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D-Limonene: safety and clinical applications.

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Abstract

D-limonene is one of the most common terpenes in nature. It is a major constituent in several citrus oils (orange, lemon, mandarin, lime, and grapefruit). D-limonene is listed in the Code of Federal Regulations as generally recognized as safe (GRAS) for a flavoring agent and can be found in common food items such as fruit juices, soft drinks, baked goods, ice cream, and pudding. D-limonene is considered to have fairly low toxicity. It has been tested for carcinogenicity in mice and rats. Although initial results showed d-limonene increased the incidence of renal tubular tumors in male rats, female rats and mice in both genders showed no evidence of any tumor. Subsequent studies have determined how these tumors occur and established that d-limonene does not pose a mutagenic, carcinogenic, or nephrotoxic risk to humans. In humans, d-limonene has demonstrated low toxicity after single and repeated dosing for up to one year. Being a solvent of cholesterol, d-limonene has been used clinically to dissolve cholesterol-containing gallstones. Because of its gastric acid neutralizing effect and its support of normal peristalsis, it has also been used for relief of heartburn and gastroesophageal reflux (GERD). D-limonene has well-established chemopreventive activity against many types of cancer. Evidence from a phase I clinical trial demonstrated a partial response in a patient with breast cancer and stable disease for more than six months in three patients with colorectal cancer.

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