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Artificial fragrances and semisynthetic perfumes: The hidden health risks

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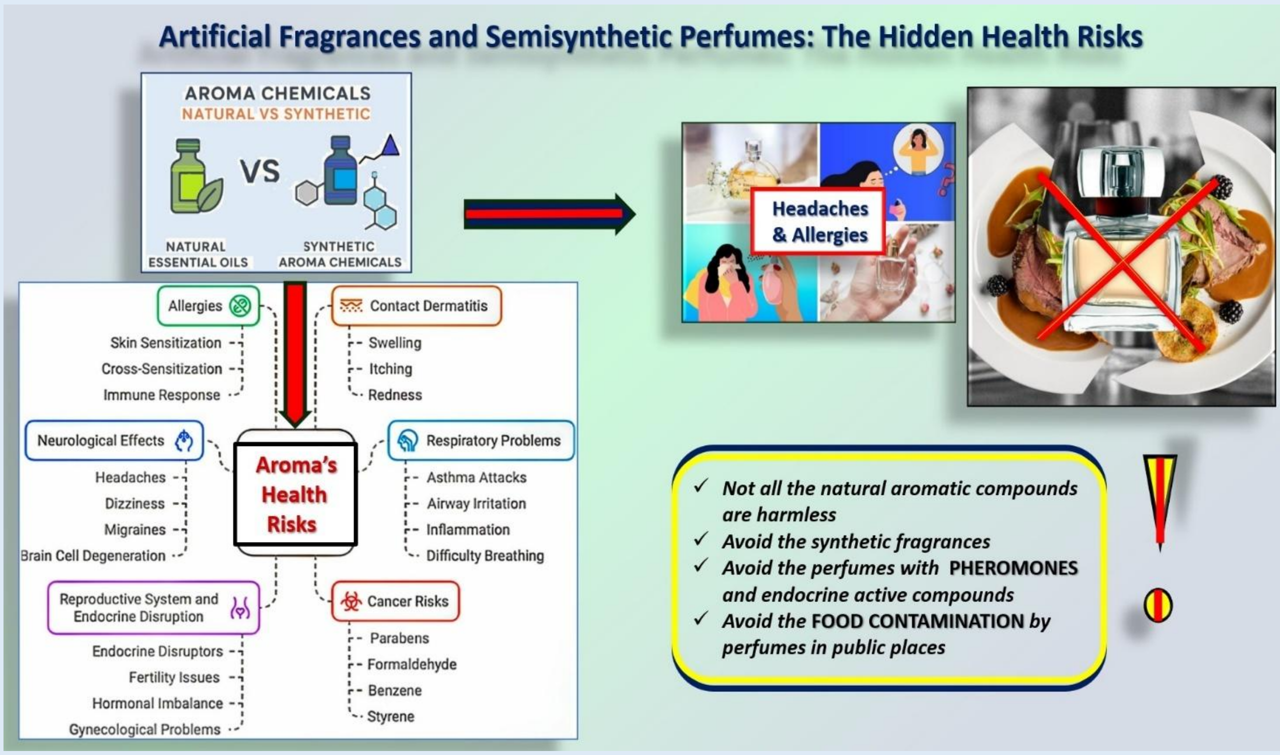
ABSTRACT

Both synthetic and natural fragrances have wide applications in personal care and household products. Their roles are to enhance the olfactory appeal and mask unpleasant odors. Some fragrances are even used in aromatherapy. However, large components of these fragrances include pheromones and volatile organic compounds (VOC), among other compounds. These have a wide range of side effects and could be dangerous to health with long-term use. They even may impact indoor plants. Thus, long-term, repeated exposure to these fragrances in indoor environments, including workplaces, may result in respiratory symptoms, skin irritation, headaches, a weakened immune system, asthma attacks, cardiovascular diseases, hormonal problems, infertility, and neurological and behavioral disorders.

This review aims to highlight the biological effects of odor-causing VOC, particularly semisynthetic and synthetic fragrances of personal care and household products, which may impair indoor air quality and negatively impact human health.

This review also synthesizes recent evidence on endocrine-active constituents in artificial and semisynthetic fragrances, car and indoor air fragrances, air fresheners, etc. highlighting underrecognized exposure pathways, plausible hormonal-disruption mechanisms, and emerging health risks across consumer settings the critical trigger for the occurrence of some acute and chronical pathologies or the aggravation of the existing ones. Moreover, the presented information links support targeted research on bioactive profiling, consumer exposure reduction, and translational guidance for safer product design, aligning with the Functional Food Science scope and priorities for future investigations.

Keywords: synthetic fragrances, semisynthetic aromatic compounds, chronic diseases, endocrine active compounds, hormone disorders



Graphical Abstract: Artificial Fragrances and Semisynthetic Perfumes: The Hidden Health Risks

INTRODUCTION:

From a phylogenetic standpoint, the chemical sense of olfaction represents the most ancient sensory modality across both terrestrial and aquatic organisms on planet Earth. For most animals, olfaction is crucial for survival, aiding foraging, detecting environmental hazards, and facilitating reproduction [1]. Unlike the other sensory systems, olfaction exhibits distinctive features: vertebrates, including humans, can discriminate among thousands of odorants owing to a large repertoire of genetically encoded olfactory receptors. These receptors have a functional lifespan of approximately one month, after which they are continuously renewed through neurogenesis in the olfactory epithelium [2]. Historically, fragrances and perfumes assumed significant cultural importance in ancient civilizations, including Egypt, Greece, and China. [3-5]. Central to their use was the belief in the supernatural efficacy of scents, categorized as “pleasant” or “unpleasant,” for purposes ranging from therapeutic interventions to religious and funerary practices, including the embalming of the deceased for the presumed afterlife, ritual purification, and the invocation of divine favor [6]. Perfumes were also employed to mask natural body odors, enhance personal grooming, and provide hedonic signals relevant to sexual selection.

In contemporary biomedical research and practice, olfaction is increasingly recognized for its diagnostic potential. Loss of smell may serve as an early biomarker for neurodegenerative disorders such as mild cognitive impairment, Alzheimer’s disease, and Parkinson’s disease, as well as for assessing inflammatory activity in conditions like multiple sclerosis. The capacity of the olfactory system to regenerate through the renewal of receptors and inhibitory interneurons underpins recovery from olfactory deficits following respiratory infections, including those associated with pandemics such as COVID-19, or after traumatic brain injury [7-9]. Moreover, neuroimaging studies of olfactory dysfunction have revealed clinically significant structural alterations within the olfactory network and its reciprocal connections with other brain systems. These interactions support higher-order cortical functions, including odor memory, emotional regulation (including both normal and psychotic reactions), cognition, dietary preferences, social behaviors, stress responses, and susceptibility to depression, thereby underscoring the profound role of olfaction in human quality of life [10-11].

The fragrances constitute some of the most common compounds in contemporary food products, perfumery, cosmetics, personal care formulations, and various household items such as dishwashing liquids, laundry detergents, room fragrances, etc. Also, they are widely used in foods and beverages as versatile flavorings [12-13]. Within cosmetic and domestic applications, their principal functions are to impart agreeable olfactory properties or to mask the malodorous substances in the consistency of a particular product [14]. These compounds might be derived from natural sources (plant-derived oils, insect-derived bioactive compounds, etc.) or be synthesized chemically as fully artificial or semi-synthetic substances, often based on naturally occurring precursors (e.g., pheromone derivatives, esters of plant-derived organic acids, waxes, essential oils, etc.) [15-16]. The use of fragrances is intended to elicit positive emotions and is associated with probable therapeutic effects, including stress reduction and enhanced memorization linked to olfactory cues [17-19]. However, fragrances can also exert adverse effects on human health and the environment, including contact dermatitis (irritant and/or allergic), non-eczematous contact reactions, photosensitivity, photo allergy, and immediate contact responses, all of which may negatively impact quality of life [20-23]. The primary sources of exposure include cosmetic products, household chemicals, industrial substances, food flavorings, oral hygiene products, and topical medications. Consequently, individuals with sensitization (and the individuals with inherited predisposition to the receptor sensitization) face the difficulty avoiding exposure to fragrances due to their ubiquity and the fact that manufacturers do not consistently disclose the composition of fragrance ingredients [24-26]. Depending on the chemical nature of a specific fragrance, a range of long-term effects may also occur, manifesting as dysfunctions of the immune, nervous, and endocrine systems, thereby producing systemic pathological consequences (Figure 1) [27].

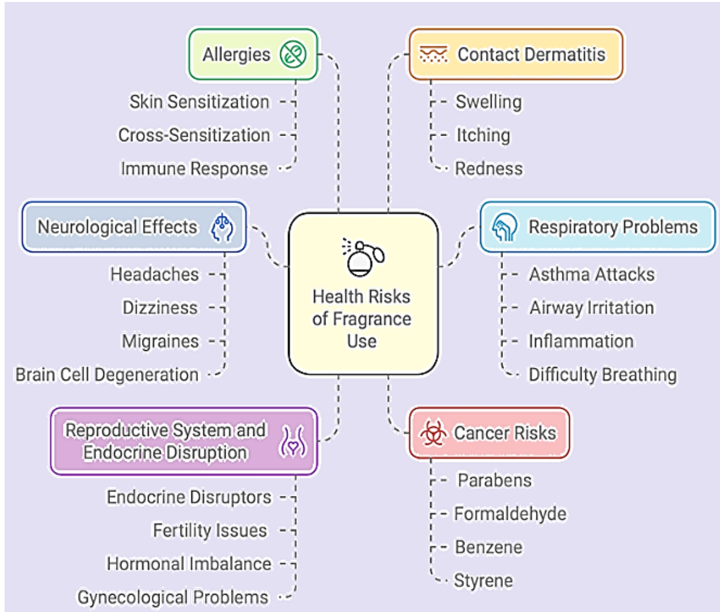


Fig. 1. The main mechanisms of negative influence of synthetic fragrances on human health [26-27].

This review investigates how both synthetic and semisynthetic fragrances can be linked to the health risks posed by the occurrence and aggravation of some chronic and acute pathologies of the human body, as evidenced by their bioactive compounds.

METHODOLOGY

Several methods are available for studying the hazardous effects of fragrances on human health, while adhering to all required ethical protocols and international standards [28-29]. The impact of pheromones, perfumes, and other aromatic substances on humans has been investigated using a wide range of methodological approaches spanning chemical, physiological, psychological, and clinical domains [30-32]. Some chemical-analytical techniques are described in literature: gas chromatography–mass spectrometry (GC-MS) and high-performance liquid chromatography (HPLC), are employed to characterize the composition of volatile organic compounds (VOC), while advanced tools like electronic noses provide odor profiling [33-36]. Physiological assessments include electroencephalography (EEG) and electrocardiography (ECG), functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), electrodermal activity, cardiovascular measurements, and endocrine markers such as cortisol, testosterone, and oxytocin, enabling the study of neural, autonomic, and hormonal responses [37-42].

Also, some cheminformatics, bioinformatics, artificial intelligence, and machine learning based methods might be found in some literature sources [43-45]. For the evaluation of the effects of fragrance components on target organs and systems, a range of biochemical analyses is applied: complementary immunological and biochemical analyses examine cytokine profiles, immunoglobulin levels, biomarkers of oxidative stress, endocrine status, etc. [46-47]. Psychological and cognitive methods, including validated questionnaires, memory and attention tasks, and implicit association tests, are applied to capture subjective and unconscious responses to odors. Behavioral paradigms assess changes in social interaction, partner preference, task performance, and fatigue following olfactory exposure [48, 49]. Finally, clinical and epidemiological studies, ranging from case reports of dermatological or respiratory reactions to large-scale cohort investigations, provide insights into the long-term health implications of repeated exposure to synthetic and natural fragrances. Together, these approaches allow for a multidimensional evaluation of effects on human physiology, cognition, and behavior [50-52].

General Types of Food Flavoring: Food flavoring substances can be categorized into three principal groups according to their origin: natural, nature-identical, and artificial. Also, they can be classified based on their functional application and chemical structure [53]. Natural flavorings include essential plant-derived oils such as lemon, mint, and cinnamon extracts (vanilla, coffee, cocoa, and various spices); fermentation products such as yeast extracts and soy sauce; and naturally occurring aroma compounds like menthol and natural vanillin. Nature-identical flavorings are synthetic substances that are chemically indistinguishable from their natural counterparts, including vanillin, limonene, and eugenol. Artificial flavorings, in contrast, represent completely synthetic compounds without direct natural analogues (ethyl maltol, butyl-phenyl-methyl-propional, γ-undecalactone, etc.). Beyond their origin, flavorings are further distinguished by chemical class, encompassing aldehydes (vanillin, citral, benzaldehyde), ketones (acetoin, ionones), alcohols (menthol, linalool), esters (ethyl butyrate, isoamyl acetate, methyl anisate, etc.), lactones (γ- and δ-lactones for peach, coconut notes), phenolic compounds (eugenol, guaiacol), terpenes and terpenoids (limonene, pinene), and diverse heterocyclic compounds: pyrazines (roasted, nutty flavors), furans (caramel, bread crust), thiophenes, thiazoles, thiols (sulfur notes in meaty flavors), pyrroles and indoles (smoky, chocolate notes), etc. [54-55]. Based on technological role and application, wherein flavorings are grouped into sweet-aromatic substances (vanillin, ethyl maltol), fruit and berry flavors (isoamyl acetate, ethyl butyrate), spicy and herbal notes (cinnamon, clove, nutmeg), meaty and broth-like compounds derived from Maillard reaction products, caramel and roasted flavors (furfural, 5-methylfurfural), and smoky or burnt/charred notes (guaiacol, cresols). Sometimes the mentioned compounds can be used not only for food, but also for vapes and cigarettes and other products for smoking, which enhances their negative impact on health [56-58]. Many of the mentioned compounds have a wide range of side effects and a significant negative impact on health in case of chronic use. The application of some of them is restricted in several countries. In contrast, in other countries, there are strict limits on their use in products, with estimated limits on their consistency in products [59-60].

Synthetic Fragrances of Perfumes and Other Household Products: Both artificial and semisynthetic agents are used to produce aromatic mixtures and fragrances. Their effects on the human body may be diverse; they depend on the chemical nature of the compounds, their combination, the dosages, and the duration of exposure (Table 1).

Table 1. Synthetic and semisynthetic fragrances bioactive compounds' effects on health [61-68].

Fragrance Chemical	Source	Known or Suspected Biological Effects
D-Limonene	Citrus essential oils, "lemon" fragrances, cleaning agents	Skin irritation and sensitization (especially oxidized forms); in male rats, renal tumors associated with *α2u*-globulin; affects the liver at high doses [60-63].
Linalool, oxides, hydroperoxides	Perfumes, cosmetics, soaps, air fresheners	Weakly sensitizing (when pure), air oxidation forms hydroperoxides that are potent contact allergens [64,86].
Synthetic musks (Galaxolide HHCB, Tonalide AHTN)	Perfumes, detergents, cosmetics as "musk" fixatives (stability agents)	Bioaccumulation in tissues, weak estrogenic and endocrine disruptor; *in vitro* enhancement of other toxins, environmental persistence [60-61].
Phthalates (diethyl phthalate, DEHP)	In fragranced cosmetics, perfumes, solvents	Endocrine disruption, reproductive toxicity, developmental effects (especially in children or fetuses), possible neurodevelopmental effects [65].

Fragrance Chemical	Source	Known or Suspected Biological Effects
Benzyl alcohol and derivatives	Component of fragrance blends, solvents, fixatives	Skin and mucosal irritation; potential neurotoxicity [62-63].
Formaldehyde-releasing aroma fixers (DMDM hydantoin)	fragranced shampoos, soaps, lotions	formaldehyde mediated irritant and carcinogen; can cause sensitization and allergies [64-67].

Semisynthetic Fragrance Compounds of Perfumes and Other Household Products: According to modern research, not only synthetic but also particular animal-derived and semisynthetic fragrances and flavoring compounds may pose risks to human health. The primary concern is endocrine-active substances, which are chemically similar to certain endocrine, paracrine, neuromodulatory, and other physiologically active compounds in the human body. They can come from multiple sources, including food, beverages, skin care products, household products, etc. Acting as mimetics of natural ligands, these endocrine active compounds (EAC) (pheromones, hormone derivatives, animal musk) can alter receptor functions, producing a spectrum of direct and indirect effects. Consequently, both short-term and long-term exposure to such compounds may lead to serious health consequences, including the development of various pathologies [63-65]. Most of these adverse effects are associated with the nervous, endocrine, reproductive, and immune systems. Also, the fragrances are among the most frequent causes of contact dermatitis, mucous membrane inflammatory reactions, respiratory problems with asthmatic manifestations, and associated conditions (Table 2).

Table 2. The main effects of common EAC of fragrances on human health [66-76].

Endocrine active compound	Source / Application	Biological Effects
Androstadienone, Androstenol, Androstenone	Synthetic or natural; used in “pheromone” scent blends; human and boar secretion products; “musky animalic” note	Nervous, behavioral effects (mood, attention, social, sexual perception of dominance, attraction); on androgen pathways, cortisol/androgenic signaling, hypothalamus (immunity decrease, obesity, anorexia, etc.) [66].
Estratetraenol	Synthetic estrogen-like volatile (used experimentally and in niche products)	Affect male sexual cognition and social perception; risks of interacting with estrogen signaling and immunity modulation; some cases of perfume form toxicity [67].
Copulins, vaginal fatty acid esters, volatile acids	Not as common as listed perfume ingredients, used in some “female pheromone” products, experimental work	testosterone increase (potential increase in aggression, immunosuppression, alteration of attractiveness and behavior; some instances of direct toxicity in perfume form [68-69]).
Civetone and/or civet extracts	Animal-derived musk (historically: civet); synthetic civetone (modern)	contact allergen, skin and respiratory irritation, sensitization potential [70-71].
Natural & synthetic muscone and macrocyclic musks	Natural muscone from musk deer or synthetic analogues	Bioaccumulation in adipose tissue, breast milk; weak estrogenic effect; induction of metabolizing enzymes, response modulation; skin irritation, allergies, and sensitization potential [72].
Bombykol (moth pheromone)	Insect pheromone, not a common perfume ingredient	Almost exclusively studied in insects; Not well-studied [73-74].
Synthetic pheromone blends, commercial “pheromone” fragrances	Marketed as “pheromone perfumes” (mixtures of the above-mentioned steroid odorants, musk, fixatives, solvents)	phthalates contamination (endocrine disruption); oxidizable terpenes (allergies, dermatitis/airway irritation); behavioral effects, chronic low-dose endocrine activity potential [75].
Macrocyclic ketones, “fixatives”: cetalox, ambroxane analogues, etc.	Common fixatives in modern perfumes (“pheromone enhancers”, long-lasting, etc.)	Skin sensitization potential, low toxicity with the range of intermediated effects (endocrine, immune, reproductive) [76].

Some compounds: 2-methyl-1,3-benzothiazole, lactones, limonene, α-pinene, etc. Carnivorous fungi synthesize VOCs to attract nematodes [77]. They are also used in some perfume compositions. Besides this, they are used in some pollinators and pest control agents. 2-Methyl-1,3-benzothiazole is a respiratory and mucosal irritant with potential neurotoxic effects [78-80]. Lactones are generally regarded as safe but may exert irritant or endocrine-disrupting actions at high concentrations. Limonene, a principal constituent of citrus oils, demonstrates antioxidant and anti-inflammatory properties. Its oxidized derivatives are allergens and respiratory irritants. α-pinene has bronchodilator and anti-inflammatory potential but can provoke irritation and sensitization upon excessive exposure [81].

The main novelty of this article is the discussion of the fact that the degree of negative influence exerted by these compounds is defined not only by their direct toxicity and other biochemical properties, but also by the genetic and epigenetic characteristics of individuals exposed to a particular substance or mixture. Fragrance constituents examined here intersect with the Functional Food Science framework through identifiable bioactive chemicals and mechanistic biomarkers (e.g., endocrine and inflammatory signaling). Our synthesis informs the functional-food pathway by clarifying exposure contexts, dose considerations, and safety/efficacy signals relevant to formulation, standardization, and post-market assessment.

Another intriguing point is that some food products (e.g., tea, coffee, milk, alcoholic beverages, citrus juices, mushrooms, etc.) can absorb some of the compounds discussed above when used and already unpackaged, potentially altering their original properties. This means unintended enrichment and, consequently, the so-called functionalization of food products by endocrine-active compounds [82-83]. In this case, it would not benefit the organism and might even be harmful to the body. The situation described is common in public food courts, traditional national restaurants, bistros, hotels, and other places where indoor air fragrances, air fresheners, and customers' perfumes come into contact with food. Furthermore, contamination through the absorption of VOCs may lead to a decrease in the nominal characteristics of bioactive compounds of genuine functional foods, thereby reducing their therapeutic effects [84-86]. Thus, control in the perfume and air freshener industries, such as the implementation of appropriate public regulations that balance ethical considerations and multicultural tolerance toward the use of aromatic products in ethnic traditions, is of critical importance, especially in the context of overwhelming globalization [87].

Recent epidemiological research highlights the notably high prevalence of diabetes in the Indian population and a sudden increase in its frequency, which may be indirectly related to the traditionally intensive use of synthetic spices and flavorings. They may contain endocrine-active compounds that contribute to the onset of diabetes [88]. Furthermore, the rise in thyroid pathologies and the growing incidence of infertility within the Armenian population may be linked to the intensified use of artificial fragrances (perfumes, deodorants, air fresheners, etc.) over the past decade, largely driven by globalization-related changes in national behavioral and social traditions [89-90].

CONCLUSION

Synthetic and semi-synthetic fragrances, as the source of endocrine-active compounds present in perfumes, cosmetics, and various household products, represent a significant but insufficiently investigated health concern. Current evidence suggests that both short- and long-term exposure may contribute to uncontrolled endocrine, immune, reproductive, neurological, and psychological disturbances. Moreover, such compounds are associated with allergic reactions, skin and respiratory irritation, and weight fluctuations that may occur independently of lifestyle factors. Given the complexity of their interactions and the paucity of long-term studies, caution is warranted in widespread use. Avoidance of unnecessary exposure should be considered a prudent preventive strategy until more comprehensive toxicological and clinical data are available.

Abbreviations: EAC, endocrine active compounds; EEG, electroencephalography; ECG, electrocardiography; fMRI, functional magnetic resonance imaging; GC-MS, gas chromatography with mass spectrometry; HPLC, high-performance liquid chromatography; MEG, magnetoencephalography; VOC, volatile organic compounds.

Competing interests: The authors declare that they have no competing interests.

Authors' Contributions: All authors contributed to this study. No competing interests were disclosed in this article.

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