A Risk Assessment of Commercial Fragrance Materials

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Abstract

The use of fragrances is central to the modern cosmetics and personal care industries, however, the widespread use of fragrances raises serious concerns about their use and impact on human health and environmental management. This paper is a critical risk evaluation of the major fragrance materials with a particular focus on their chemical composition, toxicological implication, and method of manufacture. Different components including Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) and D-limonene are examined owing to their overt sensitizing range, which usually leads to allergic contact dermatitis and respiratory irritation. The mechanisms by which these substances cause cytotoxic effects such as oxidative stress, protein haptenation, and membrane disruption are described along with the reasons for their regulation. In addition, the environmental impact of volatile organic compounds (VOCs) as a byproduct of fragrance formulations are also discussed, including their impact on water biomes and involvement in air pollution.. Regulatory tools devised by the Research Institute for Fragrance Materials (RIFM) and the International Fragrance Association (IFRA) are noted as unavoidable methodologies of protecting general health and limiting ranges of exposure to certain fragrance materials. Oversight notwithstanding barriers exist due to the lack of transparency in ingredients used, and the complexity of fragrance compositions. The importance of transparency, green chemistry, and long term scientific research can be seen by this discussion as a means to ensure consumer safety and environmental health for a better future of fragrance.

Intro

From incense to natural extracts to carefully engineered perfumes, fragrance has had a variety of uses for centuries. Modern cosmetics and cleaning utilities rely on fragrance for a sense of cleanliness, freshness, and to enhance the charm of the subject of use. The engineering process relies on human olfaction and its interactions with different compounds to then harness various chemistries to create new sensory experiences. In the field of cologne and perfume, customers are lured by different scent profiles thought to be appealing. These scent profiles include sweet, musky, spicy, citrusy, or fruity. Each scent can be attributed to the different chemical structure of the perfume. The way colognes interact with the body, whether that be through nasal inhalation or dermal absorption, leads to chemical exposure. Nasal inhalation has been known to cause adverse effects in asthmatics as well as in average people due to some odors containing carcinogenic compounds (Wolkoff & Nielsen, 2017). In addition to this, dermal absorption of fragrances is commonly the cause of contact dermatitis, which can be contracted through a number of different fragrance allergens. In order to achieve certain scents, such products have evolved to contain a copious amount of synthetic chemical compounds, which could act as allergens to a large number of users. Awareness of these allergens has brought up discussion on their long term health effects to humans. 1 out of every 5 people has been reported to be fragrance-sensitive (Klaschka, 2020). For reasons similar to these, the Research Institute for Fragrance Materials, RIFM, was founded in 1966. They aimed to evaluate and judge the safety and usages of fragrance materials in a way that would result in the least amount of possible danger to their users (Bickers et al., 2003). Similarly, in 1973, the International Fragrance Association, IFRA, was created to monitor, promote, and ensure safe usages of fragrances worldwide. Both the RIFM and IFRA play a part in determining the safety and risk of commercial fragrances, as can be seen in Figure 1. Using guidelines from these two organizations along with prior research findings, this paper will provide a risk assessment of an assortment of different men's fragrances, which will aim to identify different possible health, engineering, and manufacturing hazards of fragrances by examining their chemical compositions as well as the processes used to create them.

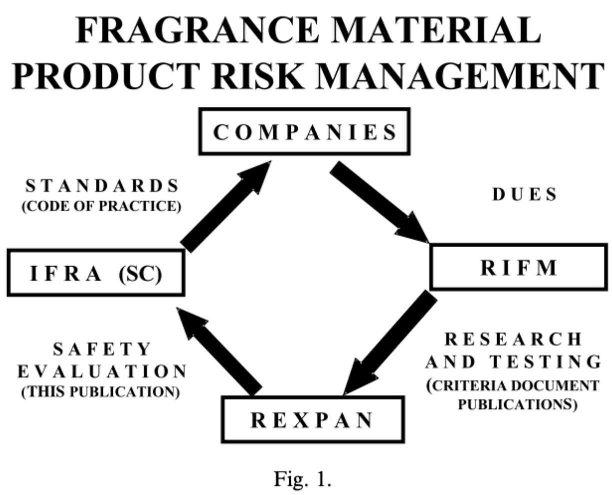


Figure 1 The process by which fragrance companies get their materials cleared for commercial use through evaluation companies including the RIFM and IFRA. Schematic depicting the cycle of fragrance evaluation involving fragrance and evaluation companies.(Bickers et al., 2003).

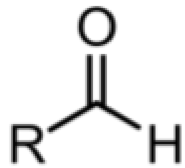
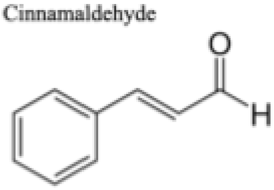
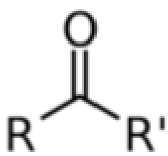
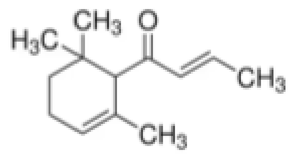
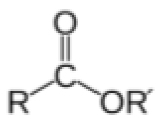
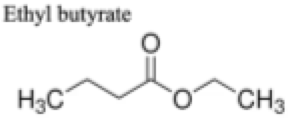
Cologne Chemistry

After spraying a fragrance, the scent is split into top, middle, and base notes. Immediately after release, the top notes are most heavily received due to those compounds being the quickest to evaporate. As the fragrance dries down, the middle notes and soon base notes are more present and continue to linger, giving the fragrance its signature scent which it would be known by. Some of these scents can be credited to different compounds in the structures of the fragrance called functional groups, which react with olfactory receptors in the nose creating the sensation of smell. Out of the many different ingredients in fragrances, some of the most commonly found ones are functional groups (displayed in figure 2) including aldehydes, ketones, and esters. Aldehydes are a type compound made up of a carbon atom singly bonded to a hydrogen and simultaneously double bonded to an oxygen. They are known to smell fruity, fresh, and soapy, and are commonly used in the fragrance industry. Ketones form a structure where a carbon atom is double-bonded to an oxygen atom and also single-bonded to two other carbon atoms or carbon-containing groups. While not widely used in the fragrance industry, ketones contribute to musky scent profiles seen in commercial fragrances. Formed through a chemical reaction between an alcohol and a carboxylic acid, esters can be attributed to a wide range of sweet, fruity, or floral scents while still complimenting a large amount of scent profiles. The chemical properties dictated by these functional groups, such as volatility (as related to how quick compounds vaporize), solubility (in skin perfumery and perfume bases), and stability to degradation are critical to the performance of a fragrance molecule. Greater volatility, for example, is found in top notes while lower volatility is more characteristic of base notes. In addition, lipophilicity (the affinity for fat/oil) causes retention to the skin.

Most perfumes are chiral compounds, meaning they can occur as stereoisomers: molecules that have the same chemical formula and connectivity but differ in the spatial arrangement of atoms. Chirality can significantly affect how odors are perceived due to olfactory sensors being chiral molecules themselves. Specific stereoisomers like (R)-(−)-carvone and (S)-(+)-carvone having this differing spatial arrangement causes the former to smell of peppermint, and the latter to smell like caraway.

Fragrance ingredients can be categorized as natural and synthetic ones, and each has a different origin and it has a different aromatic note to it. Natural ingredients are either vegetable or animal based. Some of the plant's derived elements include essential oils, resins and absolutes. The oils are obtained by distillation and associated technologies of plant materials to produce the so-called essential oils, trees to produce the so-called resins (e.g. of myrrh, vanilla), and more delicate flowers such as jasmine or rose to produce the so-called absolutes. Two animal sources that have had noticeable carryings-on in perfumery are musk over the deer and ambergris on the sperm whale, both of which assist in supplying warm and lasting backgrounds (to fragrance designs).

Table 1 Table showing certain functional groups and their structures shown alongside example chemicals real world examples and how they are perceived olfactorally

Functional Group	Formula	Example	Scent
Aldehyde		Cinnamaldehyde 	Clean, fresh, can have floral and citrus hints
Ketone		Damascone 	Broad spectrum of scents, commonly sweet, musky, and pungent
Ester		Ethyl butyrate 	Sweet, fruity

Cologne Production

Making perfume requires a meticulous process of transforming various raw botanical and synthetic materials into a fragrant product for commercial use. This journey involves several important stages starting from obtaining raw materials, to its appropriate formulation and blending, all while preserving quality of the product.

While modern colognes utilize both synthetic and natural products, about two thirds of compounds used in present day fragrances are synthetic (Duran, 2024). Compositions of most fragrances are as such oils both natural and synthetic taken from fragrant plant extracts or chemically created including the aforementioned functional groups, different substances used to change unfavorable aspects of perfumes, and solvents that oils dissolved into usually consisting of a ratio of 2 percent water and 98 percent alcohol (Herz, 2011). As a more informal experiment, a study conducted by the Nnamdi Azikiwe University in Nigeria showcased a perfume that was manufactured in a lab with pineapple rind as a base. The rind was first smashed and soon after drenched in ethanol in order to extract the solid particles, which were soon after dissolved to create the makeshift perfume (Nnoli, 2022).

Being sourced from plants, aromatic oils are produced through a variety of methods having evolved over centuries. Yet, many of those older methods, some modern realization included, are still prevalent. The methods hence stand divided: steam distillation and solvent extraction. Steam distillation is the most maintained method for "tough" oils-from lavender, peppermint, and eucalyptus plants, for instance. Steam under pressure is passed through the plant material, causing evaporation of the volatile aromatic substances. The vapor is then condensed, and since the essential oils usually do not mix with water, they are separated from the water condensate (Guenther, 1948). A schematic diagram of this method is shown in Fig. 3. The efficiency and quality of the oil extracted depend on variations in steam pressure, temperature, and length of distillation. Solvent extraction (Fig. 3) is used for delicate materials like the flowers of jasmine or tuberose, because the aroma might be changed or destroyed by the heat necessary for steam distillation. Hydrocarbon solvents (typically hexane) are alternately used to dissolve the aromatic constituents.

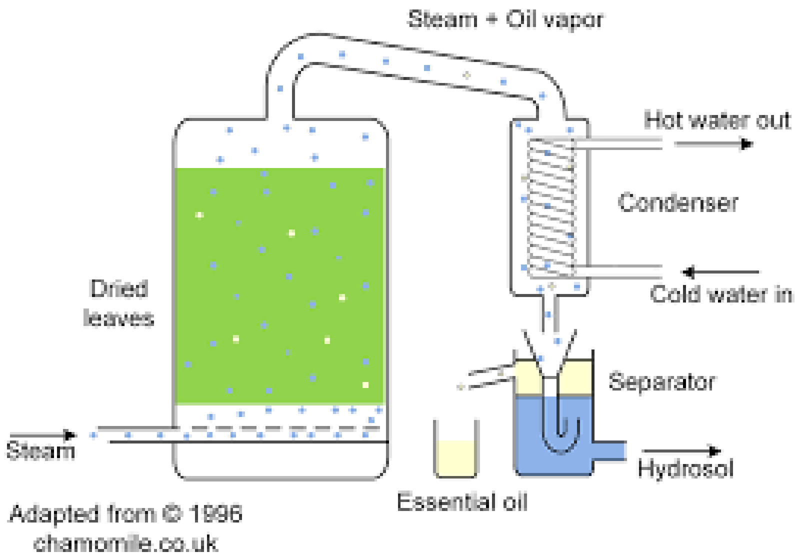


Figure 3 Diagram indicating the steam distillation process by which essential oils are extracted from natural products.

Risk Assessment

Materials extensively used in fragrances require a classic risk analysis to assess their harmfulness and prevent their possible negative consequences to human health and the environment. Fragrances, although intended to positively impact consumers, pose numerous risks due to their complex chemical makeup and their multi-route exposure, especially in regard with allergens and some essential oils.

A. Allergens and Sensitization Health Impacts

Allergic reactions related to fragrance materials, for example contact dermatitis, pose a potentially major health issue. A significant percentage of the population confirms a sensitivity to fragrances, with many reporting to have experienced physical ailments like respiratory or mucosal problems following fragrance exposure . Particular fragrance components have been discriminated against as utmost sensitizers. As an example, fragrance mix I (FM I), fragrance mix II (FM II), geraniol, Evernia prunastri (oakmoss absolute), hydroxycitronellal and methylisothiazolinone could be regularly recognized as causing dermatitis . Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), isoeugenol, atranol, chloroatranol, D-limonene, linalool and lilial also have been identified in high concentrations as being strong allergens . Geraniol, possessing typical rose odor, is found in nature in several essential oils: rose, palmarosa, geranium, citronella, jasmine and lavender oils . On the same note, R-limonene and S-limonene occur in the tea tree oil and the turpentine oil . HICC and D-limonene specifically pose the following effects.

HICC, often called Lyral, is an artificial aromatic aldehyde with a delicate floral scent. It has been identified as a powerful contact allergen in that it is able to cause allergic contact dermatitis (ACD) when consumers are exposed to it after long periods and even after minute use. Incredibly, HICC is not subject to any previous metabolism before being immunogenic as it is reacting with skin proteins to induce a sensitization sequence that would make it a pre-hapten. Both clinical and patch test evidence continues to show that HICC continues to be one of the most common perfume allergens in Europe (Schnuch et al., 2007).

Due to this increased tendency towards sensitization, regulatory agencies have imposed a blanket ban on HICC in formulating cosmetics, since August 2021 as part of the Cosmetic Products Regulation (EC) No 1223/2009 by the European Commission. Environmentally, though so far largely uncharacterised ecotoxicological information is available on these substances, the synthetic aldehydes such as HICC have been measured in waste water effluents leading to some degree of concern over their potential to generate bioaccumulative pollution with adverse effects upon aquatic microbial ecosystems.

D-limonene is a monocyclic terpene, which is naturally found in citrus fruit essential oils. It is popular in perfumery and industrial solvents, and domestic solvents. Having previously been identified as generally safe in its unoxidized state, D-limonene becomes highly sensitizing when it comes into contact with air, forming oxidisable products including limonene hydroperoxides. These oxidative derivatives cause Type IV hypersensitivity, so D-limonene is one of the most widespread reasons for fragrance-induced ACD because of these oxidized derivatives (Karlberg et al., 2008). In the environmental arena, D-limonene has been established as biodegradable although at rather low concentrations it has been found to be toxic against aquatic life forms like Daphnia magna and other fish species. Moreover, D-limonene is a volatile organic compound (VOC), and widespread releases of this substance can lead to the formation of tropospheric ozone causing the negative effect of air quality worsening and smog-related environmental pressure factors indirectly.

B. Health effects: systemic and respiratory effects

Besides the impact of dermal reactions, exposure to fragrances may result in respiratory and systemic complications. The elderly,those with weak respiratory systems, and those with asthma make up the list of people who may develop such symptoms as headaches, nausea, rhinorrhea and shortness of breath amongst some of the common chemical fragrances [1, 10]. Some of these oils are known to poison the central nervous system, kidney and respiratory ducts when they are ingested orally. Other than that, limonene which is a common odorant constituent can be subjected to ozonolysis, yielding an oxidation product such as 4- acetyl- 1- methyl cyclohexene, 4- oxopentanal and 3- isopropenyl -6- oxo heptanal. These are known to possess cytotoxic effects towards those of human bronchial and alveolar epithelium by leading to the inflammatory excretion of cytokines .

Cytotoxic activity refers to the ability of a compound to damage or kill living cells by interfering with the most basic cell activities e.g. energy production, protein action or membrane function. Even though a variety of mechanisms may be triggered by fragrance materials to cause cytotoxicity, oxidation, haptenation, or insertion into membranes are the most common. Such as D-limonene and linalool oxidize under the effects of oxygen, creating reactive oxygen species (or ROS) which destroy the cellular components and increase oxidative stress levels. The binding of HICC to cellular proteins by means of haptenation damages the normal functioning of the cell and causes immune responses by triggering it. Also, some fragrance chemicals have the ability to intercalate into cell membranes thus compromising the integrity of such structure, resulting in leakage or lysis. Such responses are of particular relevance to such cells as skin, and highlights the need to stringently test fragrance chemicals in consumer products

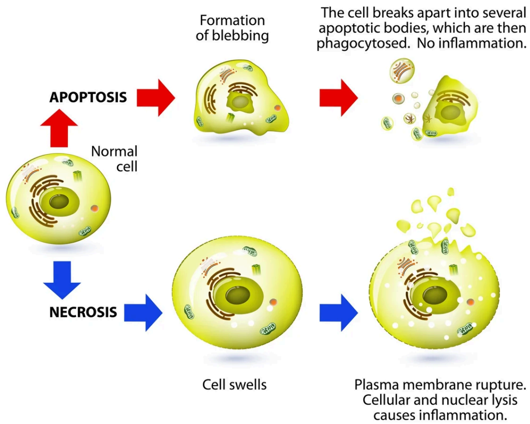


Figure 4 Features of the necrotic and apoptotic cell death as a result of cytotoxic effects (Krumm 2018)

C. Environmental aspects

Human health is normally the factor of highest interest in fragrance risk assessment, but their environmental impact on the materials used in the fragrance is also of serious concern. The majority of these fragrance chemicals are volatile organic compounds (VOCs) and present a content of air pollution along with ground-level ozone depositions. Further, the ingredients retain their shape and become very difficult to destroy, leaving some remains in the environment that may reach the water reservoirs poisoning the fish in the water. An evaluation of the risk must be thorough and must be put into consideration the human and environmental concerns.

D. Regulatory Framework and Safety Guidelines

To mitigate the risks in fragrance use, institutions such as RIFM and IFRA are important in the development of safety tips and standards in the handling of fragrance products. A large program of safety testing is done by RIFM who consider both prior information and direct entry of consumer exposure into eight major endpoints of genotoxicity, repetitive doping and reproductivity toxicity, skin sensitization, photo irritation, photo-allergenicity, and local respiratory toxicity. The results are verified and approved by a nonprofitable Expert Panel on Fragrance Safety. In its turn, IFRA interprets these scientific evaluations to practical standards, and limits the boundaries of fragrance production, so that consumers would be safe. Such standards usually entail reduction of use of some ingredients, a maximum concentration level on the finished products, or restriction of use on certain applications. A scientifically sound and effective process of fragrance safety relies heavily on the collaboration efforts of RIFM and IFRA.

Nevertheless, there are problems. There are too many ingredients in fragrances and they react together creating the difficulty in thorough evaluation. The inability to have full disclosure of ingredients as a requirement in several areas also serves to complicate consumer knowledge and avoidance issues. The way forward is to ensure greater transparency over labeling, encourage green chemistry laws in designing a fragrance, and further studies on long-term health and environmental implications of fragrance exposure.

Conclusion

Overall, the continuous addition of fragrance ingredients in common consumer items not only enhances perception, but also requires creation and sustainment of thorough risk-assessment schemes. These complex chemical formulations and diverse production processes, as well as, their possible negative health and environmental impacts associated with chemicals have been spotlighted above. In addition, it has highlighted the roles played by organizations like Research Institute for Fragrance Materials (RIFM) and the International Fragrance Association (IFRA) in establishing safety standards and their enforcement, and at the same time pointed out long-term issues associated with ingredient disclosure and the continued need for research on long-term effects. As a result, the foundation that brings together the interested parties in the industry, regulatory agency and the scientific community is necessary in advancing the concepts of green chemistry and comprehensive ingredient disclosure where the overall aim is safeguarding the health of populations and preserving environmental quality and innovation of the fragrance industry. This dedication towards standards of science and ethics will determine a future where the enjoyable value of fragrances may be experienced completely without threatening harm

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