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Perfume-Related Inhalation Allergy Review

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Abstract

Perfume allergens have been gaining importance in last few decades, but the research and analysis about inhalation exposure is still incomplete. Except for common problems of allergic dermatitis, fragrances can induce or worsen respiratory diseases due to their irritation and sensitization effect. They are thought to trigger asthma, allergic rhinitis, migraine headaches, mucosal symptoms and attention-deficit disorder. Some volatiles components of perfume can stay on the surface of clothes and skin for a long period, which is unbelievable to avoid exposure, afterwards the bioaccumulation caused long-term impact should also be taken into consideration. Furthermore, the lack knowledge of perfume ingredients that can be recognized by corresponding olfactory receptors should also be further investigated.

Method:"perfume, fragrance allergen, indoor air" were searched together with "allergic inflammation, sensory irritation, olfactory receptors, asthma, allergic rhinitis, airway effects" in Science Direct Journals, PubMed.

Keywords: Perfume; Fragrance allergen; Indoor air; Allergic inflammation; Volatile Organic Compounds (VOCs); Asthma; Allergic rhinitis; Olfactory receptors

Introduction

Perfume provides attractive scents to make the products more popular, fragranced products including commercial perfumes, air fresheners, and also cosmetics products, can emit plenty of Volatile Organic Compounds (VOCs). Perfumes are the mixtures of aromatic chemicals and essential oils, from ancient times, natural plant and their volatiles compounds, animals, synthetic spices, have been the major sources of fragrances, however, in recent decades, perfume production tends to use more and more synthetic materials and may contain lots of chemical ingredients.

Previous survey had demonstrated that 99.1% of the population are exposed to fragrance products at least once a week via personal use, other's use, or both[1]. Owing to the extremely high potential risk of perfume exposure, it is well-known that perfume and fragrance products could trigger adverse health effects, such as respiratory problems (difficulty breathing, coughing)[2,3], contact allergic dermatitis[4,5], migraine headaches[6], allergic rhinitis, mucosal symptoms (e.g. nasal congestion, sneezing)[7] and some other health problems.

Previous perfume allergy research pays more attention on skin allergy; however, the research on perfume-related inhalation allergy is unable to keep pace apparently. In terms of the nature with effumability and diffusivity, inhalation should be identified as

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one of the potential sensitization pathways, especially in indoor environments. In addition, indoor air pollution are considered to create an equal or even greater side effects on health compared to that of outdoor pollutants, for the reason that people tend to spend hours indoors (home, school and office) daily is generally higher than hours spent outdoors[8], as well, indoor environments hold a mass of allergens and higher concentration than outdoors[9].

New scientific analysis is trying their best without a break in order to ensure that the strictest standards are applied in perfume production. Allergic properties of abundant fragrance substances are being focused more nowadays, but the scientific studies regarding to perfume long-term inhalation exposure is still superficial[10]. This review is based on previous reviews with particular focus on perfume inhalation allergy.

Perfume and Perfume Allergy

Perfume Component Analysis: The perfume ingredients are extremely complicated, in modern perfume industry, perfumers can even use up to 5000 kinds of raw materials, however, approximately 1500 of them are used frequently[11]. Even one kind of common commercial perfume, which may be the mixtures of 50 - 300 kinds of individual fragrance chemicals[12], and at least 100 of those are known allergens for our human beings. Most perfume ingredients belong to one of three families: phthalates, synthetic musk, and sensitizers[13].

Main methods of perfume component analysis: At present, these are several dominant perfume analysis techniques as follows, owing to the properties of perfume ingredients are volatile and semi-volatile, Gas Chromatography-Mass Spectrometry (GC-MS) is until now the most important analytical method[11,14]. In addition to this, gas chromatography-olfactometry (GC-O) is a frequently-used method in food chemistry, but it also has the use value in perfume analysis field[15]. Human nose is a more sensitive detector for the reason that it could detect some certain ingredients at extremely low concentration[15], which brings difficulty for GC-MS to detect precisely, GC-O plays a supplementary role for GC-MS[16]. Besides, Raman spectroscopy, on the basis of multivariate data processing, gives a rapid, easy operated and also cheap method at measuring fragrance ingredients with the same ability of the standard methodology compared with GC- MS[17]. Nevertheless, it is an increasing need to learn about perfumes composition in depth, in particular focus on the potential biological activities among some certain ingredients, owing to the extremely complicated mixture; the analytical work is a challenging task without a doubt.

Basic Structural Groups of Perfume Ingredients: The previous studies classified 2155 fragrance ingredients (the majority are simple-structured as well as semi-volatile components, containing carbon, hydrogen and oxygen), according to their chemical structures, basic structural groups are sequenced by each frequency of occurrence as shown in (figure 1), esters (707), alcohols (302), ketones (259), aldehydes (207), ethers (100), hydrocarbons (82), acetals (63), lactones (61), carboxylic acids (42), phenols (40), nitriles (39), dioxanes (31), pyrans (27), miscellaneous (27), schiff's bases (26), heterocyclics (25), epoxides (25), sulfur containing (24), pyrazines (22), amines/amides (18), quinolines (14), musk (10), coumarins (4)[12]. As the existing data shows above, esters, alcohols, ketones and aldehydes took up 70 percentage approximately of all, hence perfume allergy should be focused on these four groups more in order to get potential valuable results.

Fragrance Allergens

26 Fragrance Allergens Regulated by EU: The Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) has identified 26 of these ingredients as likely to cause contact allergy. Moreover, the European Union (EU) had regulated that labeling of certain allergens contained in cosmetic and detergent products must be displayed. The 26 fragrance allergens are limonene, linalool, citral, eugenol, cinnamal, isoeugenol, citronellol, HICC, hydroxyl citronellol, cinnamyl alcohol, geraniol, farnesol, coumarin, hexyl cinnamal, butylphenyl methylpropional, alpha-isomethyl ionone, everniafurfuracea lichen extract, everniaprunastri lichen extract, amyl cinnamal, benzyl benzoate, benzylcinnamate, benzyl salicylate, benzyl alcohol, methyl2-octynoate, amylcinnamyl alcohol, anise alcohol respectively. The presence of these fragrances must be indicated in the list of ingredients when its concentration exceeds the 0.001% in leave-on products and 0.01% in rinse-off products. The use of some of the 26 fragrance compounds is already more restricted, i.e. Methyleugenol must not be the material cosmetic products[18]. The most of perfume ingredients are also restricted by the International Fragrance Association (IFRA)[19], the official fragrance institute worldwide, which is responsible for controlling the safety and standard of perfume and fragrance products.

With the widespread use of perfume and other fragrance products, a complete compounds list is scarcely ever showed on the label of such products, "fragrance mixtures" are always defined as "business secrets" and meanwhile protected by legislation[20]. It is definitely necessary for perfume manufacturer to put the correct and detailed ingredient labelling on their products. In this way, the consumers would avoid using the perfumes containing certain allergens that they cannot tolerate.

The most common perfume allergens: Limonene, linalool, benzyl alcohol, citronellol, cinnamaldehyde, and eugenol were the well- known discovered allergens, particularly linalool and limonene were found in more than a half of the fragrance products[16].

Limonene cyclohexene is a colorless liquid that is in class of cyclic monoterpene, d-limonene and l-limonene are the two optically active forms. With the exposure to d-limonene for human, the potential toxic effect may exist[21]. However, the latest research suggested that numerous positive biological effects of limonene, limonene presented an anti-inflammatory effect by decreasing reactive oxygen species (ROS) production[22], NF-κB activity and eosinophil migration[21,23].

Linalool is a colorless to very pale light liquid, although no data present evidence of linalool- related skin sensitization[24], linalool had been proved to likely undergo oxidation, oxidative products generated may bind with skin proteins indirectly[25 phthalates are commonly used in perfume as solvents for synthetic musk's, diethyl phthalate (DEP) tends to enter human body via inhalation and skin contact[26], as it has been proved

to disrupt endocrine system, the endocrine disruptors, the prolonged influence for human is still not definite[27].

The coupled exposure to combinations of two or more fragrance allergens may enhance sensitization[28]. Furthermore, the frequency of fragrance allergy could be enhanced by the autoxidative allergens under the perfume exposure in indoor air[29].

Perfume exposure: Fragranced products consist a significant part of Volatile Organic Compounds (VOCs), and are likely to increase the amount and concentration of compounds of the indoor environment[10]. Steinemann[30] reported results from the general population survey of Australians, including both asthmatics and non-asthmatics, indicating that 33% of Australians occur adverse effects after exposure from fragranced products, female presented a higher proportion than that of male (56.1% versus 43.9%). It is a remarkable fact that asthmatics were more tend to develop side effects from the fragrance exposure than non-asthmatics[31].

The most common types of adverse effects were as follows: 18.6% respiratory problems; 16.2% mucosal symptoms; 15.7% migraine headaches; 10.6% skin problems; 8.0% asthma attacks; 7.2% neurological problems; 5.8% cognitive problems; 5.5% gastrointestinal problems; 4.4% cardiovascular problems; 4.0% immune system problems; 3.8% musculoskeletal problems; and 1.7% other[1].

Sensitization Paths of Perfume Allergy: There are several routes of perfume exposure for human, respiratory tract path and skin exposure path are the two major sensitization paths, the most basic differences between skin sensitization by contact and airway sensitization or allergy from inhalation are well established at the cellular and cytokine level causing different immune responses.

Skin contact of some fragrance may cause skin allergy (allergic contact dermatitis, ACD), which is characterized by a delayed skin reaction, it is an immunological skin inflammation associated with T-helper (TH) -1-type response (lymphoyctes) [32]. By comparison, inhalation of proteins and some low molecular chemicals, e.g. acid anhydrides may cause asthma, which is another type of immunological reaction, this is preferentially orchestrated by TH2-type lymphocyte response by chemical sensitization in the airways[33]. Previous study found that perfume causes a dose-dependent non-IgE-mediated release of histamine from human peripheral blood basophils, and enhanced basophil reactivity to perfume had also been proved in patients with perfume-related respiratory symptoms[34].

The location of stimulus may also different depending on the hydrophilicity and reactivity of the volatile compounds. The high water-solubility compounds tend to deposit in the upper airways, especially nasal cavity, on the other hand, low water-solubility compounds are likely to accumulate in the low airways[35]. Those patients with asthma and allergic rhinitis are more sensitive to irritants, and generally with concentration that are many times lower than what would cause problems in the general population.

Olfactory receptors and known recognized perfume ingredients: Human olfactory system is able to recognize a large amount of odorants through about 1000 ORs merely[36], olfactory receptors genes are the foundation of detecting and sensing smells, including approximately 1000 genes and pseudogenes[37]. ORs are mainly expressed in nasal epithelium for human, and are able to detect and combine with odorants, nevertheless, previous studies had found the evidence of the ORs ectopic expression, for example, heart[38], airway smooth muscle[39], prostate[40], lung[39], skin[41], kidney[42], and several other tissues[43].

ORs located on the cell membranes of olfactory receptor neurons(ORNs), after binding with the odorants molecules, the conformational change can be detected by ORNS, and then the lyase-adenylate cyclase was activated, ATP transformed into cAMP during the process, in this way, calcium and sodium ions come into the cell, ORNs experiences depolarization, chemical signals changed into electrical signals, and then transmitted the olfactory information to olfactory bulb, finally, olfactory cortex plays translating and editing roles[44]. Each olfactory receptor attracts a group of odorants with the similar physio-chemical properties, such as hydrophobicity and hydrophilicity, likewise, one single odorant may combine with several olfactory receptors with different levels of affinity[45].

The recognizable odorants in terms of each OR are unknown to a large degree, previous study had reported several potential associations between OR and their corresponding odorants, among those, several perfume ingredients are reported to be recognized by ORs, such as OR10J5 with lyral, OR73 with eugenol, IG7 with limonene[36].

Discussion and Conclusion

Owing to the high-level of perfume exposure and the potential adverse effects, there is an increasing demand for focusing more on perfume allergy currently. As perfume are complicated mixture of plenty of individual ingredients, so study the allergens separately is inadequate, further finding should be investigated with regard to the possible combination of different perfume allergens, and an efficient method is to make a special effort to the allergens with similar physicochemical properties, especially the similar chemical structure.

Besides, studies on which kind of ingredients trigger corresponding adverse effects is still lacking, most of the previous studies took into account the allergy from skin exposure, further research will also be needed to extend our knowledge of inhalation-related allergens. Furthermore, the lack of known binding odorant molecules for ORs, especially for perfume ingredients, which makes the further research of perfume allergy challenging. Because of the unknown high-resolution of olfactory receptors, it is a effective way to simulate the binding of ORs and fragranced odorants by using homology modeling method, which is a promising direction to solve the problem of interaction between ORs and fragranced molecules, and further promotes the research in perfume inhalation allergy.

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