

Limonene: A Resource or a Danger

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Abstract

Limonene is one of the most abundant, natural, bio-based monoterpenes. In recent years, it has attracted growing attention in both industrial and scientific communities due to its versatile physicochemical properties and wide spectrum of biological activities, including antimicrobial, antioxidant, and anti-inflammatory effects. Its renewable origin and biodegradability make limonene an ideal candidate for sustainable development and as a key building block in green chemistry. The industrial relevance of limonene spans multiple sectors, ranging from its use as a solvent and flavoring agent to its application in pharmaceuticals, cosmetics, polymers, and renewable fuels. Nevertheless, despite its numerous advantages, certain limitations and safety concerns have emerged. Prolonged or high-level exposure may result in sensitization, irritant reactions, or secondary oxidation products that pose potential health risks. Moreover, its oxidative instability can lead to the formation of reactive compounds under specific environmental conditions that influence indoor air quality and may contribute to secondary organic aerosol formation. Current research focuses on several key challenges: improving extraction and purification yields through biotechnological and enzymatic pathways; enhancing oxidative stability via encapsulation or chemical modification; and standardizing toxicological assessment protocols for both occupational and clinical settings. In this review, we analyze and discuss studies published predominantly in the last five years that explore the dual nature of limonene, its valuable industrial applications and its potential environmental and health-related challenges.

Keywords: limonene; air pollution; indoor



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1. Introduction

Limonene (C₁₀H₁₆) is a cyclic monoterpene predominantly present in citrus peels and various essential oils from plants of the *Citrus* genus. It ranks among the most abundant natural terpenes and has garnered considerable interest in both industrial and scientific contexts. Its prominence in recent years is largely attributed to its unique physicochemical and biological properties, as well as its renewable origin, positioning it as a valuable building block for green chemistry. Limonene is a colorless liquid with low water solubility but high affinity for organic solvents and lipids. In nature, it occurs as two enantiomers:

(R)-(+)-limonene (D-limonene), characteristic of sweet citrus, and (S)-(-)-limonene (L-limonene), typically found in plants with a more pungent aroma (Figure 1) [1]. These enantiomers not only differ in olfactory properties but also exhibit distinct biological

activities. The stereochemistry of limonene thus plays a critical role in its organoleptic and bioactive profile, making it an attractive model for studies on chirality.

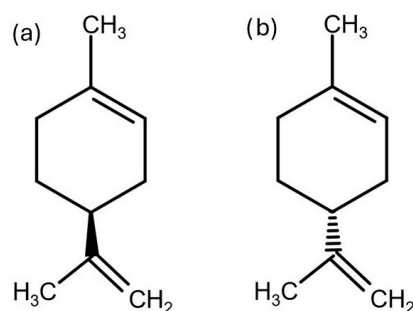


Figure 1. (a) (R)-(+)-limonene, D-limonene; (b) (S)-(-)-limonene, L-Limonene.

L-Limonene is less citrus-like compared to D-limonene and is typically associated with a characteristic pine aroma. It is found in small quantities in plants such as peppermint and pine needles and has more limited applications than its D-isomer. D-limonene, by contrast, is more prevalent and constitutes the main component of orange, lemon, grapefruit, and lime oils. It is widely employed across various industrial sectors due to its physicochemical properties and bioactivity [2]. D-limonene is renowned for its distinctive citrus scent and is extensively used in fragrances, cleaning products and cosmetics [3–5]. It exhibits numerous beneficial properties, including anti-inflammatory and antioxidant activities, which may help mitigate inflammation and protect cells from oxidative damage [6]. Studies also suggest that limonene can alleviate heartburn and improve digestive function by neutralizing gastric acids and optimizing gastrointestinal motility, thereby supporting digestion [7]. Additionally, some research indicates that limonene may have anxiolytic or antidepressant effects, providing a calming influence that helps reduce stress and anxiety [8,9]. Preliminary in vitro studies have reported potential anticancer effects including the inhibition of carcinogen formation and the induction of apoptosis in cancer cells [10]. However, these findings remain at an early experimental stage, and further research is required to confirm such effects in humans [11]. Recent studies have also highlighted the potential application of limonene as a food antioxidant and its use in mitigating or neutralizing hazardous effects induced by chemical solvents [12,13].

From a physicochemical perspective, limonene belongs to the class of terpenic hydrocarbons and is characterized by high solubility in nonpolar organic solvents (lipophilicity) and low solubility in aqueous environments [14]. These properties facilitate its interaction with the lipid structures of cellular membranes [15]. At the microbiological level, several studies have demonstrated that limonene exerts a dose-dependent antimicrobial effect, primarily through destabilization of the cytoplasmic membrane, leading to increased permeability, loss of ionic gradients, and leakage of intracellular metabolites [16]. Additionally, antioxidant activities and potential synergistic effects in combination with other phytochemicals have been reported, suggesting that limonene may have applications not only in the food and cosmetic industries but also as a bioactive molecule of pharmacological interest [17]. Its unique physicochemical properties, versatile applications, and natural abundance make limonene an exemplary case for sustainable chemistry and the bioeconomy. This review aims to provide an analysis of the evidence available in the literature, highlighting the main scientific controversies regarding both the potential benefits and the possible risks deriving from the presence of limonene in indoor and outdoor environments. In particular, the review analyzes the different interpretative approaches regarding its effects on air quality and the potential implications for human health and environmental safety. The review examines current international legislation, the main extraction and

production techniques, potential industrial and biological applications, and the impacts on packaging. A brief section is devoted to issues related to the presence of limonene in indoor environments. Finally, potential contraindications and side effects are evaluated.

2. Legislation

The global diffusion of limonene has made harmonized regulation necessary to ensure consumer safety and environmental protection. According to the International Chemical Safety Card (ICSC 0918), limonene is a flammable liquid with a flash point of 48 °C; it is irritating to skin and eyes and may form explosive mixtures in the presence of oxidizing agents [18]. The World Health Organization (WHO), in its Concise International Chemical Assessment Document No. 5 (CICAD 5), also highlights its limited acute and chronic toxicity, potential skin-sensitizing effects, and significant environmental impact in the event of release [19]. Under the European Classification, Labelling and Packaging (CLP) Regulation, limonene is classified as very toxic to aquatic life (Aquatic Acute 1), hazardous if ingested (Asp. Tox. 1), and capable of causing an allergic skin reaction (Skin Sens. 1B), although current evidence does not warrant more severe classification [20]. Similarly, the United Nations' Globally Harmonized System (GHS) categorizes limonene as a potentially irritating and allergenic substance, capable of causing skin irritation (Hazard statement H315) or allergic skin reactions (Hazard statement H317). The GHS mandates labeling with hazard pictograms, obligatory H- and P-statements, and globally harmonized safety data sheets. Furthermore, limonene is classified as a hazardous substance for international transport (UN 2052), subject to specific restrictions for maritime, air, and land shipment [18]. International regulations on limonene reflect increasing concern for environmental safety and human health. However, discrepancies between international legislations persist, which may hinder consistent risk management. In the EU, limonene is classified as an allergen and is subject to REACH regulation [21]. It requires detailed labeling which, unfortunately, varies from one member state to another. In the United States, the regulatory approach is sector-specific: it is considered Generally Recognized As Safe (GRAS) in food applications, whereas industrial uses follow different classification schemes, resulting in substantial inconsistencies [22]. In Canada and Australia, limonene is primarily treated as an irritant, with specific requirements for Safety Data Sheets (SDS) and transport regulations [23,24]. Several Asian countries permit the use of limonene as a food flavoring, while simultaneously classifying it as an allergen in cosmetic products; this likewise leads to discrepancies when compared with European standards [25]. Despite being a natural compound, limonene requires rigorous regulatory oversight. The adoption of international standards such as GHS and CLP represents a key step toward responsible and sustainable management.

3. Production

3.1. Industrial Extraction

The global limonene production derives for over 90% from the industrial processing of citrus peels, a by-product of the orange juice industry, which generates thousands of tons annually at low cost. Its industrial-scale production can be achieved through different techniques, which can be broadly categorized into extraction from natural sources and chemical/biotechnological synthesis. Extraction techniques vary considerably and exhibit distinct characteristics [26]. In cold/mechanical pressing, the peels are mechanically squeezed. Citrus peels contain 0.2–3.0% *w/w* of essential oil, with D-limonene as the dominant constituent. This process yields a crude essential oil rich in limonene (up to 90–95%) [27]. Considered the reference method for citrus oil extraction, cold pressing is a purely physical process that does not employ heat, thus preserving the freshness of the

aromatic profile. It is regarded as the method of choice because it best retains the fresh and natural aroma of the fruit, providing an oil of outstanding organoleptic quality [28]. The method is simple and cost-effective, but the resulting oil contains waxes and other impurities, requiring purification through distillation. Furthermore, it has the lowest quantitative efficiency, with a yield of only about 0.05%. Vigorous agitation with water and air creates conditions that promote hydrolysis, oxidation, and resinification reactions, which may compromise the chemical and aromatic quality of the oil. In hydrodistillation or steam distillation, the peels are treated with steam. Heat releases volatile compounds, which are condensed and separated into an oil phase. This method ensures a significantly higher yield compared to cold pressing, reaching up to 0.21%. It is one of the most widely used techniques on an industrial scale, despite the inherent risk of partial thermal degradation. High temperatures and prolonged exposure may induce chemical alterations in oil components, loss of more volatile molecules, and the formation of off-flavors [29]. The resulting aroma is often described as “pungent but different from that of the fresh fruit”. Microwave-Accelerated Distillation (MAD) is a patented, innovative, solvent-free method that exploits microwave energy for rapid and efficient extraction [30]. It is considered a green technology since it does not employ additional solvents, generates no waste, and requires less energy consumption, although optimal process control is necessary. This technique allows for higher yields but requires evaporation and purification steps to remove solvent residues. Among the most modern techniques, supercritical fluid extraction (e.g., supercritical CO₂) has emerged as a highly selective approach. Adjustable pressure and temperature enable the extraction of nearly pure limonene without the use of toxic solvents [31]. However, due to its high capital costs, this method is primarily applied in high-value sectors such as pharmaceuticals and cosmetics. Table 1 compares the key characteristics of the first three extraction methods described, the fourth being still in the optimization phase.

Table 1. Summary of the main production pathways of limonene.

	Ext. Time	Yield	Aroma Quality	Main Merit	Main Defect	Ref.
Cold Pressing	1.5 h	0.05%	Excellent	Fidelity of aroma	Very low yield	[26,27]
Hydrodistillation	3 h	0.21%	Pungent	Good performance at low cost	Thermal damage to oil	[28,29]
Microwave Distillation	30 min	0.24%	Good aroma reproduction	Speed, quality and sustainability	Requires precise control	[30]

As the comparison shows, there is no absolute “best” method, but the choice depends strictly on the final objective and the producer’s priorities. Cold pressing remains the ideal choice for high-end applications (e.g., perfumery or aromatherapy) where maximum aromatic fidelity is the only parameter that matters, regardless of yield and cost. Hydrodistillation represents a historic and economic compromise for achieving higher yields, accepting a partial alteration of the aromatic profile. It is often used to valorize industrial byproducts. Finally, microwave distillation emerges as the technology of the future: a near-perfect combination of speed, high yield, superior quality, and environmental sustainability. It is the ideal choice for modern production that accepts no compromises between efficiency and environmental impact.

3.2. Chemical Synthesis

Limonene can be synthesized from monoterpenes or isoprenoid precursors, but at the industrial level this route is less commonly employed because it is more expensive than extraction from agro-industrial by-products. The main synthetic pathways start from α -

pinene or β -pinene, C_{10} hydrocarbons present in turpentine, a resin derived from conifers. The method involves the isomerization of β -pinene, which is treated with acid catalysts (e.g., $AlCl_3$, BF_3 , or Lewis acids). A skeletal rearrangement occurs, leading to limonene with good yields [32]. A more recent study employs an acyclic diene, myrcene (another C_{10} compound), as the precursor. Conversion takes place through a thermal gas-phase rearrangement. The process is conducted in a quartz tubular flow reactor at temperatures between 300 and 600 °C, with residence times typically shorter than 1 s, achieving myrcene yields of about 80%. Nitrogen is used as a carrier gas to dilute the substrate and suppress bimolecular reactions. Subjecting myrcene to Lewis acid-catalyzed cyclization produces limonene [33]. In this case, however, the reaction can also generate other monoterpenes (such as terpinolene or α -terpinene) and therefore requires controlled conditions to ensure selectivity. Limonene can also be synthesized from C_5 alkenes: its structure is constructed by assembling two C_5 units through isoprene dimerization-type reactions. Subsequently, acid-catalyzed cyclization yields the cyclic structure of limonene [34]. Overall, the chemical synthesis of limonene is not competitive compared to the natural route. In practice, industrial production of limonene today is dominated by extraction from citrus peels, as it is far more economical than chemical synthesis. Nevertheless, synthesis from β -pinene and myrcene remains relevant as an alternative, particularly for obtaining specific enantiomers.

3.3. Microbial Production

Microbial production of limonene represents a growing field within industrial biotechnology, aiming to exploit microorganisms (e.g., bacteria or yeasts) as “cellular factories” to synthesize this monoterpene from renewable sugars such as glucose. This approach offers lower production costs and reduces dependence on citrus-derived sources. In recent years, substantial efforts have been directed toward the development of microbial platforms (e.g., *Escherichia coli*, *Saccharomyces cerevisiae*, *Yarrowia lipolytica*), for the sustainable production of this molecule [35–38]. Table 2 summarizes the main strategy, carbon source, limonene title and the productivity of the methods considered. In plants, limonene biosynthesis occurs via either the mevalonate (MVA) pathway or the 1-deoxy-D-xylulose-5-phosphate (MEP) pathway [39,40]. The two molecules produce isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), the basic building blocks of isoprenoids, which react with pyruvate or glyceraldehyde-3-phosphate, derived from glucose, to form geranyl pyrophosphate (GPP). The latter is catalyzed by lemon synthase (LS) and produces limonene.

Table 2. Comparison of main strategy, carbon source, limonene title and the productivity of the methods considered.

	Main Strategy	Carbon Source	Limonene Title (g L ⁻¹)	Productivity mg L ⁻¹ h ⁻¹	Ref.
<i>Escherichia coli</i>	Process engineering, in situ removal	Glycerol	3.6	151	[35]
<i>Saccharomyces cerevisiae</i>	Combinatorial genetic engineering	Glucose/Ethanol	2.23	13.27	[36]
<i>Yarrowia lipolytica</i>	Plug-and-play platform strain	Glucose	0.036	/	[37]

Escherichia coli currently achieves the highest reported monoterpene production titer, reaching 3.6 g L⁻¹ of limonene in the aqueous phase (7.3 g L⁻¹ in the extraction organic phase), with a space-time yield of 151 mg L⁻¹ h⁻¹. This milestone was enabled by process engineering strategies, including the use of glycerol as a carbon source, fed-batch fermentation, and in situ product removal. *Saccharomyces cerevisiae* reaches a titer of 2.23 g L⁻¹ through combinatorial engineering. This strategy integrated the enhancement of acetyl-CoA supply, elimination of competing metabolic pathways, and the implementation of an orthogonal biosynthetic route. *Yarrowia lipolytica* has been developed as a pre-engineered “plug-and-play”

platform for terpenoid production. This approach enabled a 100-fold increase in limonene production compared to the parental strain (reaching 35.9 mg L^{-1}), significantly accelerating development cycles for the production of diverse terpenoid compounds.

The microbial production of limonene offers several advantages over conventional citrus-based extraction, including the use of renewable feedstocks (e.g., sugars, lignocellulosic biomass), reduced costs and waste generation, and the ability to selectively produce a desired enantiomer through the choice of limonene synthase. Nevertheless, the production of limonene by microbial agents still presents numerous disadvantages, including a low yield compared to natural products, a probable toxicity of limonene for microorganisms and the requirement for efficient and continuous extraction processes [41]. While the technology is still under development, microbial platforms for limonene production hold considerable promise for applications within the circular bioeconomy.

3.4. Pyrolysis of Waste Products

Very recent studies have demonstrated the potential to produce limonene from the pyrolysis of end-of-life tires (ELTs) [42]. ELTs represent a significant environmental challenge, with millions of tons generated annually worldwide. Traditionally destined for landfilling or incineration, ELTs can instead be valorized chemically through processes such as pyrolysis, yielding high-value-added products [43]. Limonene has been identified as one of the potential by-products, with quantitative yields depending on tire composition [44]. During the pyrolysis of natural rubber (NR), styrene-butadiene rubber (SBR), and butadiene rubber (BR), polymer chains undergo thermal cleavage, producing a pyrolytic oil that contains D-limonene derived from the isoprene units. Under optimized conditions and in the presence of suitable catalysts, limonene yield can be increased and subsequently recovered by distillation. This “circular” source is currently under industrial exploration and implementation in various ELT recovery plants. Limonene can also be obtained from petrochemical or biobased platforms. In this approach, isoprene dimerization (via thermal, catalytic, or Diels–Alder reactions) generates a mixture of monoterpenes, which can then be enriched in limonene through isomerization steps. While technically feasible, this route remains far less common than others and cannot currently compete with citrus-derived limonene in terms of market standards [45]. Figure 2 summarizes the quantities of limonene recovered from different types of rubber. After natural rubber, tires are an important source for limonene production.

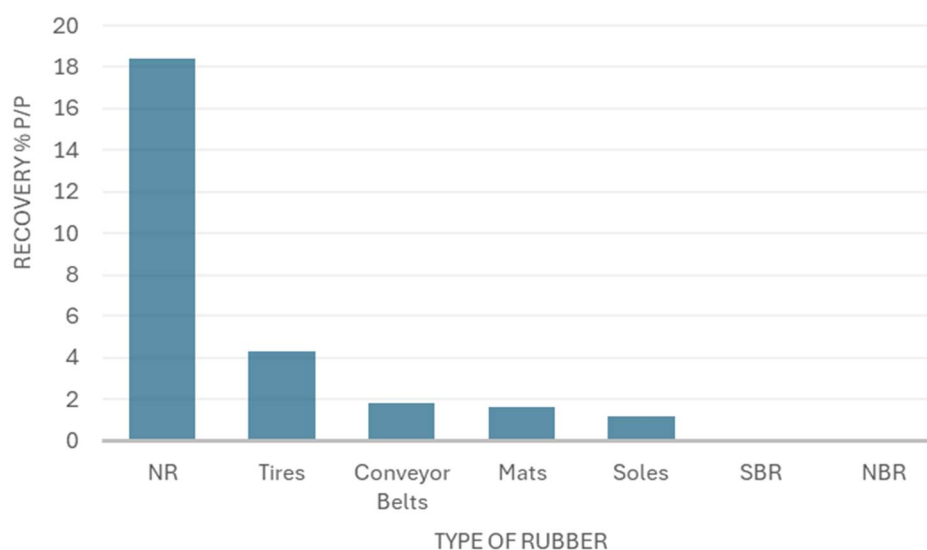


Figure 2. Recovery %p/p vs. Type of Rubber (NR: natural rubber; SBR: styrene-butadiene rubber; NBR: synthetic nitrile rubber).

4. Uses and Effects

4.1. Industrial Application

Limonene is among the most widely used natural, plant-derived flavoring compounds and is extensively applied in the food industry. It is commonly employed as an additive in soft drinks (e.g., cola, carbonated beverages, energy drinks, iced teas), confectionery, chewing gum, ice cream, yogurt, and desserts [6]. It is also incorporated into functional beverages and dietary supplements due to its potential biological properties. To enhance its bioavailability, limonene is generally delivered in microencapsulated or emulsified form [46]. In lipid-rich foods (e.g., snacks, baked goods, oils), limonene exhibits antioxidant activity by reducing lipid oxidation, thereby extending freshness, flavor, and overall stability [47]. It also serves as a deodorizing agent in food processing, helping to reduce undesirable odors and aftertastes [48]. For instance, it may be used as a natural deodorant in certain vegetable oils or food products prone to developing off-flavors. Its lipophilic nature makes it suitable as a solvent for the extraction and delivery of natural flavors from plants or spices, facilitating uniform dispersion in fat-based food matrices [49]. In addition, limonene is employed as a natural degreasing agent [50]. As a precursor in material science, limonene is used in the synthesis of biodegradable polymers and advanced materials. It has been incorporated into biodegradable films and edible coatings [51]. Which can protect fresh fruits and vegetables from microbial contamination, delay oxidation and moisture loss, and simultaneously provide a pleasant natural aroma. Limonene also finds extensive application in the cosmetic and fragrance industries, where it represents a key component of perfumes and personal care products. Beyond its olfactory role, it has been reported to improve skin appearance and reduce visible signs of aging [52]. However, due to its potential allergenic properties, cosmetic applications require careful formulation, safe concentration limits, and stabilization strategies [53]. Within the framework of green chemistry, limonene has gained attention as an eco-friendly alternative to petroleum-derived solvents. It is used in industrial cleaning formulations, adhesives, and coatings, improving their spreadability. Applications include the removal of glues, inks, and residues in recycling processes for plastics and paper, as well as the separation of components in photovoltaic panels [54]. Furthermore, limonene is being investigated as a renewable fuel or fuel additive [55]. Owing to its hydrocarbon nature and aromatic profile, it shows significant potential in the aviation biofuel sector. However, large-scale production from citrus peels remains economically impractical. An Australian research group is currently exploring the genetic modification of *Saccharomyces cerevisiae* to convert sucrose into limonene with improved efficiency and reduced costs compared to natural extraction [56]. This work involves transferring plant genes responsible for limonene biosynthesis into yeast, effectively transforming it into an industrial incubator. Although current yields remain insufficient, ongoing efforts aim to further optimize the yeast genetic background to achieve commercially viable production. The industrial applications of limonene discussed are summarized in Table 3.

Table 3. Industrial applications of limonene.

Scope	Main Uses	Benefits/Functions	Ref.
Food industry	Additive in drinks and desserts	It imparts natural flavor; stabilizes food products	[6]
Fatty foods	Snacks, baked goods, oils	Antioxidant action; maintains freshness, aroma and stability	[47]
Food deodorization	Production processes; vegetable oils and foods with unpleasant odors	Reduces unwanted odors and aftertastes; improves sensory quality	[48]

Table 3. Cont.

Scope	Main Uses	Benefits/Functions	Ref.
Solvent and aroma carrier	Flavor extraction; dispersion in fatty products	Natural lipophilic solvent; improves the distribution of aromas	[49]
Degreasing agent	Natural cleaning	Effective fat removal	[50]
Biodegradable materials and packaging	Biodegradable films, edible coatings for fruit and vegetables	Protection from microbial contamination; reduction in moisture loss	[51]
Cosmetics and perfumery	Fragrances, personal care products	Improves skin appearance	[52]
Green chemistry	Ecological solvent	Improves the extensibility of paints and adhesives; facilitates separation and cleaning processes	[53]
Energy and biofuels	Renewable fuel additive or fuel	High potential as a biofuel	[55]
Biotechnology	Production by <i>S. cerevisiae</i>	Generating limonene from sucrose with reduced costs and greater efficiency	[56]

Limonene is currently confined to the research phase and pilot-scale initiatives in the biofuels domain; however, it does not constitute a measurable or commercially established market segment comparable to its principal applications, including the food, cosmetics, and green solvent industries. Quantitative and qualitative market share analyses clearly delineate its distribution and end-use patterns (Table 4). These analyses provide a sector-based allocation of uses, within which biofuels do not emerge as a primary or dominant segment. Although limonene is classified as a bio-based compound and is theoretically suitable for incorporation into biofuel formulations, no robust or consolidated market data are available to substantiate a distinct and significant market share attributable to limonene within the biofuels sector relative to other application areas. Existing market assessments adopt a macro-sectoral segmentation approach, consistently demonstrating that limonene is predominantly utilized in established and traditional end-use sectors [57,58].

Table 4. Market share analysis.

Application	Estimated Share	Ref.
Food and beverage	33–43%	[57]
Pharmaceutical and cosmetics	20–35%	[58]
Industrial chemicals/solvents	14–27%	[57]
Agriculture, Aromatherapy, Biofuels, etc.	7–8%	[57]

4.2. Biological Activity

Limonene exhibits a broad spectrum of biological activities. Several studies have demonstrated its antibacterial and antifungal properties, supporting its potential use as a natural antimicrobial agent [59]. In particular, limonene can contribute to prolonging the shelf life of certain products, reducing the reliance on synthetic preservatives, or being incorporated into edible coatings for fresh or minimally processed fruits [60]. It also shows antioxidant and anti-inflammatory activities, being able to neutralize free radicals, unstable molecules that damage cells and accelerate aging [61]. A very recent study examines the detailed mechanisms at the molecular level and investigates the interactions of limonene with cellular pathways at the molecular scale [62]. Through this activity, limonene helps protect cellular membranes, DNA, and proteins from oxidative stress. Furthermore, limonene has demonstrated potential anticancer effects, especially in preclinical models of breast and pancreatic tumors [63]. Preliminary studies suggest that it may delay tumor onset in

the human bladder and, more generally, in the gastrointestinal tract [64,65]. Limonene's antimicrobial properties extend to a wide range of bacteria and fungi [66]. Making it a candidate for applications in food preservation and medical formulations. In addition, some investigations have proposed neuroprotective and anxiolytic effects, raising interest for its potential use in neurological disorders [67]. However, the molecular mechanisms underlying these effects are not yet fully understood, and clinical evidence remains limited.

4.3. Packaging Effects

In the context of packaging, limonene exhibits relevant effects, particularly on polymeric and composite materials [60]. It has been investigated as a natural antimicrobial agent for incorporation into active films for food packaging, with the aim of extending product shelf life [68]. However, due to its high volatility, limonene can migrate outward, potentially altering the odor of the packaging [69]. For materials intended to come into Food Contact Substance (FCS), its migration must be assessed according to European regulation (EC) No. 1935/2004. From a chemical standpoint, limonene behaves as a solvent for apolar polymers, showing particular affinity for plastics such as polystyrene (PS), polypropylene (PP), and polyethylene (PE) [70]. When present in packaged products (e.g., juices, essential oils, cosmetics), it may migrate into the packaging material and accelerate its degradation. If not foreseen in the formulation phase, limonene may soften coatings and printing inks, compromising the legibility or aesthetics of packaging [71]. This can result in swelling, loss of mechanical integrity, or even dissolution, especially in the case of expanded polystyrene [72]. Conversely, other materials such as PET, glass, metals, multilayer structures, or aluminum exhibit good resistance to swelling and degradation caused by limonene [73]. The diffusion of limonene in plastic polymers is mainly described by Fick's laws. In particular, Fick's first law describes the diffusive flux when the system has reached steady-state conditions and is expressed as:

$$J = -D \frac{dC}{dx}$$

where J is the limonene flux; the minus sign indicates that diffusion occurs from regions of high concentration to regions of low concentration; D is the diffusion coefficient of limonene in the polymer; C is the concentration of limonene in the polymer; and x is the spatial coordinate and dC/dx is the concentration gradient. This law is applicable to thin polymers, such as films, and is valid when the exposure time is sufficiently long and the conditions are constant [70].

The second law of Fick describes the temporal evolution of limonene concentration in the polymer, accounting for polymer absorption, internal migration, and release to the external environment. The second law of Fick is given by:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2}$$

where t is time, while C , x and D are defined as above. This equation relates the concentration profile to the total amount absorbed over time [74].

In both laws, the critical parameter is the diffusion coefficient D , which strongly depends on the nature of the polymer. Diffusion is faster in amorphous polymers (e.g., PE, PP, PS) and slower in glassy polymers (e.g., PET, rigid PVC), as well as being influenced by temperature and physicochemical interactions. Limonene shows a high affinity for non-polar polymers. Nevertheless, while Fick's laws provide a good first approximation, they exhibit limitations when significant polymer swelling occurs and when the diffusion coefficient D becomes concentration-dependent [70].

5. Risks and Dangers

5.1. Limonene in Indoor Environments

In indoor environments, where people spend up to 90% of their time [75], the presence of volatile organic compounds (VOCs) represents a potential concern for health and well-being. Limonene is widely present in indoor settings and has been extensively studied and monitored, with particular attention given to schools [76]. Although generally considered safe at low concentrations, its presence indoors is of growing scientific interest due to secondary reactions it can initiate. Interaction with oxidizing agents can lead to the formation of potentially harmful compounds, as formaldehyde. Understanding the mechanisms of emission and transformation is crucial for developing mitigation strategies and improving indoor air quality. The widespread use of limonene in commercial products and its high volatility make it one of the most relevant substances for indoor air studies [77]. The main sources of limonene in indoor environments include cleaning products and air fresheners, which often contain limonene as an active fragrance ingredient [76]. Additional sources include natural materials and ornamental plants, which can emit terpenes as secondary metabolites [78]. Human activities such as the use of cosmetics, detergents, and perfumes also contribute to indoor limonene levels [79]. Surface oxidation processes of organic materials, which release terpenes upon degradation, emissions can be intermittent, associated with specific activities, or continuous, associated with materials and furnishings, and may have varying persistence times [80,81]. In indoor environments, limonene concentrations exhibit strong temporal fluctuations driven not only by human activities (e.g., cleaning, use of sprays) but also by meteorological conditions. Its concentration can vary significantly from day to day. Concentrations may be transient, with sudden peaks followed by rapid decreases due to reactions with ozone or ventilation.

Indoors, limonene can undergo photochemical reactions with ozone (O_3) and radicals (e.g., $CH_3O^\bullet$, $BrO^\bullet$, $HS^\bullet$, $HOO^\bullet$, $CH_3OO^\bullet$) generating organic radicals and aldehydes, including formaldehyde [82–84]. It also contributes to the formation of secondary organic aerosols (SOA) [85–88], increasing fine particulate matter with an aerodynamic diameter less than or equal to $2.5\ \mu m$ ($PM_{2.5}$) and submicron particles [89–91]. Interacts with other VOCs, modifying the chemical composition of indoor air [92]. Reaction rates depend on factors such as ozone concentration, ventilation, temperature, and light intensity [77,93]. Monitoring studies have reported indoor limonene concentrations ranging from tens to hundreds of $\mu g\ m^{-3}$, with peaks occurring after cleaning activities [94]. Concentrations are generally higher in poorly ventilated homes and in spaces frequently using scented products. The correlation between limonene concentrations and health-protection thresholds in specific indoor environments is established through a structured comparison between environmental monitoring data and toxicological or health-based reference values derived from experimental and epidemiological studies. Limonene concentrations are generally measured in indoor air using active or passive sampling followed by instrumental analysis. In most jurisdictions, there are no legally binding indoor air quality limits for limonene. Risk assessment therefore relies on guideline values derived from toxicological studies. The No Observed Adverse Effect Level (NOAEL) and the Lowest Observed Adverse Effect Level (LOAEL) are toxicological terms indicating, respectively, the highest dose at which no observable adverse effects occur and the lowest dose at which observable adverse effects are detected. These values are typically adjusted using uncertainty factors to protect sensitive populations, including children, who constitute the predominant group in school settings. The correlation is established by comparing average concentrations (chronic exposure) and/or short-term peaks (acute exposure) with the available reference values. In most documented cases, indoor limonene concentrations are below thresholds associated with adverse systemic effects. In schools and residential environments, concentrations

reported in the literature often fall within the low tens of $\mu\text{g}\cdot\text{m}^{-3}$, with higher transient peaks occurring during or immediately after the use of fragranced products. In schools, greater attention is warranted due to the prolonged exposure of children; a conservative assessment approach is therefore favored, focusing on chronic exposure and the prevention of irritation and sub-clinical effects. In residential settings, the assessment is more variable and depends on product-use patterns and ventilation; short-term peaks are more frequent but are generally not indicative of systemic health risk. To mitigate the impact of limonene and its secondary products in indoor environments, preventive measures are recommended. These include selecting low-terpene products, ensuring adequate ventilation during and after cleaning, and implementing continuous monitoring of indoor air quality. In this context, the European project Evidence Driven Indoor Air Quality Improvement (EDIAQI), under Horizon 2020 and launched in December 2022, aims to raise awareness and knowledge regarding indoor air quality [95,96]. One of the project's objectives is the development of simple, low-cost, and user-friendly monitoring systems for a variety of indoor settings.

5.2. Contraindications and Side Effects of Limonene

Although limonene is generally considered safe for most individuals when consumed at levels typically found in foods, it does present certain risks and requires precautions. Limonene can interact with some medications or other substances, leading to potential pharmacological interactions [97]. It is therefore important to consult a healthcare professional before using limonene-based supplements, especially if other medications are being taken. There is insufficient evidence regarding the safety of limonene during pregnancy or lactation. Only few outdated studies conducted in pregnant rats suggest that the use of limonene-containing products during pregnancy may increase uterine contractility, which theoretically could pose risks such as preterm labor, although this has not been demonstrated in humans [98]. Consequently, its use during pregnancy or breastfeeding is generally not recommended. Being an unstable molecule, limonene is easily oxidized upon exposure to air, producing skin-irritating by-products. In sensitive or predisposed individuals, these oxidation products can cause skin irritation or allergic reactions, particularly if applied undiluted, leading to contact dermatitis or irritation of the skin and eyes [99–102]. The risk is further amplified in indoor environments, where concentrations are typically higher than outdoors. Ingested in large quantities, limonene can cause damage to the respiratory tract or be lethal [103]. For limonene ingestion, indicative safety values are available, unlike for indoor air exposure. These are not “legal limits” applicable to individual citizens, but toxicological reference values used in risk assessment. The currently available values are derived from the Acceptable Daily Intake (ADI) and the No Observed Adverse Effect Level (NOAEL) and are summarized in Table 5.

Table 5. Currently available values for limonene ingestion.

Reference	Value
ADI	$1.5 \text{ mg kg}^{-1} \text{ b.w. day}^{-1}$
Adult 70 kg	$\sim 105 \text{ mg g}^{-1}$
Child 20 kg	$\sim 30 \text{ mg g}^{-1}$
NOAEL	$\sim 215\text{--}250 \text{ mg kg}^{-1} \text{ b.w. g}^{-1}$

b.w. = body weight.

Its vapors can irritate mucous membranes and induce respiratory problems, while uncontrolled ingestion may cause gastrointestinal inflammation or reflux [104]. In allergologic dermatology and cutaneous toxicology, the dose–response relationship defines the association between the amount of an allergen and the probability of inducing sensitization or a cutaneous reaction. The dose–response for skin sensitization is a key parameter for

defining threshold allergenic concentrations in patch testing; supporting risk classification and the establishment of exposure limits; and setting safety margins for occupational exposures and consumer products. For limonene, tests in animal models indicate specific concentrations associated with significant skin sensitization. The Threshold Limit Value (TLV) is used to ensure a standard of safety for occupational exposure to chemical agents. The Time-Weighted Average (TLV-TWA) is the most common form and represents the average concentration of an airborne contaminant, weighted over time, during an 8 h work shift (40 h/week), to which nearly all workers may be repeatedly exposed without adverse health effects. Occupational guideline values of 25–30 ppm as an air TWA for limonene, indicative of workplace safety, have been proposed by several industrial hygiene agencies and are supported by scientific literature [105]. Despite its high volatility and biodegradability, limonene can accumulate in aquatic environments under certain conditions, potentially causing toxic effects and persistent ecological impacts. The Concise International Chemical Assessment Document No. 5 of World Health Organization (CICAD 5) provides a comprehensive evaluation of limonene toxicity [19]. In aquatic environments, limonene has been observed to exhibit high acute toxicity to fish; however, concentrations in surface waters are generally much lower than levels that would induce significant toxic effects. This suggests that, while limonene can be toxic under specific conditions, the risk to natural aquatic environments is relatively low. Nonetheless, these effects should be considered in comprehensive ecotoxicological assessments.

6. L-Limonene: Benefits, Applications, and Specific Risks

The scientific literature addressing the biochemical activity of the single enantiomer L-limonene is considerably more limited than that available for D-limonene. L-limonene represents an emblematic example of a bio-based compound with high application value but a complex risk profile. It is widely used as a solvent, fragrance, and functional additive in numerous industrial and consumer products. Owing to its biogenic origin, L-limonene generally exhibits low systemic toxicity together with favorable solvent properties [49]. It is primarily obtained as a by-product of the citrus processing industry, which confers a favorable sustainability profile in terms of resource efficiency and potential reduction in environmental impact compared with fossil-derived solvents. This characteristic has promoted its adoption in industrial formulations, cleaning products, and other bio-based applications. From a physicochemical standpoint, L-limonene is characterized by relatively high volatility, strong affinity for fats, resins, and polymers, and compatibility with a wide range of materials. These properties enable its use as an industrial degreasing agent and as a solvent for inks, adhesives, and coatings, often as a substitute for more toxic aromatic solvents. In indoor environments, L-limonene is associated with a positive perception of air quality due to its citrus-like, “clean” odor, contributing to improved perceived indoor air quality in commercial buildings, offices, and healthcare settings. However, growing scientific evidence indicates that the risk profile of L-limonene is largely determined by its oxidation and secondary reaction products, which are particularly relevant in indoor environments and occupational settings. In the presence of atmospheric oxidants, especially ozone (O₃), L-limonene acts as a precursor of secondary pollutants, leading to the formation of formaldehyde, highly reactive hydroperoxides, and secondary ultrafine particulate matter (secondary organic aerosol, SOA) [106]. These reaction products may exhibit higher irritant or inflammatory toxicity than limonene itself, making indoor risk strongly dependent on environmental context and conditions. This chemical transformation provides a mechanistic explanation for the high incidence of contact dermatitis associated with limonene exposure, particularly in occupational contexts characterized by repeated exposure, such as professional cleaning, the cosmetics industry, and mainte-

nance activities. Although occupational exposure limits are generally based on systemic and irritative effects, epidemiological evidence suggests that chronic low-dose exposure, especially via the skin, may contribute to the development of allergic sensitization even below traditional airborne exposure limits. Dose–response relationships indicate very low critical thresholds for limonene hydroperoxides. While its high reactivity represents an experimental advantage, it also requires that technology assessments include a thorough analysis of reaction by-products, and that removal efficiency be considered in conjunction with the overall chemical safety profile.

7. Conclusions

The body of scientific evidence accumulated in recent years highlights the growing role of limonene as a strategic resource for various sectors of sustainable chemistry and the bioeconomy. In light of the findings obtained, it is now possible to outline an overall assessment of the prospects and the remaining challenges associated with this molecule. Limonene represents a paradigmatic example of a bio-based molecule with broad-ranging applications, spanning the food, pharmaceutical, and advanced materials sectors. Its natural abundance, chemical versatility, and biological properties make it a key candidate for the transition toward more sustainable chemistry. However, converting a promising laboratory molecule into fully established products requires further research into efficacy and manufacturing processes. Particular attention must be devoted to safety considerations, given the potential adverse effects associated with the molecule. In particular, the development of chemical and formulation strategies to enhance bioavailability and oxidative stability is critical. Biotechnological engineering efforts are ongoing to develop microbial processes for scalable limonene production. Additional studies are also needed to design new biomaterials with controlled limonene release and to conduct well-controlled clinical trials to confirm its therapeutic potential.

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