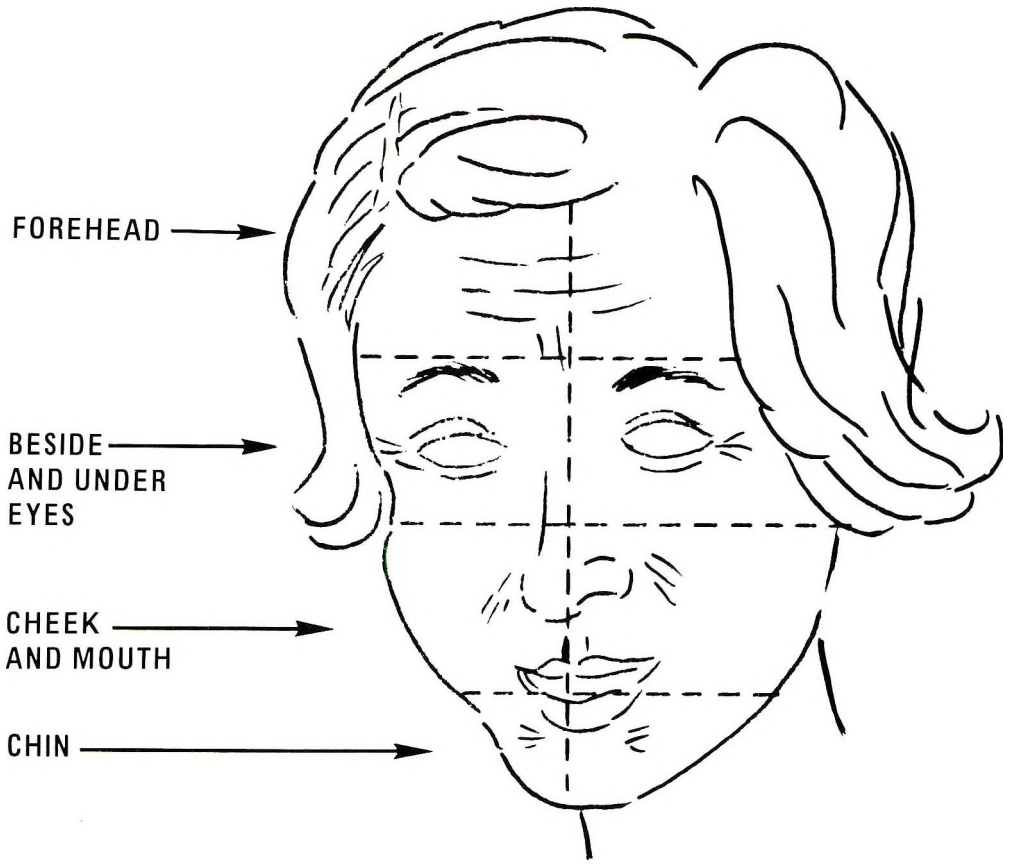

Figure 1. Scoring areas of the face

Number and depth	*Frequency Rating*	× *Depth Rating*	= *Score*
4 very shallow	2	1	2
2 shallow	1	2	2
1 deeper	1	3	3
		SFL score for the area =	7

The scores for the four component areas are summed to arrive at the score for the full half-face.

Two judges instead of one were used to provide a check on observer variation. Their training, conducted by a dermatologist, was intended to ensure uniform conditions of evaluation, such as equivalent definition of the individual facial areas from subject to subject, correct determination of frequency and depth under uniform conditions of lighting (from above) and distance (2 ft), accurate classification of lines as very shallow, shallow, deeper, or else as not SFL's, and familiarity with the requirements of a controlled scientific investigation. Both judges possessed normal visual acuity, relied on no magnification, and evaluated independently of each other without knowing the nature of the treatments used.

SUBJECTS

Twenty women, from 30 to 65 years old, were chosen for the study after initial determination that they were free of influencing diseases or allergies, and had SFL scores for the full face of 20 minimum and preferably 30 or moderately higher. This range of ages and scores excluded individuals with too few lines or with more lines than are representative of the general population. Each subject took part in each of the test series described below.

STUDY DESIGN

This half-face, single-blind study comprised five test series as follows:

Series I	No treatment *vs.* water
Series II	Moisturizer O *vs.* water
Series III	Moisturizer O *vs.* Moisture Lotion ML
Series IV	Moisturizer O *vs.* Moisture Film MF
Series V	Moisturizer O *vs.* Lotion L.[1]

We defined the extent of reproducibility in four different ways: 1. via comparison of baseline values by facial area and full half-face on Day 0 (no treatment) for the group of 5 series; 2. via comparison of baseline values on Day 0 for individual test series; 3. via comparison of inter-observer variation on the no-treatment day; 4. via comparison of the reductions achieved when the same moisturizer (O) was used in four of the test series. Once assured as to the reliability of the method, we could then test its sensitivity by examining any differing responses through time of individual facial areas in conjunction with application of the moisturizers, water, or no treatment.

TREATMENT AND EVALUATION SCHEDULES

Each series consisted of an initial no-treatment day, followed by three successive treatment days (Days 1, 2, 3). Application of the coded treatments was randomized by side of the face, through the study group, and through all test series. Test agents were applied on each treatment day to the designated half-face in the morning after the 0-hr evaluation and in the evening after the 10-hr evaluation, with the appropriate follow-up to ensure that the correct coded preparation had been used in accordance with the randomization instructions. The subjects did not use any other cosmetics or toiletries on the study areas. The SFL's were rated by the two trained judges at 0, 3, 6, and 10 hr on each no-treatment and treatment day, in accordance with the system described above. Three or more nonstudy days elapsed between treatment series to allow SFL values to return to baseline. This study took place in the fall (mid-October to December) to avoid the complicating effects of warm weather.

[1] O is Oil of Olay® (Olay Company, Inc., Wilton, Conn. 06897), containing a blend of fatty alcohols (cetyl, myristyl, and stearyl), cetyl palmitate, sodium and potassium laurates, myristates, stearates, and palmitates, mineral and castor oils, and cholesterol, in a preserved and fragranced vehicle, ML, MF, and L are marketed oil-in-water emulsions.

Table I
Baseline (*No Treatment*) Reproducibility by Facial Area SFL Score Ranges, Day 0 (All Series)

Facial Area	0 hr	3 hr	6 hr	10 hr
Forehead	4.1–4.7	4.1–4.6	4.1–4.6	4.1–4.6
Around the Eyes	7.4–8.0	7.2–7.9	7.2–8.0	7.4–8.0
Cheek and Mouth	3.9–4.2	3.8–4.2	3.9–4.1	3.9–4.2
Chin	2.3–2.8	2.2–2.7	2.2–2.7	2.2–2.8
Full half-face	17.7–19.7	17.3–19.4	17.4–19.4	17.6–19.6

RESULTS

1. REPRODUCIBILITY OF THE METHOD

Baseine values by facial areas and full half-face. Table I shows the ranges for both judges' separate scores on Day 0, averaged for the 20 subjects over the 5-test series. The ranges differed among the different facial areas, but for a particular area or for the full half-face they varied relatively little.

Baseline values by test series. Table II shows the summed scores of both judges for the full half-face, by individual test series for the no-treatment day. These scores range from a high of 38.3 to a low of 35.4.

Baseline values by judge. In Table III, the above scores are broken down by individual judge (shown for one side of the face only, for convenience) to depict the level of inter-observer variation on the no-treatment day. The scores for the other side showed a similar range of variation.

Effect of the same agent through multiple series. Use of the same moisturizer (O, Olay) in four series (II, III, IV, V) provided a test of reproducibility among series, when the values at successive time intervals within a particular series were changing. A similar pattern of change through time was detected in the 4 series, as can be seen from Table IV.

Table II
Baseline (*No Treatment*) Reproducibility by Test Series Summed SFL Scores (Both Judges), Day 0 of Each Series

		0 hr	3 hr	6 hr	10 hr
Series I	Half-face	38.3	37.9	37.9	38.2
	Opposite half-face	38.1	37.9	37.5	37.6
Series II	Half-face	35.9	35.5	35.4	35.7
	Opposite half-face	35.9	35.5	35.5	36.0
Series III	Half-face	37.0	36.0	35.8	36.5
	Opposite half-face	37.2	37.0	36.9	37.2
Series IV	Half-face	36.9	36.2	36.3	37.0
	Opposite half-face	38.1	37.9	37.8	38.0
Series V	Half-face	37.0	36.3	36.2	36.9
	Opposite half-face	38.2	37.9	38.0	38.0
	Average	37.3	36.8	36.7	37.1
	± SD	±2.7	±3.1	±3.1	±2.5

Table III
Baseline (*No Treatment*) Reproducibility by Judge SFL Scores (Half-Face), Day 0 of Each Series

		0 hr	3 hr	6 hr	10 hr
Series I	(Judge 1)	19.2	19.0	18.8	19.1
	(Judge 2)	19.1	18.9	19.1	19.1
Series II	(Judge 1)	18.0	17.8	17.6	17.8
	(Judge 2)	17.9	17.7	17.8	17.9
Series III	(Judge 1)	18.8	18.3	18.1	18.5
	(Judge 2)	18.2	17.7	17.7	18.1
Series IV	(Judge 1)	18.7	18.4	18.4	18.6
	(Judge 2)	18.2	17.8	17.9	19.1
Series V	(Judge 1)	18.9	18.7	18.4	18.4
	(Judge 2)	18.1	17.7	17.8	18.1

Table IV
Reproducibility—Effect of the Same Agent Through 4 Series Summed SFL Scores (Both Judges), Average of Days 1, 2, 3

	0 hr	3 hr	6 hr	10 hr
Series II	36.5	28.7	29.1	34.7
Series III	37.8	29.3	29.9	36.0
Series IV	37.6	29.6	30.0	35.7
Series V	38.1	29.9	30.4	36.4

II. SENSITIVITY OF THE METHOD: EFFECT OF MOISTURIZERS, WATER, AND NO TREATMENT

Results by facial area. Table V presents the per cent reductions in SFL's achieved by the various treatments, as well as the considerable variation in response by particular areas. For the two moisturizers that proved more effective, SFL's around the eyes showed the greatest reductions, followed by those in the cheek and mouth area. Lines on the forehead and chin responded noticeably less. The results for the two less effective

Table V
% Reduction in SFL's by Facial Area Average of 3 Days

Time after Application	Facial Area	Moisturizers				Water	No Treatment
		O	ML	MF	L		
3 hr	Forehead	8	4	3	3	1	0
3 hr	Around the Eyes	32	20	8	5	7	2
3 hr	Cheek and Mouth	26	15	7	5	7	2
3 hr	Chin	9	6	10	7	4	4
6 hr	Forehead	8	3	3	2	1	0
6 hr	Around the Eyes	30	16	7	4	5	2
6 hr	Cheek and Mouth	23	11	5	5	6	2
6 hr	Chin	7	6	7	6	3	3
10 hr	Forehead	3	1	1	1	0	0
10 hr	Around the Eyes	6	3	2	0	0	1
10 hr	Cheek and Mouth	6	2	1	0	1	1
10 hr	Chin	1	3	4	1	0	3

moisturizers, water, and no treatment were too limited to reveal any pronounced pattern of effect by facial area.

Water had scattered significance against no treatment for the two most responsive areas on individual study days (Wilcoxon matched-pairs signed-ranks test). Comparison of the moisturizers against water was made possible with the Friedman two-way analysis of variance by ranks. Moisturizers MF and L had no significant effects against water; moisturizer ML produced occasional significance ($P < 0.05$) at 3- or 6-hr intervals; moisturizer O was always significant ($P < 0.01$) at the eye and cheek/mouth areas at 3 and 6 hr on Days 1, 2, and 3, with frequent significance ($P < 0.05$ or better) against water at 10 hr.

Figure 2 depicts the progression through time for the most responsive facial area. As with the other areas, the peak effects recorded were at 3 hr. They continued with relatively little decrease by 6 hr, and gradually declined thereafter.

Results by full half-face. The average reductions for the full half-face represent not only the summation of the trained judges' observations, but they also represent overall effect across all four facial areas. Table VI shows these results.

Water had scattered significance against no treatment on individual treatment days; moisturizers MF and L had none against water. Moisturizer ML was occasionally significant ($P < 0.05$) against water (at 3 hr on Days 1, 2, and 3, at 6 hr on Day 3). Moisturizer O was always significant ($P < 0.01$) against water at 3 and 6 hr on all treatment days, and usually at 10 hr ($P < 0.01$ on Day 1 and $P < 0.05$ on Day 2).

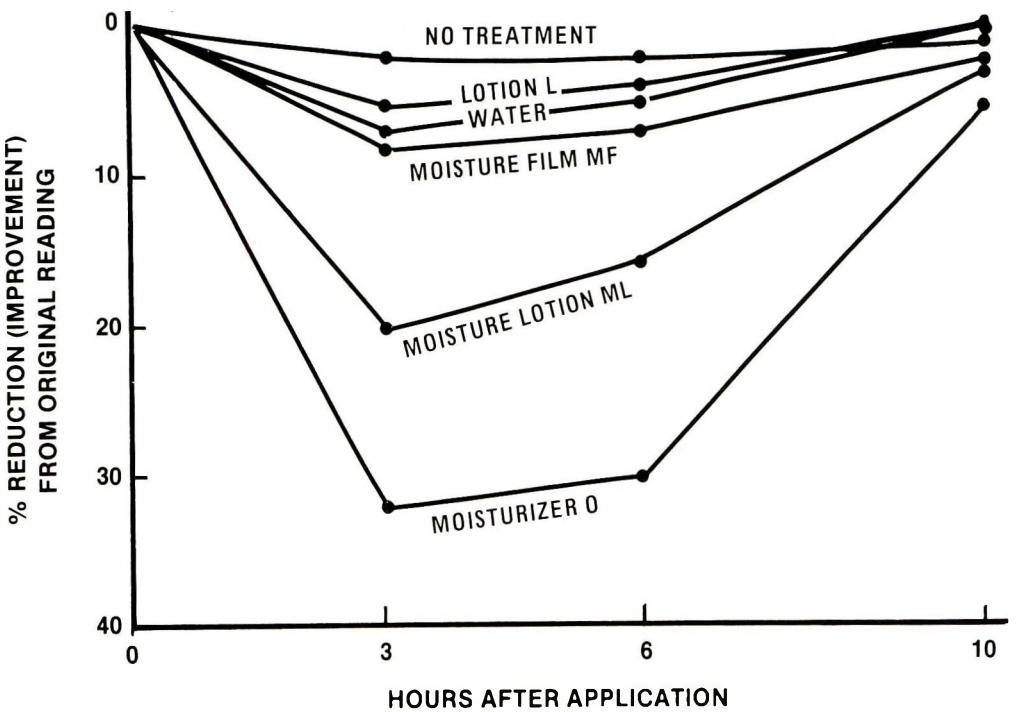

Figure 2. Per cent reduction in superficial facial lines *for the eye area.* Average values for three days of application, 20 subjects

Table VI
% Reduction in SFL's by Full Half-Face Average of 3 Days

Time after Application	Moisturizers				Water	No Treatment
	O	ML	MF	L		
3 hr	22	13	7	5	5	2
6 hr	20	11	6	4	4	2
10 hr	5	3	1	0	1	1

Figure 3 shows that overall, as with individual areas, each comparison agent displayed a similar progression through time, even though the extent of any one agent's results differed from those of other treatments.

DISCUSSION

Our goal was to develop direct visual assessment of moisturizer effect on superficial facial lines into a quantitative and methodologically objective technique. The present study with its five series, six comparison treatments, annd four component areas of the face to be evaluated was necessarily a somewhat complex one. However, this complexity permitted the comprehensive test of reproducibility and sensitivity required for a new method of evaluation.

A satisfactory level of reproducibility was ascertained through three kinds of tests in the usual static situation of baseline values (by facial area and full half-face, by series, by observer), and through the more rigorous test of seeking comparable patterns in a dynamic situation (*i.e.*, comparability of the changes produced by the same agent in four separate series).

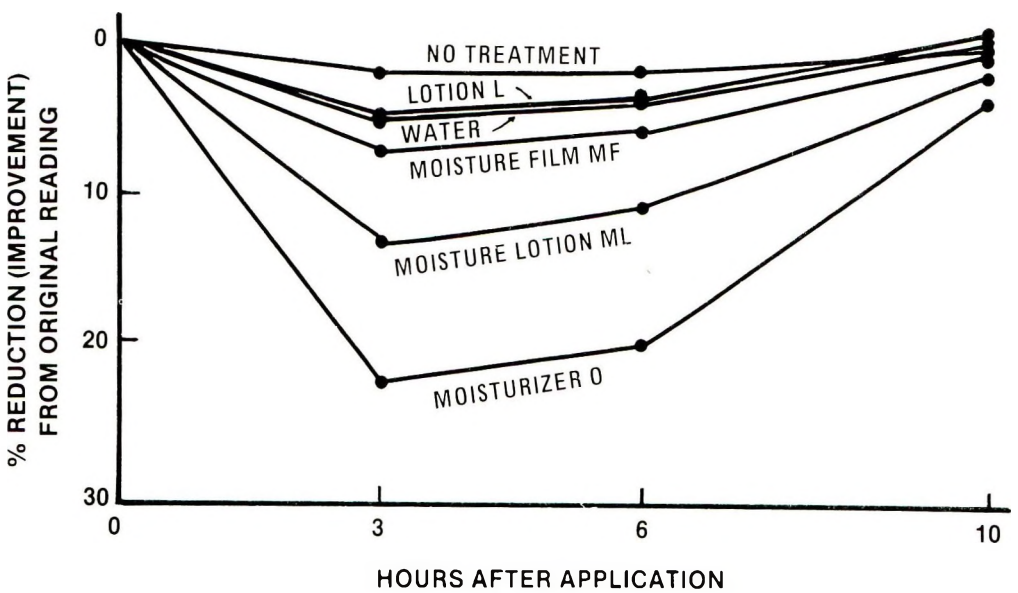

Figure 3. Per cent reduction in superficial facial lines *for the full half-face.* Average values for three days of application, 20 subjects

This confirmation of reproducibility has several implications for practical investigational work. It means that the visual appraisals of trained observers can be reliably quantified; that SFL's can be measured and their distribution by facial area determined; that the values for SFL's can remain relatively stable in the absence of treatment or of climatic change; and that these values change consistently in response to a particular treatment.

Sensitivity of the method was examined through comparison of the effects of different treatments. The blinded judges were able to discriminate among the six treatments, and to define their effects by facial area. As a particular test of sensitivity, a coherent pattern could be discerned even among the lesser results from no treatment, water, and the two moisturizers less effective in this study. Starting with the lowest percentage of reductions (*i.e.*, improvement) in SFL's after no treatment, there was then slightly more improvement for water and one moisturizer, followed by somewhat more improve-

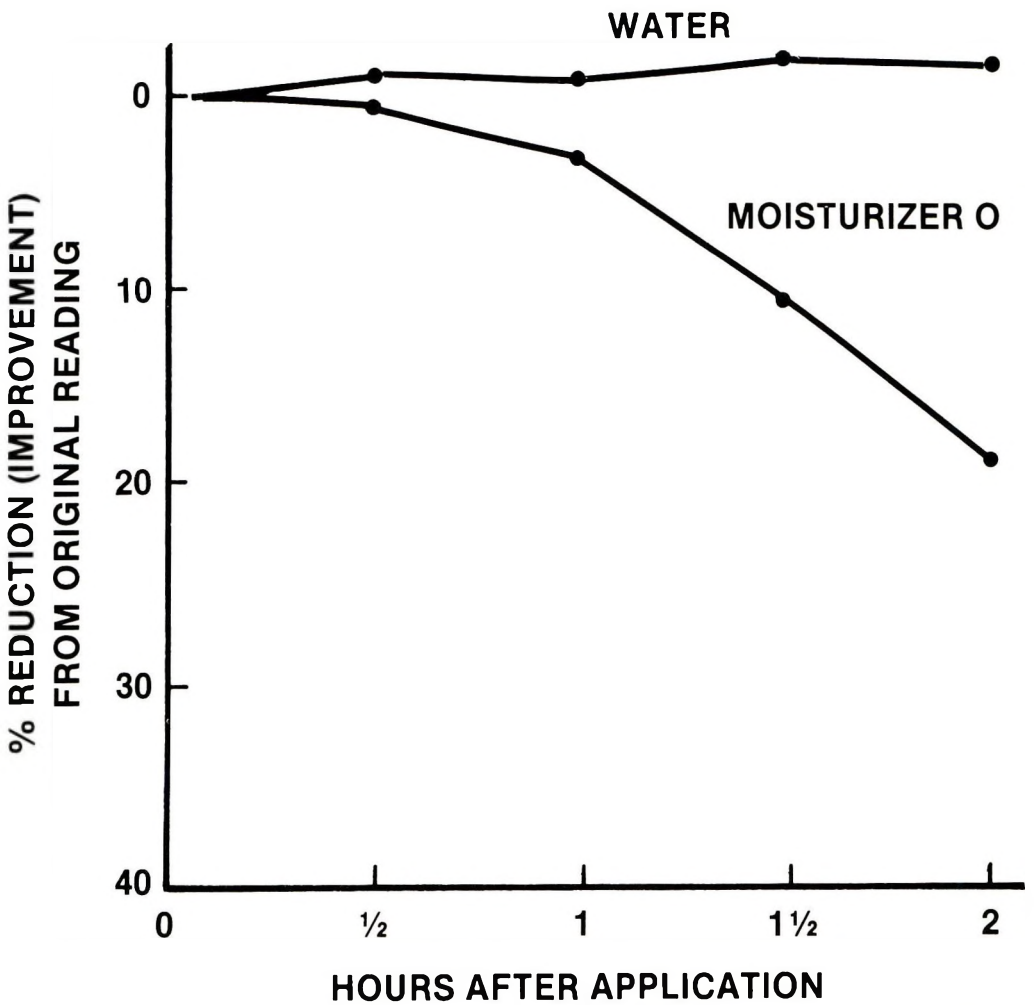

Figure 4. Determination of the time of onset of action. Per cent reduction in superficial facial lines for the eye and cheek areas. Average values for ten subjects

ment from the other moisturizer (Tables V and VI). These improvements moderated over time in a consistent manner. The pattern of change over the 10 hr is most clearly evident in Figs. 2 and 3 in the results for the two more effective moisturizers.

This led us, as a follow-up to our study, to investigate the pattern of the onset of action, with examination of the facial areas found to respond best (around the eyes and on the cheeks). Baseline SFL scores were quantified in accordance with the method described previously in ten subjects, who then applied water to one half-face and the most active moisturizer (O) to the other half-face. Two judges than independently evaluated the results every half-hour for 2 hr. Figure 4 shows that for the active treatment, reductions in SFL's began to be apparent at 1½ hr. They did not attain statistical significance against baseline until 2 hr ($P < 0.01$ around the eyes, $P < 0.05$ on the cheeks). The reductions at 2 hr were not as extensive as those recorded in the main part of our study at 3 hr, thus indicating that maximum effect occurs around 2 to 3 hr after each application.

Onset of action was slower than had been anticipated which suggests that significant reduction in SFL's by an effective moisturizer may require sufficient time for significant penetration.

This study, with detailed quantitative appraisal by two trained judges, yielded a rank order of treatments (O, ML, MF, water, L, no treatment) that provided an independent reference standard against which to compare the ranking (O, ML, MF, L, water, no treatment) from our subsequent study (8), in which a panel of untrained consumers qualitatively evaluated the overall effect of these same moisturizers in a separate group of subjects.

The results deriving from these two different methods showed certain major similarities, confirming that an untrained consumer panel could perceive qualitatively the same differences in moisturizer activity that the two trained judges ascertained quantitatively. Both methods detected and confirmed similar differences among most of the comparison treatments. Namely, both studies:

1. found O and ML to be the more effective moisturizers. The two judges determined O to be significantly more effective than ML, whereas the panel ascertained a trend toward O being more effective;
2. found MF and L to be less effective moisturizers;
3. found that water and L differed by only a few points, and thus the two studies varied in their ranking of these two treatments;
4. ranked all moisturizers and water more highly than no treatment.

The method and detailed results of the controlled panel study are described in the following article.

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CALL FOR PAPERS

1978 ANNUAL SCIENTIFIC MEETING SOCIETY OF COSMETIC CHEMISTS

Prospective authors are asked to submit abstracts of papers of 200 words or less **immediately** for the 1978 Annual Scientific Meeting of the Society of Cosmetic Chemists to be held November 30th and December 1st, at The Waldorf-Astoria in New York City.

The Program Co-Chairmen, Robert Raymond and Dr. Peter Sgaramella, have issued a Call for Papers; the subject for the papers is open. All abstracts of papers should be sent to either the Program Co-Chairmen or the SCC office at: Society of Cosmetic Chemists, 50 East 41st Street, New York, NY 10017.

The Society of Cosmetic Chemists Award sponsored by Perry Brothers, Division of Mallinckrodt, will be awarded to the best paper presented at the Annual Scientific Meeting. The award will be $1,000. In addition, if the special panel choosing the awardee feels that other papers are deserving of special recognition, they may, at their discretion and with the approval of the Board of Directors of the Society, present one or two additional awards of $500 each to papers designated as Honorable Mentions.

To be considered for the awards, all papers must be submitted to the award committee in manuscript form at least 4 weeks prior to the actual presentation. November 1st is the deadline for the 1978 Annual Meeting. The award committee will consider relevance to our industry, originality and presentation in choosing an awardee.

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The panel study as a scientifically controlled investigation: moisturizers and superficial facial lines

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Synopsis

Characteristic features of the CONTROLLED STUDY (randomized treatment, comparison agent, blinded evaluation) were incorporated into a panel investigation of the objective effects of five topical MOISTURIZERS, water, or no treatment on SUPERFICIAL FACIAL LINES, as perceived by a 12-member untrained CONSUMER EVALUATION PANEL, assessing the skin of a separate group of subjects who used the test materials. The method proved sufficiently sensitive in almost 900 single-blind, half-face comparative evaluations to demonstrate that:

1. Under the conditions of the scientific investigation, a consumer panel composed of normal users who have not been trained as professional evaluators can detect and visually evaluate the effect of moisturizers on other consumers, thereby providing an important estimate of consumer relevance to cosmetic performance.
2. The technique is sensitive enough to detect the differing degrees of performance that existed among the various treatments.
3. Three of the five moisturizers studied were significantly superior to water, which in turn was assessed more favorably than no treatment.
4. The extent of effectiveness existing for a particular cosmetic tended to prevail throughout the study group and was not concentrated in particular subjects.

INTRODUCTION

The evaluation of a cosmetic preparation, whose benefit is to be perceived by the user, gives rise to a distinctive problem for the investigator. This is different from the clinician's problem of confirming objectively an effect on an organic malfunction, perhaps a condition improved by an action not readily perceived subjectively by the

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patient. The cosmetic scientist seeks to confirm the existence of an objectively existing benefit, but it must be a benefit subjectively evident and relevant to consumers, and yet it is to be demonstrated in a scientifically viable manner.

A variety of approaches contributing to resolution of this problem has been developed by previous investigators. For example, decreased moisture loss following the application of creams or lotions has been measured objectively with desiccator assembly strapped against the inner forearm and consisting of a capped glass cylinder containing silica gel (1). Changes in roughness and dryness of the hands after use of a lotion have been assessed by an expert observer with a subjective scoring system, supplemented by the opinions and preferences of panel members (2). The effects of emollients, soaps, and water on three components of smoothness have been evaluated instrumentally via measurement of friction with a dynamometer, of topography with stylus displacement, and of scratch hardness with a variable-load stylus (3). The dynamometer has also been used to measure viscoelastic properties of skin *in vivo* and *in vitro,* following application of water, water vapor, or an emollient, through the skin's response to shearing stress, as displayed in hysteresis loops on an oscilloscope screen (4). A single-blind study of baby oil as a moisturizer on subjects selected for rough or scaly skin of the elbows, knees, heels, and tibia involved evaluation by a clinical investigator with a five-point rating scale, together with review of photographs for some subjects (5).

Our particular objective was to investigate the hydrating effect of topical moisturizers on the stratum corneum, as perceived via their action on superficial facial lines, the kind of shallow to very shallow "dry lines," not affecting the dermis, that an effective moisturizer can be expected to minimize temporarily. The term "wrinkles" is broadly used by the general population to include these lines. In accordance with this usage, a recent article on cosmetic dermatology, categorizing surface changes in the facial skin by age, describes all such manifestations as "wrinkles" (6). However, in order to best delineate the area of performance of interest to us, we selected "superficial facial lines" (SFL's) as contrasted to the more pronounced wrinkles, with a deeper, dermal involvement.

The solution described below, to the problem of defining subjectively perceived effect on such lines in objectively valid terms, consisted of designing and conducting a panel study as a controlled scientific study with its features of randomized treatment, a comparison agent, and blinded evaluation. To provide relevance, this evaluation was performed by a nonprofessional and untrained consumer panel acting as the investigators *not of effects on themselves,* as in the classic consumer test, but on a separate group of subjects who used the test materials. Our dual objectives were: 1. to ascertain the feasibility of a panel of consumers functioning effectively within the structured format of the scientific investigation, and 2. to determine the extent to which the effects of five moisturizers [previously observed as having differing degrees of performance by expert judges (7)], water, or no treatment were perceptible to these consumer-investigators.

EXPERIMENTAL

The central consideration in defining the investigational procedure was to keep it within the capabilities of nonprofessional evaluators, while adhering to the requirements of a controlled study.

SUBJECTS

Twelve females, from 30 to 65 years old, free of influencing diseases or allergies, and who regularly used various types of moisturizers, were chosen for the study after preliminary rating by two trained judges (not part of the later, evaluator panel) to determine that they had full-face scores for SFL's of 20 to 30 or moderately higher. As in our previous study (7), this age and score range includes individuals with a moderate number of SFL's and excludes those with so many lines as not to be representative of the average consumer, or those in whom lines would be so minimal as not to define treatment effects. The subjects were also selected for almost equal scores on the right and left sides of the face.

The scoring system used to select subjects for this study has been described in our associated paper on quantification (7). In essence, it makes possible reproducible visual assessment of SFL's. The result is expressed as a numerical value that takes into account the frequency and depth of these lines. This score is a multiple of the frequency rating (graded from 0 to 4) times the depth rating (1 for very shallow, 2 for shallow, 3 for deeper). For greater accuracy, the component areas of the half-face (forehead, beside and under the eyes, cheek and mouth, chin) are rated individually and then summed for each half-face score.

PROCEDURE

The six-test series, completed at the rate of one weekly, consisted of five half-face comparisons of individual moisturizers (code designations O, ML, EF, MF, and L)[1] against an active control (water), and a sixth comparison of water against no treatment. All comparisons were single-blind since the test agents could be coded and randomized but not made physically identical without altering their potential activity. For each weekly test period, the subjects were provided with two coded samples, one for each side of the face. The water was colored and faintly perfumed to mask its identity. Application of the samples was randomized for each side of the face, across subjects, and across the six weeks (*i.e.*, any one weekly test series involved a mix of the six sets of study comparisons).

Following an initial no-treatment day as a washout, the subjects applied the two samples early in the morning and ten hours later. They had been carefully instructed in the technique of achieving complete and reproducible coverage of the half-faces without mix-up or a large excess. No other cosmetics were used on the test areas during the study. After three days of application in careful accordance with their instructions, the subjects returned on Day 4 for judging by each of 12 consumer evaluators 3 hr after a final application in the morning. Our prior research had suggested that 2 to 3 hr after an application is approximately the time of onset of maximum activity of these agents in reducing SFL's.

[1]O is Oil of Olay® (Olay Company, Inc., Wilton, Conn. 06897), containing a blend of fatty alcohols (cetyl, myristyl, and stearyl), cetyl palmitate, sodium and potassium laurates, myristates, stearates, and palmitates, mineral and castor oils, and cholesterol, in a preserved and fragranced vehicle. EF is an experimental formulation containing lipids dispersed in a preserved aqueous vehicle. ML (moisture lotion), MF (moisture film), and L (lotion) are marketed oil-in-water emulsions.

EVALUATORS

Twelve women, 20 to 65 years old, were randomly chosen from regular users of moisturizers. These consumer evaluators did not receive formal training, other than the necessary instruction about procedures. With this panel, the conditions for evaluation could be better standardized than if individual subjects reported on themselves, and individual user bias in such reporting was eliminated.

These 12 judges were to evaluate for overall effect. They were to do so by determining if they could see a difference in appearance between the two sides of the face and, if so, to choose the side with fewer lines and smoother appearance. If both sides were equal in appearance, the evaluators were to so indicate. The subjects were evaluated individually in a random sequence, with separate observation forms, at a uniform distance of 2 ft, under uniform lighting conditions of light from above, with the same interval between test series (one week), and at the same time of day so as to minimize the effect of any daily variation on subjects or judges.

RESULTS

By the end of the 6 weeks, 864 evaluations had been completed, at the rate of 144 appraisals (12 evaluators times 12 subjects) for each weekly test series. The number of judgments favoring a specific treatment, as manifested 3 hr after the last application and as revealed after breaking of the code, is shown in Fig. 1. The major features of

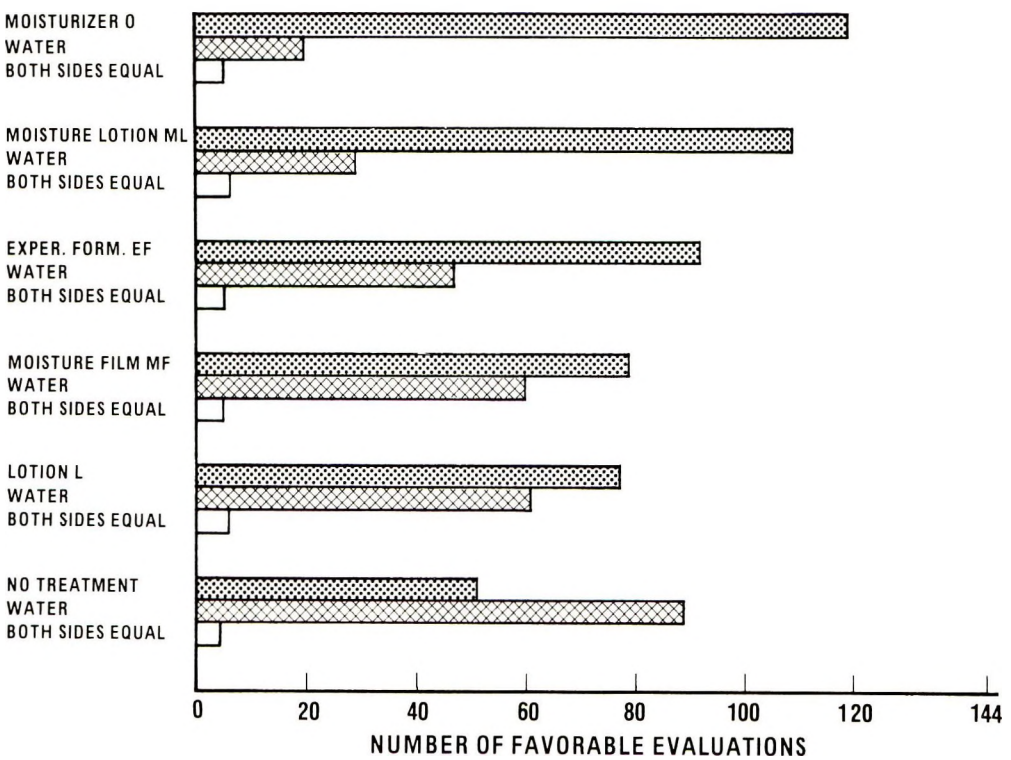

Figure 1. Overall results by treatment (total of 864 single-blind evaluations—144 in each of 6 randomized test series)

these results were:

a) Water was judged to have a perceptible effect and was significantly better ($P < 0.01$) than no treatment. In turn, moisturizers O, ML, and EF were significantly superior to water ($P < 0.001$, $P < 0.001$, and $P < 0.01$ respectively). Moisturizers MF and L were not significantly different from water.

b) A fairly distinct ranking developed in the extent to which any one of these preparations achieved a possible maximum of 144 favorable evaluations when compared against water. In percentage form and in absolute numbers this ranking was as follows:

Identity	Code	% Favorable Evaluations
Oil of Olay®	O	83% (119 out of 144)
Commercial Moisture Lotion	ML	76% (109/144)
Experimental Formulation	EF	64% (92/144)
Commercial Moisture Film	MF	55% (79/144)
Commercial Lotion	L	53% (77/144)

There was a numerical trend toward moisturizer O being assessed more favorably more often than moisturizer ML, although the difference was not statistically significant at the 95 per cent confidence level. Moisturizer O was superior to and differed statistically from moisturizers EF, MF, and L ($P < 0.001$), and similarly, ML differed from MF and L ($P < 0.01$).

c) Although water was assessed less favorably than the five cosmetic formulations, it was assessed more favorably than no treatment (89 *vs.* 51).

Table I shows the individual components of the panel ratings. The effect of the two moisturizers with the greatest lead over their control was manifested in that for every subject a clear majority of the evaluators chose the side of the face treated with one of these agents. Other preparations were proportionately less effective as their lead gradually eroded away throughout the group of subjects, rather than this lead making an abrupt, pronounced transition in particular subjects. In other words, the extent of effectiveness existing for a particular cosmetic tended to prevail throughout the study group, and was not concentrated in particular subjects.

Table I also provides the opportunity to examine the results in terms of subjects, and thereby to test the validity of the method. Overall, for the six-test series, there was no erratic pattern indicative of a failure of randomization.

Figure 2 shows the distribution of favorable evaluations by the 12-member evaluator panel for each test agent. The values clustered within one-third to less than one-half of the possible range.

DISCUSSION

Application of many of those same features, which differentiate the controlled clinical study from an open investigation, to the method of evaluation by a nonprofessional and untrained consumer panel has similarly increased the value of the results from this latter mode of inquiry. These features, in conjunction with a qualitative appraisal of comparative overall performance, appropriate for use by nonprofessional consumer evalua-

Table I

Results by Treatment and Subject

Number of Appraisals Finding Comparison Side Better/Water Side Better/Both Sides Equal in Appearance

Subject No.	Moisturizer 0	Moisture Lotion ML	Experimental Formulation EF	Moisture Film MF	Lotion L	No Treatment
1	11/0/1	10/0/2	6/4/2	7/5/0	6/2/4	4/7/1
2	9/3/0	10/1/1	7/5/0	8/4/0	5/7/0	4/8/0
3	10/1/1	9/2/1	9/3/0	8/4/0	8/4/0	5/7/0
4	10/2/0	8/4/0	9/3/0	7/4/1	4/7/1	4/8/0
5	10/1/1	8/4/0	7/5/0	5/5/2	8/4/0	4/8/0
6	8/3/1	9/3/0	8/4/0	6/6/0	8/4/0	6/6/0
7	10/1/1	10/1/1	7/4/1	5/6/1	9/3/0	5/7/0
8	12/0/0	9/3/0	6/6/0	8/4/0	6/6/0	5/6/1
9	10/2/0	9/3/0	8/2/2	5/7/0	5/7/0	4/6/2
10	10/2/0	9/3/0	8/4/0	9/3/0	5/6/1	1/11/0
11	10/2/0	10/2/0	8/4/0	6/6/0	8/4/0	5/7/0
12	9/3/0	8/3/1	9/3/0	5/6/1	5/7/0	4/8/0

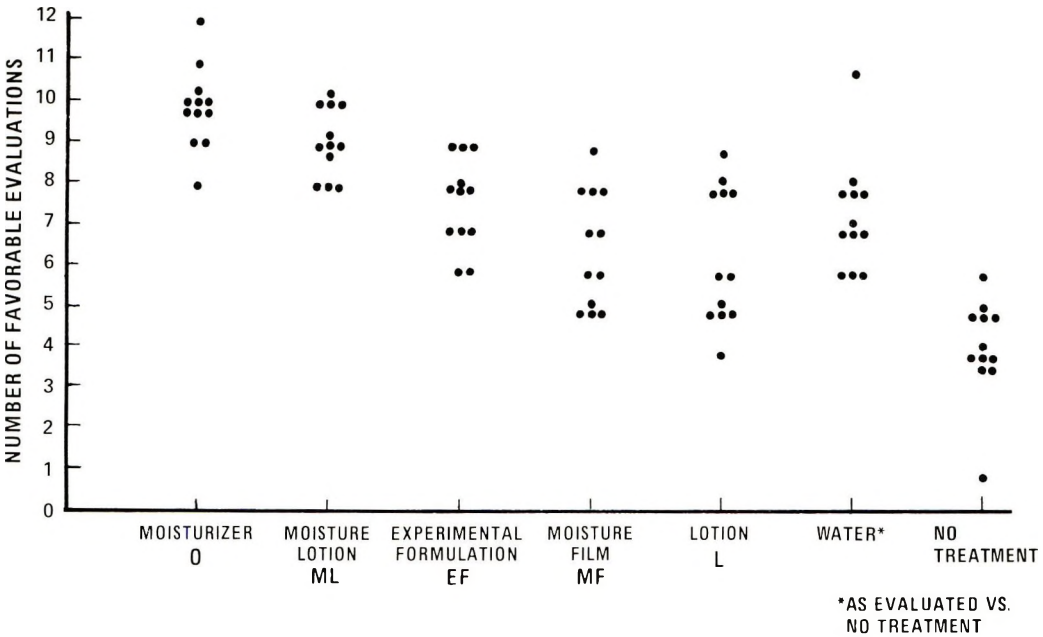

Figure 2. Distribution of favorable evaluations by treatment (each dot represents one subject)

tors, have made it possible to study more objectively the perceived effect of hydration of the stratum corneum by five moisturizers and their controls.

The classic consumer test, with users appraising results on themselves, is well suited to elicit personal preference. However, preference may be composed of other factors which do not usually affect perceived action within the skin, such as previous attitudes or opinions, fragrance, color, or tactile impression. Use of the separate evaluator panel can eliminate these factors, and can focus on the action attribute, *i.e.*, on what the test agents do to the skin that can be observed visually. The features of the controlled investigation are utilized to ensure that the appraisal is made within a setting that excludes artifact. For example, coding and randomization ensure that both the evaluator panel and the subjects are unaware of the identity of the test agents used. The crossover design provides for the same consumer panel using each moisturizer under specified, comparable conditions.

The present method also contributes to our approaching the conditions of real-life cosmetic usage (application by the users of the moisturizers under normal-use conditions, evaluation by the panel of performance as perceived outside of the home by a group of consumers and not by a single individual).

The panel study adapted as a scientifically controlled investigation could, besides being used for comparing various cosmetic products, also be appropriate for formulation research, such as for comparing an established preparation against variants of it, in the light of performance as perceived by users.

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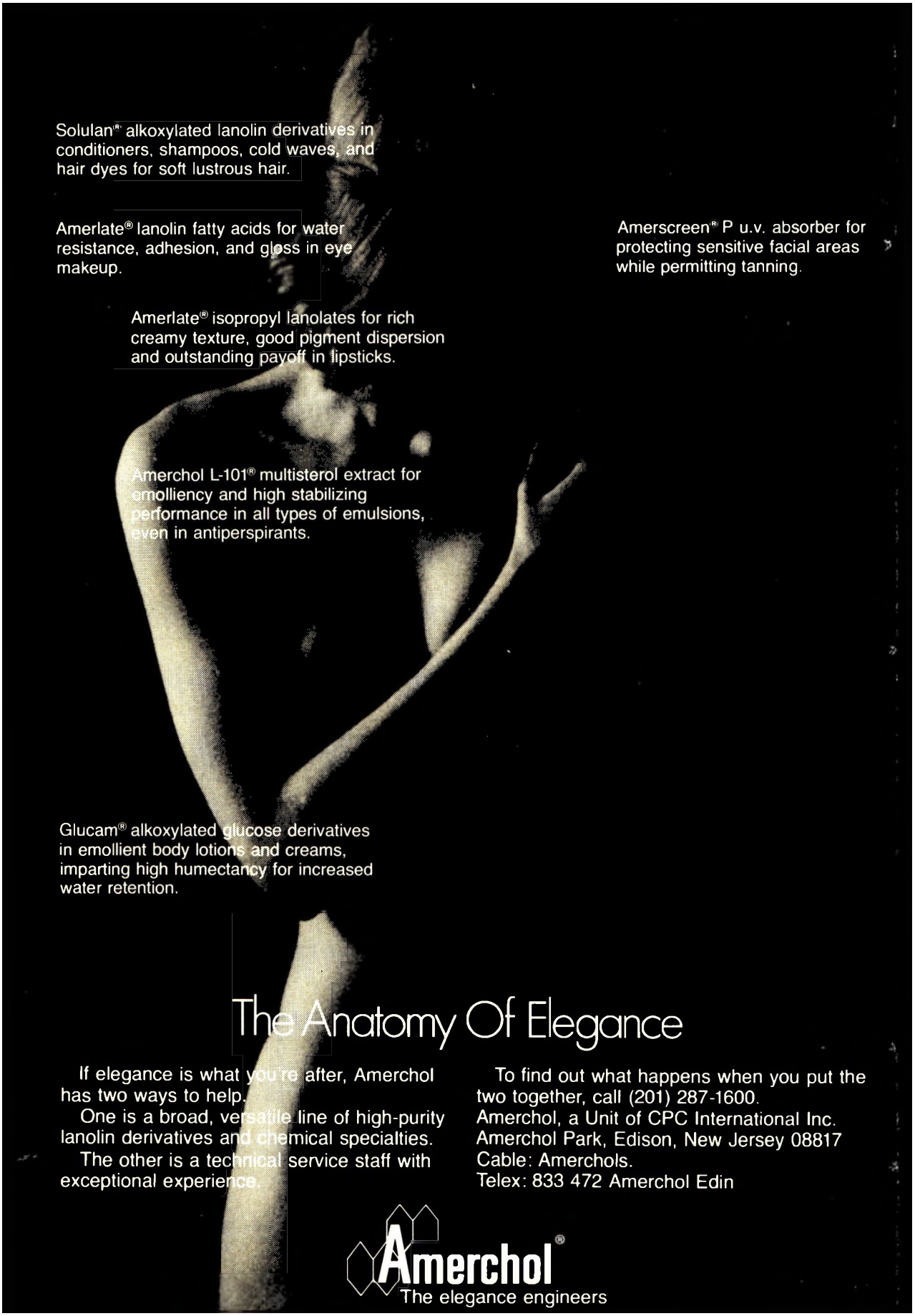

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