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Review

The FEMA GRAS assessment of aliphatic and aromatic terpene hydrocarbons used as flavor ingredients

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ABSTRACT

This publication is the thirteenth in a series of safety evaluations performed by the Expert Panel of the Flavor and Extract Manufacturers Association (FEMA). In 1993, the Panel initiated a comprehensive program to re-evaluate the safety of more than 1700 GRAS flavoring substances under conditions of intended use. Since then, the number of flavoring substances has grown to more than 2600 substances. Elements that are fundamental to the safety evaluation of flavor ingredients include exposure, structural analogy, metabolism, pharmacokinetics and toxicology. Flavor ingredients are evaluated individually and in the context of the available scientific information on the group of structurally related substances. Scientific data relevant to the safety evaluation of the use of aliphatic and aromatic terpene hydrocarbons as flavoring ingredients are evaluated. The group of aliphatic and aromatic terpene hydrocarbons was reaffirmed as GRAS (GRASr) based, in part, on their self-limiting properties as flavoring substances in food; their rapid absorption, metabolic detoxication, and excretion in humans and other animals; their low level of flavor use; the wide margins of safety between the conservative estimates of intake and the no-observed-adverse effect levels determined from subchronic and chronic studies and the lack of significant genotoxic potential.

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1. Introduction

Aliphatic and terpene hydrocarbons are ubiquitous through the food chain, therefore it is not surprising that they serve as effective flavoring ingredients. They are often used to convey citrus, pine, balsamic, woody and fruity notes. Consumers are exposed to aliphatic and terpene hydrocarbons from a variety of ingested and environmental sources (Helmig et al., 1999a,b; Guenther et al., 2000). The volume of use as flavor ingredients for aliphatic and aromatic terpene hydrocarbons prompted the FEMA Expert Panel to conduct this review of the relevant literature in support of the safe use of this group in food.

2. Chemical identity

This summary presents the key scientific data relevant to the safety evaluation of 17 aliphatic and aromatic terpene hydrocarbons used as flavoring ingredients. All substances in the group are unsaturated and include (1) three branched-chain aliphatic hydrocarbons and one structurally related unsaturated linear hydrocarbon, (2) six alkyl-substituted alicyclic and six bicyclic hydrocarbons, and (3) one alkyl-substituted aromatic hydrocarbon (Table 1).

3. Flavor use, natural occurrence in food, and exposure

The total annual volume of the 17 flavoring ingredients in this group is approximately 249,000 kg in the USA (Gavin and Williams, 2008). Greater than 99.9% of the total volume in the USA is accounted for by naturally occurring acyclic (e.g., myrcene), monocyclic (e.g., limonene), bicyclic (e.g., α-pinene), and monoaromatic (e.g., *p*-cymene) terpene hydrocarbons. The *per capita* intake[1] of each agent is reported in Table 1. The use of D-limonene (No. 5) itself accounts for approximately 92% of the total annual volume reported in the USA. The *per capita* intake of D-limonene in the USA is 27,905 μg/person per day. β-Caryophyllene (No. 16), α- and β-pinene (Nos. 12 and 13), α-phellandrene (No. 9), terpinolene (No. 6), myrcene (No. 2), and *p*-mentha-1,4-diene (No. 8) account for the majority of the reported annual volumes of use for other terpene hydrocarbons. The daily *per capita* intakes of these other flavoring agents are in the range of 114–760 μg/person per day.

All 17 substances (Nos. 1–17) are ubiquitous in the food supply and have been reported to occur naturally in coffee, alcoholic beverages, baked and fried potato, heated beans, tea, bread and cheese (Nijssen et al., 2010).

Substances in this group are products of plant biosynthesis formed via the isoprene pathway. Quantitative natural occurrence data for 17 aliphatic terpene hydrocarbons in the group demonstrate that their consumption occurs predominantly as natural components of traditional food (i.e., consumption ratio > 1) (Stofberg and Kirschman, 1985; Stofberg and Grundschober, 1987). Their ubiquitous presence in plants is reflected by the fact that essential oils derived from fruits, spices, vegetables, tree barks, roots, leaves, etc. have been shown to contain many of these terpene hydrocarbons (see Table 1).

4. Absorption, distribution, excretion, and metabolism

4.1. Absorption, distribution and excretion

4.1.1. Acyclic branched-chain hydrocarbons

Greater than 70% of an oral dose of 400–700 mg/kg bw of myrcene given daily for 2 days to male albino rabbits was excreted in the urine as diol metabolites collected over 3 days (Ishida et al., 1981). The same metabolites were observed in the urine of adult male IISC rats given 800 mg/kg bw of myrcene daily by oral intubation for 20 days (Madyastha and Srivatsan, 1987).

4.1.2. Monocyclic hydrocarbons

Monocyclic hydrocarbons, such as D-limonene, administered orally are rapidly absorbed and distributed throughout the body. Following oral administration to humans, D-limonene was distributed preferentially to fatty tissues; this is probably due to high oil–blood partition coefficient and a long half-life during the slow elimination phase (Falk et al., 1990a; Falk-Fillipsson et al., 1993).

[1] Intake (μg/person/day) calculated as follows: [((annual volume, kg) × (1 × 10^9 μg/kg)/(population x survey correction factor × 365 days)], where population (10%, "eaters only") = 28 × 10^6 for the USA; where correction factor = 0.8 for the Gavin et al., USA survey representing the assumption that only 80% of the annual flavor volume was reported in the poundage surveys (Gavin et al., 2008). Intake (μg/kg bw/d) calculated as follows: [(μg/person per day)/body weight], where body weight = 60 kg. Slight variations may occur from rounding.