

The effect of perfume "ageing" on the allergenicity of individual perfume ingredients

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An ingredient of a perfume which is a sensitizer may become hypoallergenic by interacting with other ingredients during the ageing process of the perfume. Thus, a patient with an exquisite allergic sensitivity to cinnamic aldehyde tolerates two perfumes containing cinnamic aldehyde without acquiring a dermatitis.

There are several theories of why cinnamic aldehyde can become a non-sensitizer in a perfume mixture. Testing with a mature perfume may be much more significant than testing with individual ingredients.

Key words: ageing of perfume – interaction of individual ingredients – rendering a sensitizing ingredient non-allergenic – testing with mature perfumes.

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Several recent issues of Contact Dermatitis contain articles dealing with the problem of perfume allergy. Collins and Mitchell (1975) stress the difficulties in a meaningful search for the cause of allergic reactions to perfumes stating that it is unlikely that much progress will be made without close biochemical-dermatological collaboration, and feel that resolution of the problems of dermatitis from aroma chemicals will have to await the development of a "computerized *in vitro* system of testing for delayed hypersensitivity". The fact that a perfume may contain as many as fifty ingredients, according to these investigators, is probably an excellent state of affairs since the more compounds that are present, the less likely it may be that any one ingredient will reach a threshold sensitizing level.

Schorr (1975) has found that cinnamic

aldehyde, an ingredient in many perfumes, is a common sensitizer and cross-reacts with cinnamon compounds in topical agents and foods.

Larsen (1975) reported a patient with perfume allergy who had positive patch test reactions to many individual perfume ingredients, and stresses the difficulty of finding out which perfumes contain the particular components to which the patient is allergic.

Fisher (1975) prepared a list of potential individual sensitizers in perfumes with their concentration and diluents suitable for patch testing.

Recently the North American Contact Dermatitis Group (NACDG) has selected sixteen ingredients for a Perfume Screening Series (Table 1). The NACDG plans to test many individual perfume ingredients in the

Table 1. North American Contact Dermatitis Group perfume screening series

1. Cinnamic aldehyde, 1 % in pet.
2. Cinnamic alcohol, 5 % in pet.
3. Benzyl salicylate, 2 % in pet.
4. Methyl salicylate, 2 % in pet.
5. Benzyl benzoate, 2 % in pet.
6. Benzyl alcohol, 5 % in pet.
7. Musk ambrette, 5 % in ethyl alcohol
8. Eugenol, 2 % in pet.
9. Isoeugenol, 2 % in pet.
10. Coumarin, 5 % in pet.
11. Hydroxycitronellal, 4 % in pet.
12. Jasmin absolute, 10 % in pet.
13. Jasmin synthetic, 10 % in pet.
14. Costus root oil, 0.1 % in pet.
15. Oil of sandalwood, 2 % in pet.

hope that once the most frequent offenders are defined, they could be eliminated from perfumes and thus reduce the incidence of perfume sensitivity.

Nakayama et al. (1974) have drawn up an "Allergen Controlled System" to manage perfume dermatitis. The "System" is based on the results of patch test reactions to a series of individual perfume ingredients and to seven perfumes made with the cooperation of the Takasago Perfumery Company of Tokyo. Table 2 lists the individual perfume ingredients and the seven perfumes designated "A" to "G". These Japanese investigators claim that patients with perfume allergy can avoid perfumes to which they are sensitive through the interpretation of results of patch tests with their perfume screening series. For example, if a patient is found to be allergic to cinnamic derivatives, the patient is advised to use perfume "A", "B" or "C" which are known to be free of such derivatives.

Opdyke (1975) on the basis of studies made by the Research Institute for Fragrance Materials (RIFM) recommended to perfume manufacturers that the ingredients listed in Table 3 be eliminated from perfumes. The (RIFM) Institute was estab-

Table 2. Japanese perfume screening series

1. Jasmin oil, 20 % in pet.
2. Cananga oil, 15 % in pet.
3. Ylang-ylang oil, 5 % in pet.
4. Lavender oil, 20 % in lan.
5. Patchouli oil, 20 % in pet.
6. Balsam of Peru, 10 % in pet.
7. Rose oil Bulgaria, 20 % in pet.
8. Geranium oil, 20 % in pet.
9. Geraniol, 20 % in pet.
10. Sandalwood oil, 10 % in pet.
11. Benzyl salicylate, 5 % in pet.
12. Benzyl alcohol, 20 % in pet.
13. Hydroxycitronellal, 10 % in lan.
14. Hydroxycitronellal, 10 % hydrophilic ointment (JP)
15. Methoxycitronellal, 10 % in pet.
16. Cinnamic alcohol, 1 % lan.
17. Eugenol, 5 % in pet.
18. Methyl salicylate, 10 % in pet.
19. Perfume A, 10 % in pet.
20. Perfume B, 10 % in pet.
21. Perfume C, 10 % in pet.
22. Perfume F, 10 % in pet.
23. Perfume G, 10 % in pet.
24. Hydrophilic ointment, as is

Table 3. Fragrances recommended to be eliminated by the Research Institute for Fragrance Materials, Inc.

Allergens

Alantroot oil
Anisylidene acetone
Benzylidene acetone
P-T-Butyl phenol
Cassia oil
Cinnamon bark oil
Costus oil
Dihydrocoumarin
Ethyl acrylate
Hydroabietyl alcohol
Peru balsam

Phototoxic oils

Angelica root oil
Bergamot expressed
Cumin oil
Lemon oil expressed
Lime oil expressed
Orange oil bitter
Rue oil

lished in 1966 by the principal suppliers of raw materials to the fragrance industry. At present, RIFM is supported by fifty of these companies, representing most of the industry in the United States, Europe and Japan. The sole purpose of RIFM is to assure the safety of perfumery raw materials.

The chief parameters selected by the RIFM for toxicological screening of all these materials include tests for allergenicity and phototoxicity on human skin; tests for general toxicity in animals by the oral and dermal route, and other procedures where required by an international panel of experts drawn from outside the industry.

Difficulties in the reliance of the study of individual perfume ingredients in the management of perfume allergy

Although the elimination of certain individual perfume ingredients, particularly phototoxic agents, from perfumes makes such perfumes less likely to cause dermatitis, the following case report illustrates the fact that although a patient has been shown to be allergic to a specific perfume ingredient, nevertheless, perfumes containing that allergen may not produce dermatitis in the sensitized individual.

Report of a case of a patient with cinnamic aldehyde sensitivity who tolerates perfumes containing this ingredient

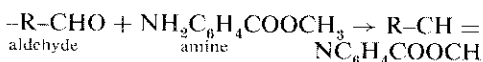
A 45-year-old woman was shown to be exquisitely sensitive to a certain perfume and to cinnamic aldehyde and balsam of Peru. The manufacturer of the perfume to which this patient was shown to be sensitive was not certain that the perfume contained cinnamic aldehyde. However, two other perfumes definitely known to contain cinnamic aldehyde did not produce any dermatitis.

There are several possible explanations

when a patient with cinnamic aldehyde sensitivity can use a perfume containing this chemical without acquiring dermatitis.

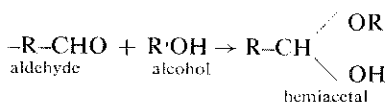
1. The concentration of the cinnamic aldehyde is too low in the perfume to produce sensitivity.

2. The cinnamic aldehyde reacts with an amine in the perfume in the following manner:



with the formation of "Schiff base" between an aldehyde and an amine. The Schiff base may not be a sensitizer in the cinnamic aldehyde sensitive individual.

3. A perfume aldehyde may react with alcohol as follows:



The cinnamic aldehyde sensitive individual may not react to hemiacetal.

4. In the ageing process the cinnamic aldehyde is oxidized to cinnamic acid. Our patient with cinnamic aldehyde sensitivity did not react to cinnamic acid.

5. Opdyke in a personal communication states that investigations are under way which may further explain why cinnamic aldehyde may become "hypoallergenic" in a perfume mixture.

Dooms-Goossens (1975) in introducing a study of the effects of "ageing" of perfumes on individual ingredients states that the individual ingredients of a perfume, whether used in fine perfumes or in common detergents, are mixtures of two basic ingredients. The first are "essential oils" - "essential" meaning "a concentrated derivative" - that come from such natural items as flowers, plants, fruits and trees. The essential oils of truly international character are made from jasmin flowers in North Africa, sandalwood trees in India, pine scented fir trees in the United States, la-

vender flowers in France and patchouli shrubs in the Far East, to name a few.

The other basic ingredients in fragrances are aromatic chemicals, which are synthetic odorous materials created in the laboratory. In most cases, these chemicals, of which there are thousands, attempt to imitate the odor of one or more of the essential oils.

Thus, the individual ingredients of a perfume can be quite simple, such as cinnamic aldehyde, benzyl alcohol, or eugenol, while other components are complex, such as Jasmin "absolute" which contains benzyl acetone, benzyl alcohol, d-linalool, linalyl acetate, jasmone, indole, methylanthranilate (Wells 1974).

At present, perfumers store their perfume mixture for three to twelve months to "mature" the perfume. This ageing process leads to the improvement of the odor of the perfume-mixture during storage. During this ageing period, chemical changes are taking place by interaction of the perfume ingredients, until a state of equilibrium has been reached. Finally, the perfume complex remains "balanced" and "stable" during storage. In addition, when an individual uses a perfume, air and light come in contact with the perfume mixture producing further changes (Schuller 1974).

Thus, it is not unlikely that an originally allergenic perfume ingredient may become non-allergenic due to the neutralization by another chemical ingredient of the perfume-mixture or to the chemical interchanges between the two components (Bedoukian 1952).

There is also the theoretical possibility that a non-allergenic perfume ingredient becomes allergenic when "aged" with another perfume ingredient. Such a possibility means that a patient may be allergic to a perfume-mixture, but not to any individual ingredient of the perfume.

An ideal approach would be to analyze

the aged perfume mixture which caused the allergic reaction. This means all the different ingredients present in the perfume-mixture have to be identified, not only the basic raw materials, but also the products formed by chemical reactions. Patch testing with all of these individual ingredients separately might lead to the identification of the agent in the mature perfume which is causing the dermatitis. This "ideal" method is impractical since the analysis would require a complex apparatus and because of the great number of individual ingredients or combinations of ingredients which would have to be tested. Such "research" would be very time consuming and costly.

A somewhat more practical approach to the problem of the identification of the "culprit" in a perfume could consist of performing a selective chemical extraction in order to identify the different chemical groups, such as aldehydes, ketones, esters etc. Patch tests with these various fractions would enable us to obtain information concerning the general nature of the allergen in the perfume and may more readily lead to the identification of a specific ingredient in the perfume which is actually producing the allergic reaction in perfume *after* it has aged and is in actual use by the individual with perfume allergy.

Finally, unless we can give a perfume-sensitive patient more specific advice, such an individual should request that a sample of the desired perfume be sprayed on both forearms before any purchase is made. One forearm should be covered with a patch to detect ordinary allergic contact sensitivity. The other forearm should be exposed to sunlight, if possible, to detect a photo-sensitivity reaction.

Furthermore, many perfume-sensitive individuals can utilize perfumes to which they show positive patch test reactions by the simple expedient of applying the perfume to their hair or clothing. Such a man-

ever, of course, cannot be used for perfume allergens in soaps, cosmetics and topical agents which are applied directly to the skin.

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