

Review

# Essential Oils and Their Single Compounds in Cosmetics—A Critical Review

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Received: 5 December 2017; Accepted: 3 January 2018; Published: 12 January 2018

**Abstract:** Essential oils are widely incorporated in cosmetic products, perfumes and related household products due to the variety of their properties but mainly due to their pleasant odour. The composition of these volatile natural complex mixtures may vary depending on the quality of plant material from which they were obtained and the extraction method by which they were derived. These factors are also important in ensuring the safe use of essential oils in personal care products. As they contain compounds with varied chemical structure and effects, skin sensitivity and irritations as well as other symptoms may arise after their application. Although essential oils are considered as safe and nontoxic when used at low concentrations, available scientific literature indicates that essential oils and their compounds may possess a strong allergy potential. This review focuses on side effects and allergy contact dermatitis caused by selected essential oils and their single compounds in cosmetic products, summarizing data from the most recent scientific literature.

**Keywords:** activity; allergy; contact dermatitis; fragrance; side effects; regulations

## 1. Introduction

Essential oils as well as their isolated compounds are widely used in cosmetic products as they offer a variety of benefits. Their biological activities range from analgesic, antiseptic, antimicrobial, carminative, diuretic, spasmolytic to hyperaemic and stimulatory. The main reason for their usage in cosmetics is their pleasant aroma. Fatty acids, fatty oils and surfactants used in the production-process of cosmetic products often exhibit an unpleasant scent. Effective perfume mixtures are therefore added to these products in order to mask it. If such a product is not explicitly labelled as “fragrance-free”, “contains no perfume” or “scented-free” it can be assumed that it contains fragrance chemicals [1].

There is a variety of cosmetic and personal care products on the market for the purpose of cleaning, nourishing, beautifying and perfuming of the human body in order to protect and retain improved condition of the body and to promote its attractiveness. EU Cosmetics Regulation (Regulation (EC) No. 1223/2009) defines cosmetics as “any substance or mixture intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours” [2].

Due to the antimicrobial and antifungal impact of essential oils, cosmetic preparations such as creams, gels and ointments do not necessarily require an additional chemical preservative if they contain an essential oil or a single compound as an active agent (e.g., rosemary oil, eucalyptus oil) [3].

Essential oils mainly consist of lipophilic, small and non-polar molecules. They can easily penetrate the skin and unfold effects there. Friedl and co-workers [4] determined blood and plasma levels of 1,8-cineole in humans after dermal application compared to inhalation. The compound not

only appeared earlier after inhalation but also the levels in blood and plasma were approximately ten times higher in that condition. These results could be due to accumulation of 1,8-cineole in the fatty tissue after dermal application. In cosmetic products, the concentration of terpenoids is very low and therefore a pharmacological effect seems to be rather unlikely according to these findings. But as the growing importance of essential oils in pharmaceutical and cosmetic products was recognized, Lucia Montenegro and co-workers [5] investigated topical effects of rosemary oil on skin hydration and skin elasticity in human subjects. In this study two application forms of rosemary oil were compared: A gel containing free rosemary essential oil and another gel containing lipid nanoparticles loaded with rosemary essential oil. The results of the study indicated that the oil loaded lipid nanoparticles offered more benefit to dehydrated skin with poor elasticity. Van Vuuren and colleagues [6] proved the high antimicrobial effect of selected essential oils against a wide range of dermatological pathogens.

However, these substances do not only have positive effects; as essential oils and fragrances can be sources of potential allergens, experts gathered at the international organization IFRA (International Fragrance Association) defined which essential oils and which components of them represent a potential allergy risk. They also determined the maximum concentration of them in order to produce safe cosmetic products [7].

The present review provides an update on side effects and allergy contact dermatitis caused by selected essential oils and their compounds that are often added to cosmetic- as well as household-products and therefore appear in our everyday lives. Although many essential oils are also recommended in the treatment of certain dermatological problems due to their activities, we focused on substances that are used to improve a product's odour and/or storage life.

## 2. Allergy Contact Dermatitis

Allergy contact dermatitis, also called contact allergy, is a form of contact dermatitis developed due to an allergic response to an allergen after it came in contact with the skin. It is a hypersensitivity reaction which occurs 48 to 72 h after exposure to the allergen. CD<sup>4+</sup> T-lymphocytes recognize an antigen on the skin surface and release cytokines which then activate the immune system. As immune response, dermatitis is developed. Most common symptoms of contact dermatitis are inflammation of the skin, skin redness and itchy blistered as well as dry and thickened skin. These symptoms can affect any area of the body but most commonly hands and face. Contact dermatitis can be developed by jewellery due to nickel contact allergy or due to fragrance contents in cosmetics and household products but also due to acrylates used in hair extensions and nail cosmetics. Sometimes contact allergy occurs after a certain chemical has been applied to the skin and then exposed to sunlight (photo-contact dermatitis) [8].

Two case reports described patients who developed phototoxic skin reactions within 48 to 72 h after they came in contact with bergamot aromatherapy oil and then were exposed to ultraviolet radiation: A 54-year-old Austrian woman developed facial phototoxic reaction followed by red and oedematous lesions after having applied bergamot aromatherapy oil for few days and later being exposed to sunlight. Using high-performance liquid chromatography (HPLC) the bergamot aromatherapy oil preparation was identified to contain a higher concentration of bergapten (5-MOP) than allowed in cosmetics and tanning agents (0.1 ppm) in Austria. Another 41-year-old patient was treated with bergamot aromatherapy oil in a sauna. When visiting a tanning salon, the patient was exposed to ultraviolet radiation which caused photo-contact dermatitis [9].

The cause of allergy contact dermatitis is commonly determined by using patch tests (contact delayed hypersensitivity allergy test). Small patches containing small amounts of potential allergens are applied to the patient's skin. After 48 h, they are removed to observe the skin for allergic reactions. If a patient is allergic to any of the test substances, a red, itchy bump will appear on the skin. The patch test is repeated but then interpreted 72 to 96 h after application [8].

### 3. Essential Oils

Essential oils are consisted of numerous individual substances which, depending on their concentration, can be divided into main (20–95%), secondary (1–20%) and trace components (less than 1%) [10]. The chemical composition and therefore the quality of essential oils derived from one plant species can vary depending on several factors like the time of harvest, the location of the crop, the part of the plant, as well as the production method.

The International Organization for Standardization (ISO) defines an essential oil as product manufactured by either water- or vapour distillation, by mechanical processing of citrus rinds or by dry distillation. In addition to natural oils of herbal origin, synthetic oils are becoming more and more important. These can be identical to natural oils, called “nature identical essential oils”. When synthesized they are referred as synthetic oils. Only essential oils are used for medical purposes and they must meet the Pharmacopoeias standards for quality. Natural identical oils are only approved by Pharmacopoeia when it comes to mono-substances like vanillin, thymol or camphor. Synthetic oils are most often used in the perfume industry, mainly because they are much cheaper than essential oils. Pharmaceutical products whose composition is almost the same as the cosmetic composition, such as bath salt and bath oil, are allowed to contain natural or synthetic oils [11].

In the literature, the term “essential oil” can often be found incorrectly used for numerous products extracted from plant material by methods other than distillation or cold pressing. Absolutes, aromatic waters and concentrates are such products which are produced from plant material but are not essential oils. These products are used either as part of a cosmetic product or as cosmetic product per se like aromatic waters. These hydrolates are aqueous solutions of the essential oils that remain after steam distillation of the plant material (e.g., “rose water”). Concretes are products extracted from fresh plant material with solvents such as hexane or supercritical fluids such as CO<sub>2</sub>, which are then partly or totally removed. Steam distillation is considered not to be suitable for products obtained from some flowers like jasmine, narcissus and violet leaves since they contain compounds sensitive to high temperature. Absolutes are products obtained mainly from concretes, resinoids, supercritical fluid extracts, or pomades by using ethanol as solvent. These products do not just contain volatile fragrances but all lipophilic components and also some fatty compounds. Absolutes are widely used in the fragrance industry. Most important are jasmine and violet leaf absolutes [12].

Essential oils belong to a substance group that is very often exposed to counterfeiting. They are used as a strong marketing advantage in sale and promotion of numerous beauty as well as personal care products but the prices of natural oils are always higher than those of synthetic oils. Some oils sold on the Internet are labelled as “pure”, “natural” or “100% natural”. According to ISO/TC 54 standard, essential oils must be generally natural and pure, so such labels are unnecessary and do not guarantee good quality of the oil. Adulteration, contamination, incorrect oil production and aging are consequences of low quality oils [13]. Most common ways of counterfeiting essential oils, for financial reasons, are [14]:

- a. Adding of single raw materials,
- b. Adding cheaper essential oils of the same plant but from another country—adjuncts,
- c. Adding of cheap synthetic compounds (identical to natural) isolated from other oils,
- d. Adding of individual synthetic substances to oils and aromatic raw ingredients,
- e. Labelling one essential oil as another,
- f. Blending with less expensive essential oils of the same plant taken from a different part of the plant.

To verify the purity of an essential oil many tests can be performed. For all analyses of essential oils and their mixtures comparison with the standard profile for essential oils is of high importance.

Another issue is the storage of these products. According to the requirements of the European Pharmacopoeia essential oils need to be protected from light in a tightly closed and fully filled container [15]. Photoisomerisation, photocyclisation, oxidation, peroxidation and decomposition

of alcohols and ketone hydrolysis are consequences of inappropriate storage conditions. Safety of essential oils and single compounds can be altered through degradation. In order to avoid such consequences of degradation, the ISO publishes standards for essential oils. The ISO/TS 210:2014 standard prescribes general rules for packaging, conditioning and storage of essential oils [16].

Annex II and Annex III of the EU Cosmetics Regulation settle the use of essential oils and single compounds in cosmetic products. It states that potential allergen substances must be declared on the packaging. General rules for labelling are regulated by the ISO/TS 211:2014 standard. Twenty-six possible allergenic fragrances have been defined, 18 of which can be found as ingredients of essential oils (Table 1). For this reason, they must be declared on the packaging or in the information leaflet if the concentration of these allergenic fragrances is higher than the permissible concentration of 0.01% in shower gels and baths (rinse-off products) and higher than 0.001% in body oils, massage oils and creams (leave on products) [17]. The Cosmetic Directive also requires that a product containing other fragrances must be labelled as aroma, fragrance, or perfume.

**Table 1.** List of the 26 allergenic fragrances in accordance with EU Directive.

| Fragrances  |
|---|
| Amylcinnamal  |
| Amylcinnamyl alcohol  |
| Anisyl alcohol  |
| Benzyl alcohol  |
| Benzyl benzoate   |
| Benzyl cinnamate  |
| Benzyl salicylate   |
| Cinnamyl alcohol  |
| Cinnamal  |
| Citral  |
| Citronellol   |
| Coumarin  |
| Eugenol   |
| Farnesol  |
| Geraniol  |
| Hexyl cinnaminaldehyde  |
| Hydroxy-citronellal   |
| Hydroxy-methylpentylcyclohexenecarboxaldehyde                 |
| Isoeugenol  |
| D-Limonene  |
| Linalool  |
| Methyl heptin carbonate                                       |
| 3-Methyl-4-(2,6,6-tri-methyl-2-cyclohexen-1-yl)-3-buten-2-one |
| Oak moss and treemoss extract                                 |
| Treemoss extract  |
| 2-(4-tert-Butylbenzyl) propionaldehyde                        |

In a recent study Bennike and co-workers investigated the exposure of the general population to these 26 fragrance contact allergens [18]. The study was conducted on 5,588 cosmetic products. A new non-profit smartphone application was used to identify the compounds. It was designed to provide users with information about the chemical substances of their cosmetic products. 85.5% of the tested products contained one of the 26 fragrance allergens, 73.9% of the products contained at least two or three of them. Among all investigated products linalool (49.5%) and limonene (48.5%) were most often labelled. 5.9% of investigated products had one or more of the 26 allergens labelled but did not mention “perfume/fragrance/aroma” on the label. Additionally, hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lycral<sup>®</sup>) was found in 13.5% of the tested deodorants, which is a widely used synthetic fragrance for personal care and household products with allergen potential [19].

A retrospective study based on data from the Department of Dermatology and Allergology, Copenhagen University Hospital Gentofte, investigated the frequency of sensitization to these 26 individual fragrances. 1508 eczema patients were patch tested and 115 (7.6%) patients developed a positive reaction to at least one of these ingredients. 60.9% patients reacted positive to one fragrance when patch tested while 39.1% of patients had a positive reaction to more than one allergen. In a total of 196 patients (13.0%) a sensitization to a fragrance ingredient was determined when all of the fragrance screening markers (Lycral<sup>®</sup>, Fragrance Mix I, Fragrance Mix II and *Myroxylon pereirae*—balm of Peru) were included [20].

The obligatory labelling of the 26 allergens on cosmetic products is highly important as it helps to optimize the diagnosis of contact allergy to fragrance ingredients. For a patient with diagnosed contact allergy to one of these 26 fragrances it is of great importance to be informed whether the desirable product contains the allergenic fragrance since it could lead to reoccurrence of allergy symptoms [21].

### 3.1. Selected Essential Oils in Cosmetic Products

#### 3.1.1. Immortelle Essential Oil

*Helichrysum italicum* essential oil is a pale yellow to red, oily liquid with a strong, honey-like aroma. The flower of *H. italicum* (Roth) G. Don does not wither and the lively colour stays even if the flower is collected and dried. Therefore, it is called “Immortelle”—immortal. In Europe, the oil has mostly been used as an infusion or as tea to treat respiratory tract infections such as asthma and chronic bronchitis but it has also been applied against headache, migraine, skin burns and allergies. Nowadays, immortelle is one of the most popular essential oil in cosmetics as it stimulates the blood circulation in the skin, strongly regenerates the skin and helps to reduce the appearance of fine lines and wrinkles. Due to its scent, immortelle essential oil is used as a fragrance in soaps, cosmetics and perfumes. Several studies on composition of *H. italicum* essential oil can be found which varies according to geographical regions: *H. italicum* oil collected in Montenegro was characterized by a high number of oxygenated monoterpenes (43.9%) and sesquiterpene hydrocarbons (41.2%). GC/MS analysis identified neryl acetate (28.2%) and  $\gamma$ -curcumene (18.8%) as the main compounds while neryl propionate (9.1%) and  $\alpha$ -curcumene (8.3%) existed in significantly lower concentrations [22]. Oil extracted from *H. italicum* collected in Greece contained high amount of geraniol and geranyl acetate [23]. Furthermore, three different chemotypes for the essential oils of *H. italicum* were described: one was rich in nerol, another contained the majority of  $\alpha$ - and  $\beta$ -selinene and the third chemotype was characterized with high concentration of  $\gamma$ -curcumene [24].

Despite this large diversity of its chemical contents, several studies have shown that immortelle oil has an antimicrobial and antifungal activity [25]. It has been effective against bacteria and fungi that can cause skin irritations, infections and delay wound healing. A very strong hematoma-dissolving effect makes immortelle oil one of the best effective oils in treatment of hematomas [26]. In one study a contact toxicity test was performed with six essential oils (*Achillea millefolium*, *Myrtus communis*, *Rosmarinus officinalis*, *H. italicum*, *Foeniculum vulgare* and *Lavandula angustifolia*) against the stored food insect *Sitophilus zeamais* Motsch. Essential oils of *A. millefolium*, *L. angustifolia* and *F. vulgare* showed highest toxicity at any concentration while *H. italicum* essential oil showed low toxicity rate up to a dosage of 0.5 mL per insect [27].

Due to the anti-allergen effect of Immortelle essential oil no publications on allergy contact dermatitis existed in the literature.

#### 3.1.2. Lavender Essential Oil

Lavender essential oil is a clear, colourless to pale yellow liquid with a characteristic odour which is extracted by steam distillation from the flowering tops of *Lavandula angustifolia* Mill. According to ISO standard, the oil should contain linalyl acetate (25–47%), linalool (max. 45%), terpinen-4-ol (max. 8%), camphor (max. 1.5%), limonene (max. 1%) and 1,8-cineole (max. 3%) [28].



There are two varieties of lavender essential oil:

- Lavender essential oil, the classic lavender, is distilled from the flowers of *L. angustifolia*. It has a sweet floral aroma and contains a high percentage of esters, mostly linalyl acetate. It does not contain camphor which distinguishes it from other lavender varieties. The oil is often used for its anti-inflammatory, calming, headache relieving, sedative and skin healing properties. One of the rarely known effects and qualities of *L. angustifolia* oil is its ability to relieve menstrual pain [29,30].
- Spike lavender essential oil is obtained from flowers of *L. latifolia* Medik. This species of lavender contains high percentage of 1,8-cineol and camphor and therefore has a strong camphoraceous odour. Due to these components, spike lavender oil is recommended for skin damages (cuts, burns, stings), as a pain reliever, for headache treatment and for its antimicrobial properties. It has anti-bacterial, antiviral, antimycotic, anti-inflammatory and nourishing properties and is one of most common used and best investigated oil in aromatherapy. It is used for relaxing and stress relief, for nose and throat infections, for skin care, in wound treatments and for stomach problems. It has a pleasant aroma. Lavender oil is also commonly used in pharmaceutical products and as a fragrance ingredient in soaps, cosmetics and perfumes [31].

In Japan, a study was conducted over nine years to estimate the tolerability of lavender oil. Contact dermatitis was diagnosed with patch tests. The results were positive to lavender oil in 13.9% of the patients [32]. One case report described photoallergic contact dermatitis caused by lavender oil in topical ketoprofen, administered in Fastum<sup>®</sup> gel. A 45-year-old patient suffered from erythematous and itching plaque which started on patient's left foot and then spread onto the left leg. The patient was patch positive to 2% lavender oil and to Fastum<sup>®</sup> gel which indicated that lavender oil caused photoallergic contact dermatitis and ketoprofen caused contact dermatitis [33]. One review article summarized 19 publications on allergic contact dermatitis caused by lavender oil. In some of these case reports, patients allergic to lavender oil also showed positive patch test results to linalool [34].

As aforementioned, main components of lavender oil are linalool and linalyl acetate, which are easily oxidized when exposed to oxygen as it happens when the oil is applied onto skin. The oxidized fragrance increases the irritancy on the skin. One study using 6% oxidized lavender oil investigated the frequency of contact allergy caused by oxidized lavender oil. 2.8% of the patients had positive reactions to oxidized lavender which indicated that oxidized compounds of lavender oil are a common cause of contact allergy [35].

### 3.1.3. German Chamomile Oil

Essential oil of German chamomile is one of the most used essential oil in cosmetics. The blue chamomile oil is steam distilled from the flowers and flower heads of *Matricaria chamomilla* L. (Syn. *Chamomilla recutita*, *Matricaria recutita*) [36]. During the steam distillation process, colourless proazulene forms matricin, matricarin, guajazulen and chamazulene, which is responsible for the blue colour of the essential oil. The oil has a sweet herbaceous odour and bitter aromatic flavour. When exposed to air, the light oil changes its colour to brown. It contains a high percentage of sesquiterpene and a low amount of monoterpenes. Important components are  $\beta$ -farnesene, farnesol, chamazulene,  $\alpha$ -bisabolol oxides A and B which are responsible for the anti-inflammatory, antiphlogistic, spasmolytic and antiseptic properties of the oil. Chamomile oil is often adulterated with cheap pure bisabolol extracted from *Vanillosmopsis erythropappa* (DC.) Sch.Bip., which can be detected by IRMS and GC-IRMS [36].

The oil is often used external in skin-creams, skin oils and as bath additives as it is considered to be effective in the treatment of skin inflammation. It can also be found in mouthwash-products, toothpastes, decorative cosmetics and shampoos [37].

Lee and co-workers determined the antipruritic effects of chamomile essential oil in relieving atopic dermatitis symptoms. Patients in the essential oil group experienced a lower scratching frequency compared to patients in the control group [38]. Peristomal skin problems can cause numerous

unpleasant symptoms such as skin discoloration, pain, full-thickness wounds and itching. Patients are often treated with topical corticosteroid preparations whose long-term use can cause serious side effects. One study was conducted to compare the effects of a German chamomile extract and 1% topical hydrocortisone ointment in colostomy patients diagnosed with peristomal skin lesion. The results implicated that German chamomile oil can be recommended in treatment of peristomal skin lesions as it showed anti-inflammatory and antipruritic effects [39].

A randomized controlled clinical trial exerted that topical application of chamomile oil to patients diagnosed with knee osteoarthritis was effective as patients used less of acetaminophen, a known pain reliever. In this study, no adverse reaction to essential oil of *M. chamomilla* was reported [40]. Despite the fact that German chamomile oil is most commonly used in cosmetics and personal care products, barely any reports of contact allergy or allergic contact dermatitis have been described in the scientific literature [36].

#### 3.1.4. Neroli Essential Oil

Neroli essential oil is extracted from the flower of *Citrus aurantium* var. *amara* L., also known as bitter orange. It is an extremely expensive essential oil since for the production of 1kg of oil, 850 kg of bitter orange flowers are necessary. The citrus tree produces three different kinds of essential oils. Neroli essential oil is steam-distilled from the flower, petitgrain oil is produced from the leaves and orange oil comes from the orange peel [41]. Neroli is a pale yellow to coffee brown essential oil with a sweet, fresh and floral odour. Due to its very fine fragrance, it is one of the most important oils in perfume and soap industry. The oil has antimicrobial [42], antidepressant, antiseptic, carminative, antispasmodic and sedative properties. In cosmetics, it is generally used to refresh a tired skin, either sensitive or oily [43].

A comprehensive two-dimensional GC-TOF-MS analysis was used to identify terpenoid compounds, such as linalool,  $\beta$ -pinene,  $\alpha$ -terpineol, limonene, sabinene, nerol, nerolidol, linalyl acetate and  $\alpha$ -pinene as main chemical compounds of neroli essential oil [44].

Neroli essential oil is generally recognized as a non-irritant, non-sensitizing and non-phototoxic oil but it does contain known allergens [45]. However, occupational contact dermatitis was reported due to use of essential oils including neroli essential oil [46]. From May 2001 to June 2002, Belgian Contact & Environmental Dermatitis Group investigated 20 patients suspected of developing dermatitis caused by Fastum<sup>®</sup> gel (ketoprofen) with open patch and photo-patch tests. Fastum<sup>®</sup> gel base contains 5% of lavender oil and 5% of neroli oil in alcohol and 2% of lavender oil and 2% of neroli oil in white petrolatum. The results showed that three patients out of 17 had a positive photo-patch test and two patients had a positive patch test to 5% neroli oil in alcohol. Out of 20 only one patient showed positive photo-patch test to 2% neroli oil in white petrolatum [47].

#### 3.1.5. Peppermint Essential Oil

Peppermint essential oils are extracted from *Mentha piperita* L., a cross between watermint (*M. aquatic* L.) and spearmint (*M. spicata* L.) [48]. The main active ingredients of peppermint oil are (-)-menthol (33–55%) and (-)-menthone (14–33%). Other chemical compounds are 1,8-cineole, methyl acetate, methofuran, isomenthone, limonene,  $\beta$ -pinene,  $\alpha$ -pinene, germacrene, trans-sabinene hydrate and pulegone. Peppermint oil is commonly used as a fragrance in soaps, cosmetics and as spice since it possesses a fresh, minty and cooling effect due to menthol. Added to bitter tasting capsules, peppermint is able to mask the bitterness when orally applied [49]. Due to this flavouring property, peppermint is often found in chewing gums, toothpastes and mouthwashes. For medical use, peppermint oil can be taken orally as a dietary supplement for gastrointestinal complications.

One case report described four patients with allergic contact cheilitis (inflammation of the lip) after being exposed to peppermint oil contained in a lip balm product. The patients' lips and the skin around the lips were inflamed. The lip balm product which they were using contained potential allergens such as lanolin, propolis, coconut oil, almond oil, vitamin E and peppermint oil. The patch-test results

were positive to peppermint oil and indicated that peppermint oil was the most likely cause of allergic reactions in these patients [50]. Another case report noted allergic contact cheilitis caused by menthol in a toothpaste and throat medication [51]. In the period of 2000–2009, positive patch test reactions or positive usage tests to the patients' own cosmetic products were investigated. In this nine year period one patient had positive reactions to peppermint oil which was contained in his cosmetic product [52]. Furthermore, there was one report on allergic contact dermatitis due to use of a product for depilation which contained peppermint oil [53].

### 3.1.6. Rosemary Essential Oil

*Rosmarinus officinalis* L., also known as rosemary, is an aromatic plant which belongs to the Lamiaceae family and is native to the Mediterranean region. Rosemary essential oil is produced by steam distillation from the flowering tips of the plant yielding a colourless to pale yellow liquid with a strong, warm, woody, balsamic aroma. The main chemical compounds in rosemary essential oil are eucalyptol (19.4%) and  $\alpha$ -pinene (14.7%). Camphor (9.5%), bornyl acetate (9.1%), camphene (6.9%),  $\beta$ -pinene (6.7%),  $\beta$ -myrcene (5.8%), limonene (5.2%) and borneol (5.0%) are also found in the oil [54]. Due to its stimulating effects, it is widely used in aromatherapy. Rosemary forms three different chemotypes depending on the location, climate and environment:  $\alpha$ -pinene chemotype, camphor chemotype and 1,8-cineol chemotype. As such, they have different chemical and physical properties. The composition of 1,8-cineol chemotype was analysed with GC/MS and three main compounds were identified:  $\alpha$ -pinene (37–40%), camphor (41.7–53.8%) and 1,8-cineole (58.7–63.7%). The camphor chemotype contains 41–53% of camphor while the  $\alpha$ -pinene chemotype contains 37–40% of  $\alpha$ -pinene [55].

Rosemary essential oil is often an ingredient in bath salts, bath oils, liniments, gels and ointments. It can also be found in cosmetic products such as lavender water, cologne water and as fragrance in soaps. The essential oil of rosemary is widely used for hair care as it nourishes the hair, promotes hair growth and helps against dandruff. It is also recommended in hair-loss treatment as it is believed that it has similar function to Minoxidil, an antihypertensive vasodilator medication, which revitalizes hair follicles that are damaged. Rosemary oil widens blood vessels and opens them and makes blood and nutrients more available to the follicles which are then stimulated into producing new hair. In 2015, one study conducted on patients with pattern hair loss (androgenic alopecia) compared the effectiveness of rosemary oil vs. 2% Minoxidil in the treatment of androgenic alopecia. It was discovered that rosemary oil was as effective as 2% Minoxidil and that patients in the rosemary group experienced less side effects compared to patients in the Minoxidil group [56].

Allergic contact dermatitis due to rosemary oil has been reported in a few publications. Three of them were related to the essential oil from rosemary. An aromatherapist, a physiotherapist and a masseur were diagnosed with occupational contact dermatitis due to exposure to rosemary oil [57].

### 3.1.7. Rose Oil

Rose oil is extracted from the flowers of the *Rosa x. damascene* Mill., also known as damask rose as the flower was initially brought to Europe from Damascus. The literature often mentioned different varieties of rose flower essential oil extracted from different rose species such as *R. canina*, *R. centifolia*, *R. galica*, *R. moschata* and *R. rugosa*. However, most of the commercial rose oil derives from *R. damascene* including rose oil produced in Bulgaria and Turkey which are the world's biggest producers of rose essential oil. Rose oil is widely used as a fragrance in different types of cosmetic products (soaps, body lotions, face creams etc.) and also as a flavouring agent in food products such as jam, ice cream, pudding and yoghurt [58].

Next to rose oil, rose absolute, rose water and rose concrete are important basic materials in cosmetic industries. For the production of 1 kg of rose oil 3500–4000 kilograms of rose flowers are necessary. Due to its expensive industrial production and also to high importance in the cosmetic industry, rose oil is often called "liquid gold" [59]. The most common chemical compounds present in



essential rose oil obtained from *R. damascene* are citronellol, geraniol, nerol, farnesol and androse oxide, which is a fragrance attributed to rose [60,61].

Mohamadi and co-workers [62] investigated the effect of storage on essential oil content and composition of *R. damascene* under different conditions. The authors concluded that it was better to use fresh petals for essential oil production. As the petals collected in large amount cannot be steam distilled all together at the same time, some parts of the petals can undergo various fermentation processes until distillation which influences the rose oil composition. Therefore, it is important to store petals until the time of distillation and to freeze them without water, which has been proven to be the best storage method.

The pharmacological properties of *R. damascene* are numerous including hypnotic, analgesic and anticonvulsant, antidiabetic, antimicrobial, anti-HIV, anti-inflammatory and antioxidant. Furthermore, in Persian traditional medicine the essential oil of *R. damascene* has been used for treatment of male sexual dysfunction and also for libido stimulation. It is considered that lipophylic constituents of *R. damascene* were responsible for most of these effects [63]. Due to its antibacterial properties, it is very effective in moisturizing dry skin and it is often recommended for acne treatment. Rose oil cleanses the skin from bacteria that cause acnes and then hydrates the skin.

Four cases of allergic contact dermatitis to rose essential oils occurred in three aromatherapists and in one chemist with a particular interest in aromatherapy. Patch tests in all four cases were positive to 2% Bulgarian rose oil, which makes it the only oil to which all four patients were positive [64]. In general, patch positive reactions were reported in persons working with the essential oil. Geraniol and citronellol are considered to be the most relevant allergens [65].

### 3.1.8. Tea Tree Oil

Tea tree oil, also known as melaleuca oil, is the essential oil obtained by distillation from leaves and terminal branchlets of *Melaleuca alternifolia* (Maiden et Betche) Cheel (narrow-leaf tea tree), *M. linariifolia* Smith (flax-leaf tea tree) or *M. dissitiflora* F. Muell (creek tea tree).

*M. alternifolia*, Australian tea tree, is either a tall shrub or small tree which belongs to the Myrtaceae family and is native in the coast of New South Wales and Queensland, Australia. It has been used by the Aborigines in traditional medicine. They crushed tea tree leaves in order to extract the oil, which was then inhaled for treatment of cough and cold or applied directly onto the skin for healing. It has antiseptic, antifungal and anti-inflammatory properties and its dilution is used as a topical antiseptic for the treatment of acnes.

Tea tree oil is a clear, colourless to pale yellow, volatile liquid and has a characteristic, intensive aromatic fresh camphoraceous odour.  $\alpha$ -Pinene,  $\beta$ -pinene, sabinene, myrcene,  $\alpha$ -phellandrene,  $\alpha$ -terpinene, limonene, 1,8-cineole, p-cymene, linalool, terpinen-4-ol and  $\alpha$ -terpineol are the most common chemical compounds found in tea tree oil [66]. In order to be defined as "tea tree oil", it must contain the following 15 components in specified amounts, according to the ISO standard given in Table 2 [67].

In the presence of oxygen, high temperature, light and humidity the composition of tea tree oil changes and antioxidant compounds  $\alpha$ -terpinene,  $\gamma$ -terpinene and terpinolene are converted to p-cymene. As it is sensitive to oxidation, the European Cosmetics Association recommended that the presence of tea tree oil in cosmetic products should not exceed the concentration of 1% and that it should be specially packed to secure minimal light exposure. Tea tree oil targets Gram-positive and Gram-negative bacteria such as *Staphylococcus*, *Streptococcus* and *Pseudomonas aeruginosa*. It is also effective against *Candida albicans*, *Dermatophytosis* and *Herpes simplex* virus. Applying 5% of tea tree gel to acne lesions was more than threefold as effective in reducing the number of lesions than a placebo [68].

**Table 2.** ISO 4730 (2004)—Tea tree oil composition.

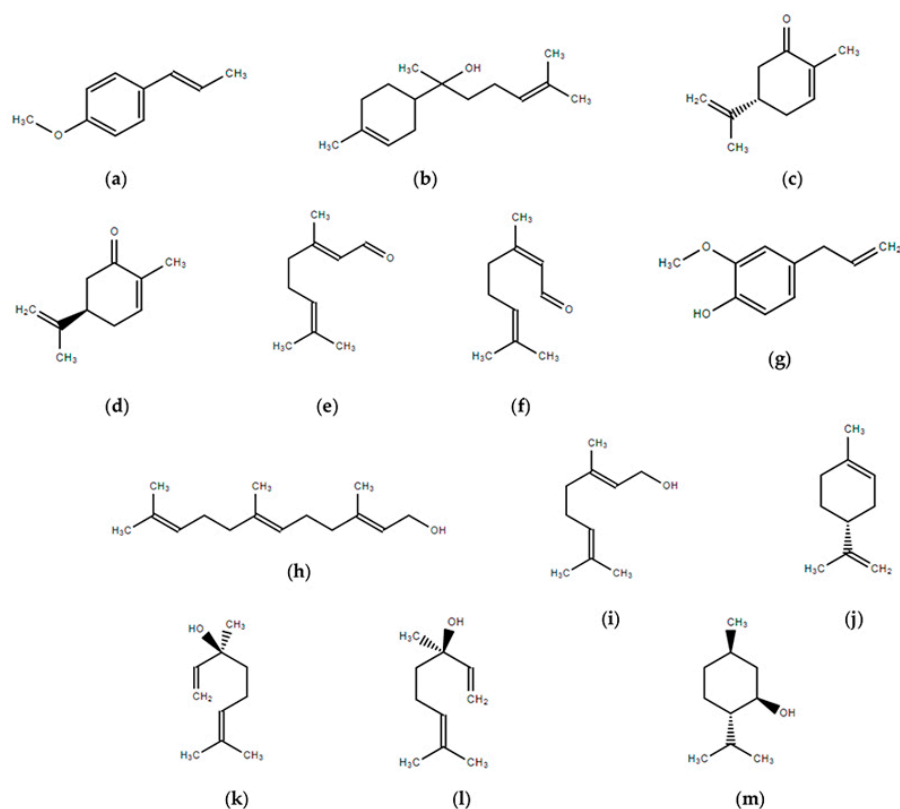
| Component           | Concentration |
|---------------------|---------------|
| Terpinen-4-ol       | 30–48%        |
| $\gamma$ -Terpinene | 10–28%        |
| 1,8-Cineol          | traces-15%    |
| $\alpha$ -Terpinene | 5–13%         |
| $\alpha$ -Terpineol | 1.5–8%        |
| p-Cymene            | 0.5–8%        |
| $\alpha$ -Pinene    | 1–6%          |
| Terpinolene         | 1.5–5%        |
| Sabinene            | traces-3.5%   |
| Aromadendrene       | traces-3%     |
| $\delta$ -Cadinene  | traces-3%     |
| Viridiflorene       | traces-3%     |
| Limonene            | 0.5–1.5%      |
| Globulol            | traces-1%     |
| Viridiflorol        | traces-1%     |

Tea tree oil is also used in the treatment of fungal nail infections. It can be used as a chemical-free mouthwash since it helps to fight bad breath and dental plaque. Several studies suggest that tea tree oil might be effective against germs that cause tooth decay and bad breath [69,70]. If administered orally, tea tree oil is toxic. One case report noted that an 18-month-old boy suffered from serious injuries after accidentally swallowing tea tree oil [71]. One study compared the effects of different treatments for contact dermatitis and tea tree oil. Tea tree oil reduced symptoms by 40% and was more effective than standard medications used on the skin. Surprisingly, there have been many case reports of allergic contact dermatitis, the conditions that tea tree oil may help to treat, reported as a cause of using tea tree oil [72]. One case report noted that five patients developed allergic contact dermatitis due to the topical application of tea tree oil [73]. A review article which summarized the chemical compounds but also case reports and case series of contact allergy to tea tree oil, stated that of all essential oils, tea tree oil has caused the most allergic reactions with the first case reported in 1991 [74]. It is also worth mentioning that the use of tea tree oil in pets may be unsafe: more than 400 dogs and cats developed tremors and other problems of the nervous system after administration of 0.1–85 mL of tea tree oil orally or onto the skin [75].

#### 4. Individual Fragrances

##### 4.1. Anethole

Anethole (Figure 1a) is a phenylpropane derivative and the main aromatic component of anise, anise myrtle and fennel oil. It can also be synthetically obtained. Anethole exists as *cis* and *trans* isomer but the *trans* isomer is used more often. Anethole can have a form of white crystals or a liquid. It has a sweet taste and pleasant odour of anise oil [76]. Anethole has antibacterial, antifungal, antispasmodic and mucokinetic properties and is often used as an expectorant and carminativum. Since it is thirteen-fold sweeter than sugar, it is widely used as the flavouring agent in alcohol drinks, ouzo and raki and in cosmetic products for oral care. It is also used as fragrance in soaps and as a flavouring agent in pharmaceutical products. In some perfumes, the fennel fragrance can often be found while star anise fragrance is used in detergents [77].



**Figure 1.** Chemical structures of most common fragrances. (a) *trans* Anethole; (b)  $\alpha$ -Bisabolol; (c) S-(+)-Carvone (caraway); (d) R-(-)-Carvone (spearmint); (e) Geranial (citral A); (f) Neral (citral B); (g) Eugenol; (h) Farnesol; (i) Geraniol; (j) D-Limonene; (k) S-(+)-Linalool; (l) R-(-)-Linalool; (m) (-)-Menthol.

There have been a few reports of allergy contact dermatitis reactions: A 63-year-old woman suffered from a six-year history of persistent cheilitis. The symptoms were pain, persistent itch and blistering lips. The patient did not use any lipsticks but she was using lip balms and toothpaste produced in China. The ingredients were not listed on the package of the toothpaste. A patch test showed a positive reaction to anethole, which was found in the toothpaste [78]. Another 55-year-old female patient experienced cheilitis for three months. The patient complained about crust on her lips, intra-oral burning sensation, dry mouth and loss of taste. She was patch tested to cosmetics, dental products, fragrances and bakery product series and to her own toothpaste. The patch test was positive to anethole and *trans*-anethole. On all of her dental care products, “aroma” was listed as an ingredient. The producers of the oral products that she used revealed that almost all of the contained anethole [79]. Recently a similar case report indicated a 15-year-old girl with perioral dermatitis due to the usage of toothpaste. Patch test reaction was positive to anethole. On the toothpaste, “flavour” was listed as the only ingredient, which was later confirmed to be anethole by the manufacturer [80].

#### 4.2. Bisabolol

$\alpha$ -(-)-Bisabolol (Figure 1b), also called levomenol, is a monocyclic sesquiterpene alcohol which is one of the main active compounds found in an essential oil from German chamomile. It is a clear, pale yellow liquid.  $\alpha$ -(+)-Bisabolol is an enantiomer which is very rare in nature. Bisabolol can also be produced synthetically as a racemic mixture. Due to its pleasant sweet floral odour, it is used in fragrances and in personal care and cosmetic products. Bisabolol has anti-inflammatory, healing, soothing and antimicrobial properties and it is often a component in moisturizers, sun creams, face creams, cleansers and lipsticks [81].

One case report described seven paediatric patients with a history of intolerance to moisturizers that contained bisabolol. Atopic dermatitis was reported by six patients, while in 14 patients a patch test was performed with 0.5% and 1% bisabolol (three patients) and with 1% and 5% bisabolol in petrolatum. The patients were also patch tested for other moisturizer components. Results showed that four patients were patch positive to 1% and 5% bisabolol. Bisabolol positive patients reacted also positive to Compositae Mix. The rest of the 16 patients with intolerance to the same moisturizer had no positive reaction to patch testing with 1% and 5% bisabolol [82]. In another report, a 14-year-old girl suffered from acute cheilitis over a period of two months. She complained about her red and very dry lips after she had been using a lip-care stick a few times per day for two months. Patch tests were performed on the patient with the European baseline series and with the patient's own cosmetics. Patch test reactions were positive to the girl's lipstick and to Fragrance Mix I as well as nickel. A patch test was also performed with ten ingredients of the stick released by the manufacturer. Two ingredients were patch positive: Bisabolol 5% pet. and Parsol® SL [83].

#### 4.3. Carvone

Carvone is a volatile monocyclic terpenoid which can be found in many essential oils but it is mostly concentrated in caraway, spearmint and dill. Carvone forms two enantiomers with different biological properties: (S)-(+)-Carvone (= D-carvone) (Figure 1c) is found in caraway seeds and has a caraway odour. Its enantiomer (R)-(-)-carvone (= L-carvone) (Figure 1d) is found in mint leaves and is responsible for mint odour [84]. For thousands of years, both carvones have been used in spices and as flavouring agents in food products. L-carvone is a pale yellow to colourless pleasant-smelling liquid which is often added to liqueurs, toothpastes, chewing gums as well as to soaps and perfumes to improve their aromas. It is also widely used in aromatherapy and in complementary medicine [85].

Carvone is considered as a potential allergen since there have been several case reports of hypersensitivity of skin and allergy contact dermatitis due to L-carvone [86–88]. It is not obligatory to be labelled on cosmetic products according to European Cosmetics Regulation. A recent study performed in Sweden analysed a total of 66 toothpastes available on the Swedish market with straight-phase HPLC. The products containing limonene were also chosen since L-carvone can be produced from D-Limonene by various methods. The results showed that L-carvone was found in 64 of 66 toothpastes with the concentration of 0.00005–0.35%. In ten toothpastes on which limonene was labelled, the concentration of L-carvone was higher than 0.1% [89]. One control study investigated whether contact allergies due to potential allergens were causing oral lichen lesions in patients exposed to a variety of dental material. This study included 83 patients with oral lichen lesions and a control group of patients with dermatitis. Patients in both groups were patch tested and examined intraorally. The results indicated that patients with oral lichen lesions had developed contact dermatitis to mercury and carvone more often compared to patients with dermatitis, while the number with contact allergy to nickel and colophony was higher in the group of dermatitis patients. Therefore, carvone is suspected to be one of the main causes of oral lichen lesions. Hypersensitive patients with oral lichen lesions should be advised to avoid carvone-containing products for oral use [90].

#### 4.4. Citral

Citral is a pale yellow liquid and can be obtained from lemongrass oil which contains 70–80% of this monoterpene. It is also found in other essential oils such as verbena oil, citronella oil, orange oil and lemon oil. Citral can be synthetically produced from myrcene, ionone and methylionone. It is an isomeric mixture of two aldehydes, geranial (Figure 1e) and neral (Figure 1f). Neral (citral B) is the (Z)-isomer, while geranial (citral A) is the (E)-isomer. Due to its pleasant lemon odour, it is widely used in perfumes and as a flavouring agent [91].

Several single cases of allergic contact dermatitis in masseuses working in the same health spa were reported by De Mozzi and Johnston [92]. These nine massage therapists were directly exposed to the essential oil as they were massaging their clients. In all of nine masseurs which suffered from

hand dermatitis, patch tests with British baseline series were performed. Six persons who had positive patch test reactions were later diagnosed with allergic contact dermatitis. One person gave a positive reaction to Fragrance Mix I, five of the nine masseurs were positive to Fragrance Mix II and all nine had positive reactions to citral.

As a compound of Fragrance Mix II, citral is often patch tested and as such it is considered to be a potential allergen. Due to EU Cosmetic Regulation it has to be labelled on consumer products (Table 1).

#### 4.5. Eugenol

Eugenol (Figure 1g) is a pale yellow to colourless aromatic oily liquid. It is a cinnamate derivative of the shikimate pathway. It belongs to the chemical group of phenylpropanoides. Eugenol is the main component in clove essential oil (70–85%) and in allspice oil (60–90%). It can also be found in the essential oil of Ceylon cinnamon (10%) as well as in nutmeg, basil and pepper but in lower concentrations. As isoeugenol, eugenol is used for the production of synthetic vanillin [93]. Eugenol is used in perfumes and also as a flavouring agent and in dentistry, due to its antiseptic and anaesthetic properties. It can be mixed with zinc oxide and then used for temporary fillings.

A study was conducted to investigate antifungal activity of eugenol and essential oils containing eugenol (pimento oil, bay oil, clove oil and cinnamon oil) against 38 clinical isolated strains of *Candida albicans*. The results led to the conclusion that antifungal effects of the investigated oils were strongly related with their concentration of eugenol [94].

Eugenol is hepatotoxic and can cause serious health issues when used in high concentrations. As a component in personal care and dentistry products, it can cause allergic reactions such as contact dermatitis and contact stomatitis. One case report described a 34-year-old woman who was diagnosed with occupational asthma and dermatitis due to eugenol in a cleaning product. She used a mop spray which contained chemical substances including eugenol. After one month of using this spray, the woman developed maculopapular erythema on parts of her body which were exposed to the spray. Maculopapular erythema was also followed with other symptoms such as cough and dyspnoea. After an antihistaminic treatment, the symptoms were reduced and after her holiday, all symptoms had vanished. A specific bronchial test was performed in a challenge chamber with two minutes inhalation of eugenol at the corresponding dilution. The patient showed positive spirometric reactions to eugenol and it was later considered as the main allergen [95]. Another case report noted a 53-year-old female patient who suffered painful oral mucosal lesions after she had received a new dental bridge. The patient was skin patched with the standard series recommended by the German Contact Allergy Group. The patient had no positive reaction to any of the tested substances at either 48 or 72 h after testing. Since it is often used in combination with zinc oxide in dentistry, eugenol as a single substance was tested and the reaction was positive to eugenol after 72 h, a fact that revealed that eugenol caused delayed-type sensitization [96].

#### 4.6. Farnesol

Farnesol (Figure 1h) is a sesquiterpene alcohol which is extracted from citronella oil, neroli oil, cyclamen oil and tuberose oil. It is a colourless to pale yellow liquid with flowery, weak-citrus odour and therefore it is used in aftershave lotions, cleansing products, colognes, deodorants, eye lotions, hair care products, moisturizers and skin care products. It is also used as a co-solvent to regulate the volatility of the odorants, primarily in lilac perfumes. It can also be found in food as a flavouring agent, as an additive in cigarettes and due to its antibacterial properties in hygienic products [97].

Farnesol is a compound of Fragrance Mix II along with lylal, citral, citronellol, farnesol, coumarin and hexyl cinnamic aldehyde. Since farnesol has a strong allergen potential but is at the same time a key ingredient in perfumes, EU Cosmetic Regulation requires that it has to be declared on personal care and cosmetic products (Table 1). A multicentre study that took place in Hungary investigated the contact hypersensitivity due to Fragrance Mix II and its compounds by patch testing a total of



565 patients. According to the results, 163 patients developed contact hypersensitivity due to one or more tested compounds of the mix. Patch tests were positive to Fragrance Mix II in 97 patients while contact hypersensitivity was noted to coumarin in 29 cases, to citral in 19 cases, to farnesol in 14 cases and to citronellol in seven cases [98]. The published data indicate that farnesol has a sensitization potential but more data is required to determine whether farnesol alone is the main causative allergen in personal care and cosmetic products [99,100].

#### 4.7. Geraniol

Geraniol (Figure 1i) is a monoterpenoid alcohol. It is a colourless to pale-yellow oily liquid that has a sweet rose, floral odour. It occurs naturally in rose oil, citronella oil and palmarosa oil but it can also be found in other essential oils like lemon, geranium, bergamot and lavender oil in lower concentrations. Due to its pleasant rose odour it is commonly used in perfumes, body lotions, creams, after shave lotions and hygiene products. Geraniol is also widely used as a flavouring agent to induce the flavour of fruits such as pineapple, raspberry, peach, grapefruit, plum, red apple, lime, watermelon, orange and lemon. As a flavouring agent it can be found in candies, ice creams and baked food products to improve the smell of the foods. Geraniol has antiseptic, antibacterial and anti-inflammatory properties [101].

As one of the 26 fragrances identified as a potential causes of allergy contact dermatitis by the EU Scientific Committee for Consumer Safety geraniol must be labelled on personal care products (Table 1).

Geranial and neral, two sensitizing compounds, are formed from geraniol by autoxidation and skin metabolism and they are considered as a possible cause of allergy reactions on the skin. Hagvall and co-workers [102] tested the hypothesis that oxidized geraniol caused more cases of contact allergy dermatitis than pure geraniol. From January 2006 to August 2010, 2227 patients were patch tested with Swedish base line series. 14 out of 2227 patients were patch positive to one or more of the tested substances. From these 14 patients three were patch positive to geraniol, 11 reacted to oxidized geraniol, 11 to geranial, five to neral and seven to citral. In a follow-up study, they investigated the relationship between cross reactivity of citral and geraniol and allergic reaction to oxidized geraniol. The patients were tested for pure geraniol, citral mixture (66% geranial and 34% neral), geranial and neral. Patch test results showed that 19 of 655 tested persons reacted positive to one or more tested compounds. Out of these 19 patients, 13 reacted positive to geranial [103].

#### 4.8. Limonene

Limonene (Figure 1j) is a monoterpene and a component of the essential oil of oranges. At room temperature, it is a clear colourless liquid and it exists in two isomer forms: (R)-(+)-Limonene (=D-limonene) and (S)-(-)-limonene (=L-limonene). Limonene has a strong odour of orange and as such, it is widely used as a fragrance and flavouring agent in cosmetic products, pharmaceuticals, perfumes and foods [104]. When exposed to air, it can be easily oxidized to carvone, carveole and limonene oxide, compounds that can cause skin irritation and dermal sensitization.

Several studies reported that the oxidation products of limonene were causes of allergy contact dermatitis [105]. In Spain 3639 patients were recently tested with three different concentrations of limonene, limonene hydroperoxides and linalool hydroperoxides. The results showed that 292 were patch positive to one or both hydroperoxides and 187 of them (5.1%) developed positive patch reaction to limonene hydroperoxides [106].

Since hand cleansers and cleaning products often contain limonene, one study investigated allergy contact dermatitis caused by oxidized limonene in people who were often exposed to such products. From a total of 511 patients which were tested in one clinic with oxidized limonene, 21 patients were patch positive to oxidized limonene. In 14 patients, occupational contact dermatitis caused by limonene was determined [107]. Additionally, Christensson and co-workers [108] summarized clinical data on

2900 patch tested patients with dermatitis in Australia, Denmark, United Kingdom, Singapore, Spain and Sweden. The results showed that 149 patients reacted positive to oxidized limonene.

#### 4.9. Linalool

Linalool is naturally a monoterpene alcohol which can be found in many essential oils, such as that of spearmint, rose, cypress, lemon and cinnamon. (S)-(+)-Linalool (Figure 1k), known as coriandrol and licareol or R-(-)-linalool (Figure 1l) are two stereoisomers of linalool. Linalool is a colourless to pale yellow liquid with a sweet odour similar to that of bergamot oil and French lavender. It is used as fragrance in air care, cleaning and laundry products and also in personal care products as well as a flavouring agent and insecticide [109].

During 2010 to 2015, 6004 patients with dermatitis were patch tested with the 26 fragrance allergens (Table 1). Results from this cross-sectional study showed that out of 6004 patients, 940 were patch positive to one of these fragrances. Among these 940 patients, most of them showed patch positive reactions to linalool-hydroperoxides [110]. A recent case report described a 45-year-old woman from Sweden who suffered from an eczematous reaction after she wore Footner<sup>®</sup> exfoliating socks' (Nordic Consumer Health, Nacka Strand, Sweden) on both feet for one hour as it was stated in the instructions. She had used this product three times before and had not experienced any side effects. She was then tested with the Swedish baseline series and reacted patch positive to nickel sulphate, palladium chloride but also to oxidized linalool which was considered as one of possible sensitizers [111].

#### 4.10. Menthol

(-)-Menthol (Figure 1m), also known as levomenthol, is an organic compound extracted from peppermint or mint oils. In European Pharmacopoeia, two menthol monographs can be found. One is naturally occurring (-)-menthol and the second is the synthetically produced racemic menthol (*Mentholum racemicum*). (-)-Menthol has sweet minty, cooling and fresh scent while (+)-menthol has a weak minty herbaceous scent. When applied topically, menthol expands blood vessels and has a refreshing cooling effect. As such, it relieves pain and symptoms of pruritus. (-)-Menthol reacts with TRPM8 thermoreceptors which are responsible for the cooling effect of methanol when it is applied on the skin. It has ten-fold stronger cooling effect on the human skin than (+)-menthol. Menthol is used as a flavouring agent in food and pharmaceutical products. In low concentrations (0.1–1%) as a part of topical preparations, menthol exerts antipruritic and anti-inflammatory properties and is used for the treatment of pruritus and urticarial. In higher concentrations (1.25–16%), it can cause skin-sensitizing and irritant properties [112].

Allergic contact cheilitis due to menthol content in toothpaste and throat medication has been reported. A 29-year-old male patient had an eight-year history of erythematous, scaling and redness of the lips. Cheilitis started at both corners of the mouth and later spread to the upper and lower lip. The patient was treated with several medications but was never patch tested before. Patch test reaction was positive to menthol, peppermint oil and the menthol-containing throat spray. Semi patch test for his toothpaste which contained menthol was also positive [113].

Another 69-year-old patient developed anaphylactic reaction after he had consumed a peppermint candy. Symptoms were hard breathing, lip and tongue swelling, throat tightness and cough. A skin test was positive for menthol and peppermint oil and therefore considered as a cause of serious anaphylactic reactions. The patient was advised to avoid all products with traces of menthol and peppermint [114]. A case report of a two-month old infant that experienced an anaphylactic reaction after menthol containing-cologne was applied to his face was reported. The infant, which developed facial oedema, short breath and urticarial lesion, was treated with several medications but was never skin patch tested to menthol as the parents refused the further diagnostic. Parents were advised to avoid menthol containing products [115].

## 5. Conclusions

Essential oils and their fragrance compounds are a very important part of perfume and cosmetic industry as they can serve as natural or natural-like chemical preservatives and, at the same time, offer various benefits for skin and body. Additionally, these chemicals increase the value of cosmetic products due to their pleasant odour. The cosmetic and perfume industry therefore are unimaginable without these precious substances. However, it should be taken into account that essential oils and their components could cause allergic reactions and symptoms. These reactions can be gleaned in the scientific literature. According to de Groot and Schmidt, 79 different essential oils have caused contact allergy or allergic contact dermatitis until 2015 [116]. Most of the reports described only single cases of allergy contact dermatitis caused by essential oils and many of the studies were performed on persons whose allergic potential was above average as well as on patients suffering from dermatitis or other dermal diseases. For these individuals, the application of cosmetic care products or perfumes containing potential allergens might be a risk. Therefore, the labelling of potential allergens is mandatory to enable persons with skin problems to avoid products containing critical substances. The demands for appropriate storage and handling of products containing fragrance compounds are also very important during all stages (industry, trade and consumer).

If the number of allergic reactions to essential oils and their compounds is compared to how widely these substances are applied, we can conclude that the use of essential oils in perfumes and cosmetic products could be considered as safe for the majority of the population.

**Author Contributions:** Asja Sarkic did the literature search and wrote this review. Iris Stappen supervised, rearranged, completed and corrected the manuscript.

**Conflicts of Interest:** The authors declare no conflict of interest.

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