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Comedogenicity and irritancy of commonly used ingredients in skin care products

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Synopsis

A survey, using the rabbit ear, of the comedogenicity and irritancy of several groups of skin care products indicates that many contain follicular and surface epithelial irritating ingredients. These ingredients fall into several chemical classes. Certain generalizations can be deduced by examining the results: (1) medium-chain-length fatty acids are more potent than short- or long-chain fatty acids in producing follicular keratosis, (2) the comedogenicity and irritancy of an organic material can be reduced by combining the molecule with a polar sugar or a heavy metal, (3) increasing the degree of ethoxylation in a molecule tends to reduce the comedogenicity and irritancy of the chemical, and (4) the longer chain lipids, i.e., waxes, appear too large to produce a reaction. By following the guidelines developed in this study, it is possible to formulate nonirritating, noncomedogenic moisturizers, sunscreens, hair pomades, cosmetics, and conditioners.

INTRODUCTION

The possibility of comedogenicity and irritancy of facial skin care products has been well documented (1–3). Because of this work and an increasing public awareness, facial products that are less comedogenic are now becoming available (4). However, other skin care products such as hair conditioners, hair pomades, moisturizers, sunscreens, and even acne treatment products may be a source of cosmetic acne. By taking these products apart, testing their ingredients, and putting them back together and retesting them, an extensive ingredient listing has been created. By studying this list, the cosmetic chemist can begin to be selective in developing formulas for less irritating and less comedogenic products.

The rabbit ear assay has been used since the mid-1950s as a method of measuring follicular keratinization by externally applied compounds (5). The advantage of this rapid screening tool is that it takes only two weeks to develop follicular impactions in the rabbit ear, while it may take six months to develop similar reactions on human skin. The disadvantage of the model is its extreme sensitivity. The fragile, protected epithelium of the inner ear is extremely sensitive. Not everything that irritates this model will also irritate human skin. However, this extensive screening of cosmetic formula-

tions and their ingredients would not have been possible without the use of this animal model. We have now extended the model to include an index of surface skin irritancy as well as of follicular hyperkeratosis.

METHODS

Ingredients are mixed in propylene glycol at a 9 to 1 dilution for testing unless otherwise indicated (10% concentration). A colony of New Zealand albino rabbits that has genetically good ears and is free from mites is used. Three rabbits, weighing two to three kilograms, are used for each assay. Animals are housed singly in suspended cages and fed Purina Rabbit Chow and water *ad libitum*. Animals are maintained on a 12-hour light and 12-hour dark cycle. A dose of 1 ml of the test material is applied and spread once daily to the entire inner surface of one ear five days per week for two weeks. The opposite untreated ear of each animal serves as an untreated control. Follicular keratosis is judged both macroscopically (visually) and microscopically with a micrometer to measure the width of the follicular keratosis. The macroscopic response is determined by averaging the measurements of the width of six follicles using a Mitutoyo Dial Micrometer (#536-724). A similar microscopic micrometer measurement is obtained by averaging the width of six follicles under a magnification of 430× after a 6-mm biopsy specimen is fixed in formalin, sectioned at six microns, and stained with hematoxylin-eosin. The results are then combined on a scale of one to five:

Micrometer reading	Grade	
0.009 in or less	0	No significant increase in follicular keratosis
0.010 in–.014 in	1	
0.015 in–.019 in	2	A moderate increase in follicular keratosis
0.020 in–.025 in	3	
0.025 in–.029 in	4	An extensive increase in follicular keratosis
0.030 in or more	5	

Grade 5 is the presence of large comedones throughout the ear, similar to those induced by the application of our standard "positive" testing agent, isopropyl myristate. As reported in our previous studies, a minimal grade of 0 to 1 is not considered significant. Grade 2 to 3 is borderline. However, a grade of 4 to 5 is uniformally reproduceable and considered positive.

The irritancy produced by the repeated application of a chemical or skin care product on the surface epidermis in the rabbit ear is also evaluated on a similar scale of 0 to 5. The grades are summarized as follows:

0 No irritation
1 Few scales, no erythema
2 Diffuse scaling, no erythema
3 Generalized scaling with erythema
4 Scaling, erythema, and edema
5 Epidermal necrosis and slough

To study the effects of different vehicles on comedogenicity and irritancy, several fatty acids and the D&C red pigment #36 are reexamined in different solvents. The fatty

acids are dissolved in either a volatile solvent or sunflower oil. The D&C red #36 pigment is tested in mineral oil, propylene glycol, polyethylene glycol 400, and pentaerythrital tetra capra/caprylate.

RESULTS AND DISCUSSION

Cosmetic acne was first reported by French dermatologists in the mid-forties. They reported on brilliantines and hair pomades causing flareups on the temple and forehead facial regions. They attributed the problems to impurities in the brilliantines (6). In 1970, Kligman requested that Gerd Plewig and I examine over 700 men to find some with normal facial skin. Much to our chagrin, the majority had cosmetic acne (7). About 70% showed some evidence of follicular keratoses on the forehead and temples. Occasionally the eruptions were noted on the cheeks down to the jawline area. The lesions were usually noninflammatory, closed comedones. A few lesions developed into small inflammatory papules. However, there were no cases of severe, cystic inflammatory acne. Histologically, the comedones from pomade acne cases were identical to biopsies taken from comedones of classic acne vulgaris patients. In surveying the hair care preparations, we felt that the actual ingredients and not trace contaminants were offenders. Interestingly, very few of the subjects attributed their follicular eruptions to their daily use of a hair pomade. This study stimulated us to examine other skin care products and ingredients.

In 1972 Kligman and Mills reported on *acne cosmetica* in their survey at the Acne Clinic at the University of Pennsylvania (1). Approximately one third of the adult women had a low-grade, persistent acne in the cheek area, consisting of closed comedones quite similar to those found in pomade acne. This appeared more frequently in women after age twenty and may explain one of the reasons for epidemic adult acne in women in the 1970s and 1980s. In 1976 and 1984, Fulton published results on actual cosmetic lines and on ingredients, and proposed the development of noncomedogenic cosmetics using ingredients that were nonoffenders in the rabbit ear assay (2,3). Several major cosmetic manufacturers have now produced these types of products. However, our screening indicates that work is still needed on many skin care formulations.

It became apparent during our research into potential noncomedogenic ingredients that several hypotheses could be developed: (1) In order for an ingredient to be comedogenic, it must penetrate into the follicle, and (2) once in the follicle, the chemical must produce the follicular reaction of "retention hyperkeratosis" (8). In addition, the overall penetratibility of the molecule may be related to (1) the water/oil partition coefficient of the compound (HLB balance) and (2) the relative molecular weight of the ingredient. The ingredient appears to have the most potential if it is fairly soluble in both water and oil (HLB around 10 to 12) and has a range of molecular weight between 200 and 300. The comedogenicity of an ingredient may be reduced by adding a large constituent (i.e., polymers of PEGs), by adding a charged molecule (i.e., sugars), or by adding a heavy metal (i.e., zinc or lithium). This often relates to raising the HLB balance to above 12.

Examples of this concept of water/lipid solubility and molecular weights are apparent in each class of chemicals examined (Table I). Among the lanolins, the classic anhydrous lanolins are not as comedogenic as the moderately ethoxylated derivatives (laneth 10).

Table I
Ingredients and Their Comedogenicity and Irritancy

Ingredient	Grade (0–5) Comedo.†	Irrit.‡
I. Lanolins and derivatives		
Acetylated lanolin	0	0
Acetylated lanolin alcohol	4	2
Anhydrous lanolin	0–1*	0
Lanolin alcohol	0–2*	0
Lanolin oil	0–1*	0
PEG 16 lanolin (Solulan 16)	4	3
PEG 75 lanolin	0	0
Laneth-10	2	1
PPG 12 PEG 65 lanolin oil	2	0
II. Fatty acids and their derivatives		
Caprylic acid	1	3
Capric acid	2	2
Lauric acid	4	1
Myristic acid	3	0
Palmitic acid	2	0
Stearic acid	2–3*	0
Eicosanoic acid	2	0
Behenic acid	0	0
Ascorbyl palmitate	2	0
Behenyl erucate	0	0
Butyl stearate	3	0
Cetyl acetate	4	2
Cetyl ester NF	1	1
Cetyl palmitate	0	0
Decyl oleate	3	0
Di (2 ethylhexyl) succinate	2	0
Dioctyl malate	3	1
Dioctyl succinate	3	2
Diisopropyl adipate	0	0
Diisopropyl dimerate	0	0
Ethylhexyl palmitate	4	0
Ethylhexyl pelargonate	2	3
Isodecyl oleate	2–3*	1–2
Isopropyl isostearate	5	0
Isopropyl linolate	4	2
Isopropyl myristate	5	3
Isopropyl palmitate	4	1
Isostearyl neopentanoate	3	3
Isostearyl isostearate	4	1
Myristyl lactate	4	2
Myristyl myristate	5	2
Octyldodecyl stearate	0	0
Octyldodecyl stearoyl stearate	0	0
Stearyl heptanoate	4	0
Tridectyl neopentanoate	0	3
III. Alcohols, sugars and their derivatives		
SD alcohol 40	0	0
Isopropyl alcohol	0	0
Myristyl alcohol	2	4
Cetyl alcohol	2	2
Isocetyl alcohol	4	4
Cetearyl alcohol	2	1
Oleyl alcohol	4	2
Stearyl alcohol	2	2
Cetearyl alcohol + ceteareth 20	4	1
Ceteareth-20	2	3
Propylene glycol	0	0
Butylene glycol	1	0
Hexylene glycol	0–2*	0–1
PG caprylate/caprate	2	2
PG dicaprylate/caprate	1	0
PG dipelargonate	2	2
PG laurate	0	3
PG monostearate	0–3	0–1
Ethylene glycol monostearate	0	0
Glucose glutamate	0	0
Sorbitol	0	0
Sorbitan laurate	1–2*	1–2
Sorbitan sesquinoleate	0–1*	0
Sorbitan oleate	3	0
Sorbitan stearate	0	1
Sorbitan isostearate	1–2*	0
PEG 40 sorbitan laurate	0	0
Polysorbate 20	0	0
Polysorbate 80	0	0
Glycerin	0	0
Glycereth-26	0	0
Glyceryl-3-diisostearate	4	0
Glyceryl stearate NSE	1	0
Glyceryl stearate SE	3	2
Glyceryl tricapylo/caprate	1	1
Behenyl triglyceride	0	0
Pentaerythrital tetra isostearate	2	0
Pentaerythrital tetra capra/caprylate	0	0
Wheat germ glyceride	3	2
Polyglyceryl-3-diisostearate	4	0
Polyethylene glycol (PEG 400)	1	0
Sucrose distearate	0	2
Sucrose stearate	0	0
PEG 120 methyl glucose dioleate	0	0
PEG 8 stearate	3	1
PEG 20 stearate	1	0
PEG 100 stearate	0	0

Table I (continued)

Ingredient	Grade (0–5) Comedo.†	Irrit.‡	Ingredient	Grade (0–5) Comedo.†	Irrit.‡
PEG 100 distearate	2	0	Sesame oil	3(1)**	0
PEG 150 distearate	2	0	Corn oil	3	0
PEG 200 dilaurate	3	2	Avocado oil	3(2)	0
Laureth-4	5	4	Evening primrose oil	3	2
Laureth-23	3	0	Mink oil	3(2)	1
Steareth-2	2	2	Soybean oil	3	0
Steareth-10	4	3	Shark liver oil	3	2
Steareth-20	2	1	Cotton seed oil	3	2
Steareth-100	0	0	Peanut oil	2	0
Oleth-3	5	2	Olive oil	2(1)	0
Oleth-5	3	2	Sandalwood seed oil	2	0
Oleth-10	2	1	Almond oil	2(1)	0
Oleth-20	1	0	Apricot kernel oil	2(1)	0
Oleth-3 phosphate	2	2	Hydrogenated polyisobutane	1	2
Triacetin	0	0	Castor oil	1	0
PPG 5 Ceteth 10 phosphate	4	2	Hydrogenated castor oil	1	0
PPG 2 myristyl propionate	3	2	Chaulmoogra oil	1	0
PPG 10 cetyl ether	3	1	Babassu oil	1	0
PPG 30 cetyl ester	0	0	Squalane	1	0
PPG 50 cetyl ester	0	0	Maleated soybean oil	0	0
PEG 78 glyceryl monococoate	0	1	Safflower oil	0	0
PEG 8 castor oil	1	1	Sunflower oil	0	0
PEG 40 castor oil	0	0	Mineral oil	0–2	0
Polypentaerythrital tetralaurate	0	0	VII. Pigments		
IV. Waxes			D & C red #3	3	0
Candelilla wax	1	0	D & C red #4	2	1
Carnuba wax	1	0	D & C red #6	1	0
Ceresin wax	0	0	D & C red #7	1	0
Beeswax	0–2*	0	D & C red #9	1	0
Lanolin wax	1	0	D & C red #17	3	0
Jojoba oil	0–2*	0	D & C red #19	2	0
Sulfated jojoba oil	3	2	D & C red #21	2	0
Emulsifying wax NF	0	0–2*	D & C red #27	2	0
V. Thickeners			D & C red #30	3	0
Carboxymethylcellulose	0	0	D & C red #33	1	2
Carboxypropylcellulose	1	0	D & C red #36	3	0
Hydroxypropylcellulose	1	0	D & C red #40	2	2
Magnesium aluminum silicate	0	0	Ultamarine violet	0	0
Carbomer 940	1	0	Iron oxides	0	0
Bentonite	0	0	Carmine	0	0
Kaolin	0	0	Titanium dioxide	0	0
Talc	1	0	VIII. Silicones		
PVP	0	0	Simethicone	1	0
VI. Oils*			Dimethicone	1	0
Cocoa butter	4	0	Cyclomethicone	0	0
Coconut butter	4	0	IX. Sterols		
Hydrogenated vegetable oil	3	0	Cholesterol	0	0
			Soya sterol	0	0
			Peg 5 soya sterol	0	0

(continued)

Table I (continued)

Ingredient	Grade (0–5) Comedo.†	Irrit.‡	Ingredient	Grade (0–5) Comedo.†	Irrit.‡
Peg 10 soya sterol	0	1	XII. Miscellaneous		
Choleth 24	0	0	Octyl dimethyl PABA	0	0
Sterol esters	0	0	Oxybenzone	0	0
Phytantriol	2	2	Octyl methoxycinnamate	0	0
X. Vitamins and herbs			Octyl salicylate	0	0
A & D additive	2	0	Acetone	0	0
Tocopherol*	0–3*	0–3*	Ethyl ether	0	0
Tocopheryl acetate	0	0	Diethylene glycol monoethyl ether	0	0
Black walnut extract	0	0	Ethylene glycol monomethyl ether (EGME)	0	0
Papain	0	0	Xylene	4	3
Chamomile extract	0	0	Lithium stearate	1	0
Vitamin A palmitate	1–3*	1–3*	Magnesium stearate	1	0
Panthenol	0	0	Zinc oxide	1	0
XI. Preservatives and additives			Zinc stearate	0	0
Methyl paraben	0	0	Triethanolamine	2	0
Propylparaben	0	0	Stearic acid: TEA	3	2
Phenoxyethyl paraben	0	0	Amoniomethylpropinate	0	0
Allantoin	0	0	Sodium PCA	0	0
Hydantoin			Hydrolyzed animal protein	0	0
Sodium hyaluronate	0	0			
Chondroitin sulfate	0	0			
Precipitated sulfur	0	0			
Water-soluble sulfur	3	0			

† Comedogenicity or ability of test substance to produce follicular hyperkeratosis.
‡ Irritancy or ability of test substance to produce surface epithelial irritation.
* Results depend on source of raw material.
** Parentheses indicate results using "refined"oil.

The higher ethoxylated derivatives with HLBs above 12 are more water-soluble and noncomedogenic and nonirritating (PEG 75 lanolin). Two of the lanolin derivatives studied require special comments: (1) The acetylated lanolin alcohols are both comedogenic and irritating, not because of the acetylated lanolin but because of the cetyl acetate additive (Figure 1), and (2) PEG 16 lanolin (Solulan 16) is quite comedogenic and irritating, perhaps secondary to the combination of nonlanolin additives: ceteth-16, oleth-16, and steareth-16.

Among the fatty acids and esters a similar analogy is found. The mid-chain-length fatty acids, such as lauric acid and myristic acid and its analogs cause follicle hyperkeratosis. As the molecular weight of the fatty acid becomes larger and the effective charge of the overall molecule is reduced, less follicular reaction is produced. When the fatty acid is esterified with a small- to mid-size alcohol, the combination becomes more potent than the fatty acid itself. The cousins of isopropyl myristate, such as myristyl myristate, isopropyl isostearate, isostearyl neopentanoate, butyl stearate, and decyl oleate, are all comedogenic (Figure 2). Also, when branched-chain fatty acids are used, the derivatives may be more comedogenic. Large molecular weight esters, such as behenyl erucate and cetyl palmitate, are not a problem.

Figure 1. The key ingredient is acetylated lanolin alcohol—cetyl acetate—is not only comedogenic, but it is also an irritant.

Similar analogies are apparent with the alcohols, ethers, glycols, and sugars. Short-chain alcohols do not cause a reaction. The mid-chain-length alcohols are comedogenic and more irritating than their fatty acid analogs (Figure 3). In the glycol series, as the hydrocarbon component becomes more dominant, the compound is more effective at producing comedones. The pure sugars are noncomedogenic. However, if they are combined with penetrating fatty acids, they may become follicular irritants. Also, if they are combined with another irritant, as in glyceryl stearate (SE), which contains added sodium or potassium stearate, the combination becomes more comedogenic. The increasing addition of polyethylene glycols to the fatty acids increases the HLB balance, reduces the follicular irritancy, and appears to prevent hyperkeratosis. An example is the oleth 3, 5, 10, 20 series (Figure 4).

Among the waxes, the hydrocarbon chains appear too long to penetrate unless the wax is modified, such as in sulfated jojoba oil. In the case of beeswaxes and jojoba oils, some commercial preparations are more comedogenic than others. This suggests more contaminants or irritants in some of the preparations. Emulsifying wax NF may be irritating, depending on the concentration of longer-chain alcohols such as cetearyl alcohol.

Chemicals such as cellulosic polymers, the silicates, and the carbomers used in the pharmaceutical and cosmetic industry to thicken lotions and creams are not usually a problem. The clays, bentonite, and kaolin are also not a problem. Neither is talc.

Clinically, natural oils such as cocoa butter and coconut butter have long been known to cause problems with pomade acne. This is confirmed in the rabbit ear assay. Also,

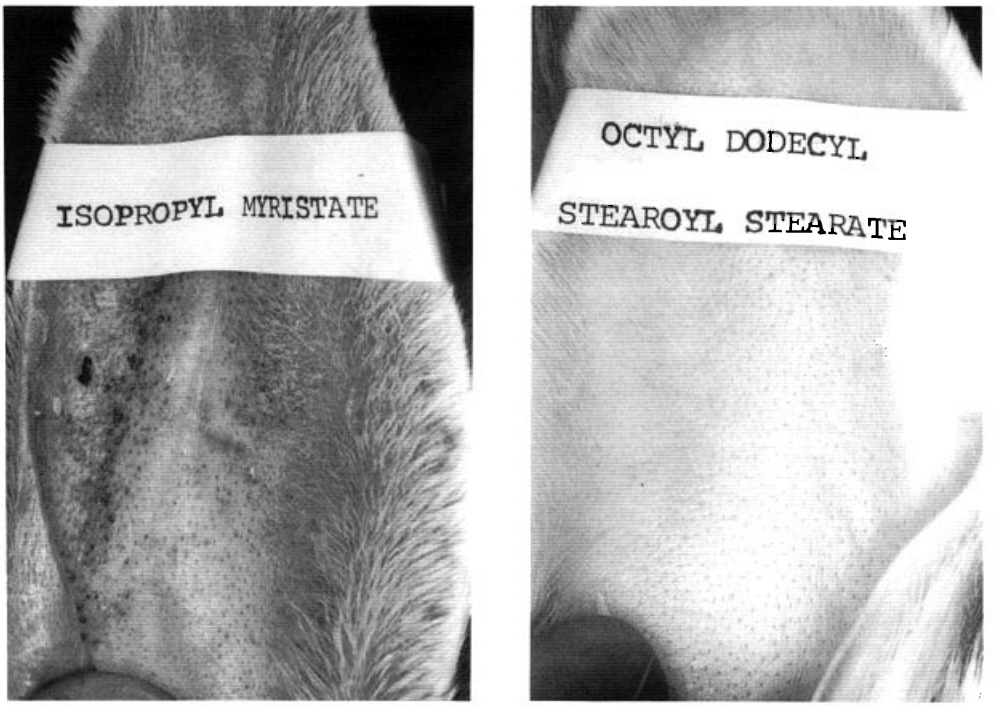

Figure 2. Ingredient testing in the rabbit ear assay—the macroscopic view of the results from testing isopropyl myristate. Microscopic examination confirmed the comedogenicity seen visually. Note that the ingredient is also an irritant compared to a potential substitute, octyl dodecyl stearoyl stearate.

hydrogenated vegetable oil (Crisco®) appears to contain residual irritating lipids. Among the natural oils such as sesame oil, avocado oil, and mink oil, the results are improved when a more refined oil is used. However, it seems easier to use safflower oil and sunflower oils, which are naturally less comedogenic. Mineral oil presents a complex problem: some sources are acceptable; others are not.

D&C red colors represent a perplexing mixture of different types of red dyes and pigments. Some are mildly comedogenic; others are not. The common pigments used in powder blushers (D&C red #6, barium lake; D&C red #7, calcium lake; and D&C red #9, barium lake) are relatively noncomedogenic. However, the vehicle is also particularly important for the D&C red colors. A dry compressed powder or powder suspended in an evaporating vehicle such as propylene glycol may be noncomedogenic. The same dye incorporated into a nonevaporating oil can be comedogenic (Table II, Figure 5). Carmine, which is a red dye obtained from insect wings, is noncomedogenic and may be used as a substitute. The iron oxides, chromium hydroxide, and titanium dioxide are not a problem.

The silicones and sterols do not appear to be a problem. Among the vitamins, tocopherol is a follicular irritant. Tocopherol has been advocated by the layman for years to increase wound healing and reduce scar formation. However, it should not be used on acne-prone skin because of its potential to produce follicular hyperkeratosis. The derivative, tocopheryl acetate, is noncomedogenic, and research needs to be done to see if it is an acceptable substitute.

Figure 3. The branched-chain alcohol is more comedogenic and more irritating than the straight-chain alcohol.

As for the miscellaneous items, the usual sunscreen active ingredients are noncomedogenic. Among chemical solvents, acetone, ether, and EGME are not problems, but xylene is comedogenic and an irritant. When metallic bases, such as lithium, magnesium, and zinc stearate, are added to the fatty acids, the metal appears to prevent the comedogenic reaction. Among bases, triethanolamine is more comedogenic than aminomethylpropylamine. The classic formulation of a cold cream often involves a salt bridge between stearic acid and triethanolamine. In testing different ratios [4:1, 1:1, 1:4] of stearic acid to triethanolamine (stearic acid:TEA) in a cold cream base, all combinations were found to be comedogenic.

The influence of the vehicle or solvent on the comedogenicity and irritancy of a chemical appears quite significant. For example, the use of rapidly evaporating vehicles such as acetone or ether reduces the comedogenicity of fatty acids when compared to the results obtained with sunflower oil, a nonvolatile vehicle (Table III). The effects on irritancy are reversed. Fatty acids are less irritating when delivered in a nonvolatile vehicle. As with the fatty acids, the vehicle or carrier for the D&C red pigment is extremely important. Whereas the D&C red color may be noncomedogenic in volatile propylene glycol, it may be more comedogenic in mineral oil. Possible alternatives for mineral oil, such as pentaerythrital tetra capra/caprylate and polyethylene glycol 400, also reduce the comedogenicity of the red color (Table II). We have chosen propylene glycol as the routine diluent for these studies, as it gradually evaporates and leaves a concentrate of the raw material to be tested. Also, lot after lot of propylene glycol has proven to be nonirritating and noncomedogenic.

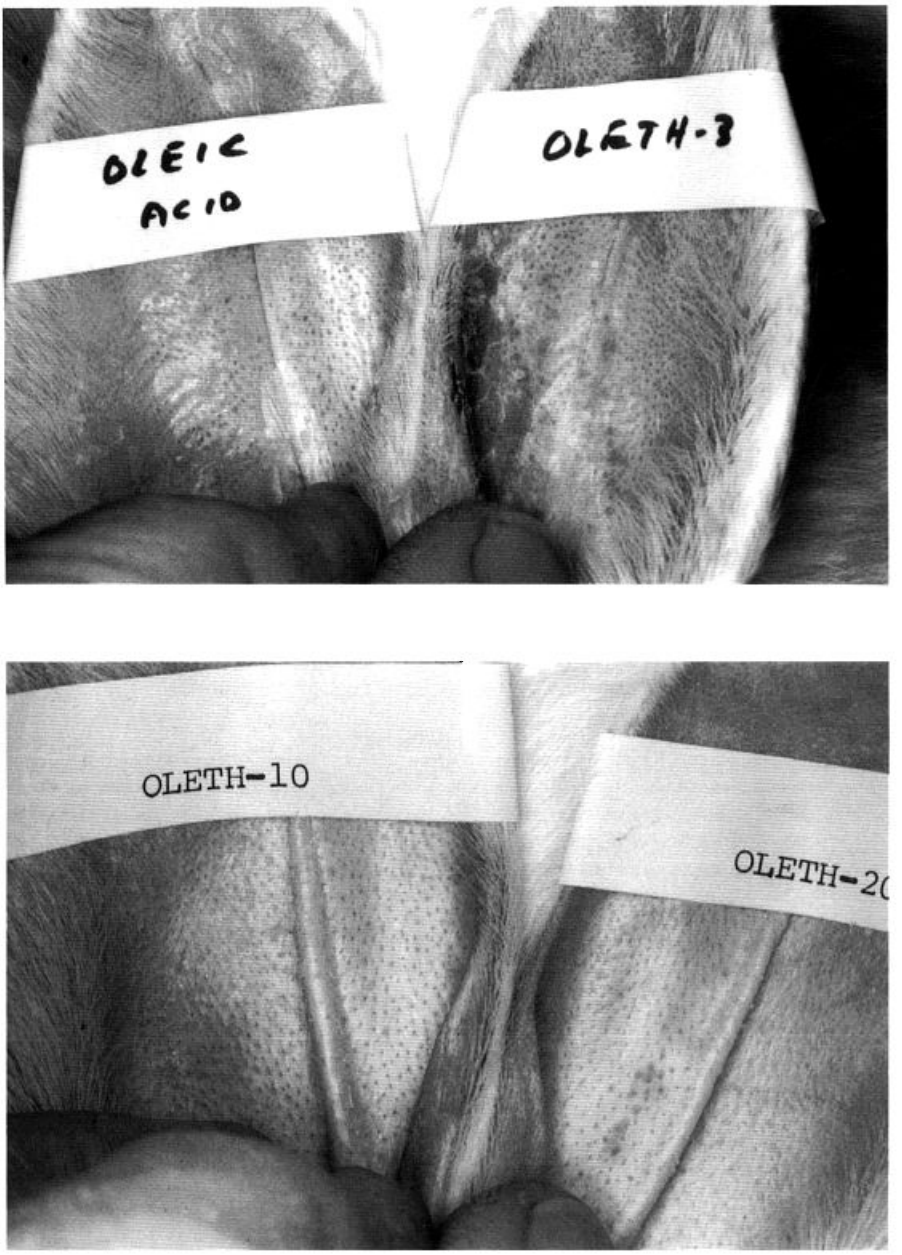

Figure 4. Oleth-3 compared to oleic acid. The initial additions of ethylene glycols to potentially comedogenic and irritating ingredients appear to increase this propensity. Further additions of ethylene glycols, such as oleth-10 and oleth-20, tend to reduce reactions.

Some ingredient combinations—for example, the combination of glyceryl stearate with potassium stearate (available commercially as glyceryl stearate S.E.) and also the combination of D&C red #36 and mineral oil—appear more comedogenic than the individual compounds themselves. These synergistic reactions need to be studied further.

Table II
Comedogenicity of D&C Red #36 Dye in Different Vehicles

	Grade (0–5)	
	Comedo.	Irrit.
D&C red #36 in mineral oil	3	0
D&C red #35 in pentaerythrital tetra capra/caprylate	2	0
D&C #36 in propylene glycol	1	0
D&C red #36 in PEG 400	0	0

The opposite is also possible. For example, the combination produced by the ingredient D&C red #36 and the vehicle polyethylene glycol is less comedogenic than D&C red #36 when incorporated into other vehicles. The cosmetic chemist may be able to take advantage of these findings in the future to custom design noncomedogenic products.

SUMMARY

These studies indicate that skin care preparations that are nonirritating and noncomedogenic can be made. Nonreactive ingredients can be used to make elegant products, and borderline ingredients can be combined with other ingredients to reduce the reactions to acceptable levels. In spite of these guidelines, new formulations must always be examined with the rabbit ear assay before the cosmetic chemist can be assured that his ideas work.

Figure 5. The comedogenicity of D&C red #36 when incorporated into two different vehicles. The vehicle may increase or decrease an ingredient's ability to produce follicular hyperkeratosis.

Table III
Effects of the Solvent on Comedogenicity and/or Irritancy of Fatty Acids

	Organic solvent* Grade (0–5)		Sunflower oil Grade (0–5)	
Fatty acids	Comedo.	Irrit.	Comedo.	Irrit.
Caproic acid	0	4	2	2
Caprylic acid	1	3	1	1
Capric acid	2	2	3	1
Lauric acid	3	1	4	1
Myristic acid	1	0	3	0
Palmitic acid	0	1	2	0
Stearic acid	0	1	2	0
Archidic acid	1	1	2	0
Behenic acid	1	0	1	0

* Ethyl ether or acetone.

The rabbit ear assay remains important to the rapid evaluation of new ingredients and the cosmetic chemist's formulations. Both the visual and microscopic evaluations of the rabbit ear need to be done simultaneously (9). Materials found to be noncomedogenic in the rabbit assay appear to be noncomedogenic in the human model (10). Whether highly comedogenic ingredients in the rabbit ear assay are always comedogenic in humans still remains uncertain. Currently, it is more prudent to avoid these offenders.

The major offenders, such as isopropyl myristate, acetylated lanolin alcohol, and lauric acid derivatives such as laureth-4, should be used with caution in skin care products. We are not convinced of the statement that lower concentrations of these compounds can be safely used with no comedogenic consequences (11). Human skin studies have been used to give that statement credence, but the back skin of human volunteers is relatively insensitive (7). However, when the rabbit ear assay is positive but the human back skin results are negative after only eight weeks' exposure, the results from the rabbit ear assay should not be dismissed. The reaction may take longer or the back skin may not be the ideal testing surface.

An additional "bonus" of the rabbit ear assay is detection of the potential of an ingredient or finished product to produce an epithelial irritant reaction. It is easy to keep track of the surface irritancy while doing the follicular studies. The stratum corneum of the rabbit ear is very thin and undeveloped. This results in an extreme sensitivity of the skin to exposure to irritants. If this test finding is confirmed by others, we may find it unnecessary to use the Draize rabbit dermal irritancy test.

This paper is meant to be a survey of the ingredients used in skin care and hair care products. The survey is not at all definitive but simply designed to stimulate research, so that new noncomedogenic products will become available for those of us with acne-prone complexions. This subject has recently received an excellent review by the American Academy of Dermatology Invitational Symposium on Comedogenicity (12).

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