Memorial Sloan-Kettering Cancer Center

D-limonene

Scientific Name

p-mentha-1,8-diene

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Common Name

R-limonene, orange peel oil, citrus peel oil, citrene

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Clinical Summary

Derived from the peels of citrus fruits, D-limonene is used by patients to prevent and treat cancer and has been promoted as a treatment for gastroesophageal reflux. Following oral administration, D-limonene is rapidly metabolized to limonene-1,2-diol, perillic acid, dihydroperillic acid, and uroterpenol [(1) (2) (3)].

In vitro and animal studies suggest that D-limonene has anti-inflammatory [(13)] and anticancer effects [(14)]. It was also shown to enhance the activity of docetaxel against prostate cancer cells [(15)].

An epidemiological study reported an inverse relationship between citrus peel consumption and squamous cell carcinoma [(4)], but an early clinical trial in breast cancer patients failed to support the observations [(5) (6)].

Further research is necessary to determine if D-limonene has a role in the prevention or treatment of cancer.

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Purported Uses

- Cancer prevention
- Cancer treatment
- Heartburn and GERD (gastroesophageal reflux)

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Constituents

- Monocyclic monoterpene

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Mechanism of Action

Although the exact mechanism of action is unknown, D-Limonene and its metabolites, perillic acid, dihydroperillic acid, uroterpenol, and limonene1,2-diol, may inhibit tumor growth via inhibition of p21-dependent signaling and apoptosis resulting from induction of the transforming growth factor beta-signaling pathway [(9) (10)]. D-Limonene metabolites also cause G1 cell cycle arrest, inhibit posttranslational modification of signal transduction proteins, and cause differential expression of cell cycle- and apoptosis-related genes [(6)]. Animal studies show activity of D-limonene against pancreatic, stomach, colon, skin, and liver cancers [(5)]. Data also indicate that D-limonene slows the promotion/progression stage of carcinogen-induced tumors in rats [(11) (12)].

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Pharmacokinetics

Following oral administration, D-limonene is absorbed rapidly and metabolized to perillic acid (PA), dihydroperillic acid (DPA), limonene1,2-diol, and uroterpenol. D-Limonene metabolites distribute throughout the body to all sites, including adipose tissue, and are eliminated as glucuronide metabolites in the urine [(1) (2) (3)].

How It Works

Bottom Line: D-limonene has not been shown to be an effective cancer treatment in humans.

D-limonene is made from the peels of citrus fruits. Scientists are not exactly sure how it works, but it showed some anticancer activity in laboratory studies. These studies suggest that D-limonene alters the signaling pathways within cancer cells in a way that stops cancer cells from multiplying and causes their death (this is called “apoptosis”). In animals, D-limonene slowed the growth of pancreatic, stomach, colon, skin, and liver cancers. It also slowed formation of tumors and their progression in animals exposed to cancer-causing substances. However, these anticancer effects have not been shown in humans.

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Purported Uses

- **To prevent and treat cancer**
  Although test tube and animal studies show that D-limonene has anti-cancer activity, this effect was not found in early clinical trials.
- **To treat heartburn and gastroesophageal reflux**
  There is limited evidence to support this use. More studies are needed.

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Research Evidence

Cancer treatment:

Researchers conducted a two-part study to assess the effectiveness of D-limonene in treating solid tumors that had not responded to other therapies. In the first part, 32 patients with solid tumors received a range of doses of intravenous D-limonene in order to identify how high the doses could go without causing toxic side effects. Because one breast cancer patient showed a partial response (shrinkage of her tumor), ten additional breast cancer patients were added to the study and were given 8 g/m^2/day of D-limonene. However, none of these patients showed any tumor shrinkage. This small study does not support d-limonene as a cancer treatment.

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Patient Warnings

- This product is regulated by the F.D.A. as a dietary supplement. Unlike approved drugs, supplements are not required to be manufactured under specific standardized conditions. This product may not contain the labeled amount or may be contaminated. In addition, it may not have been tested for safety or effectiveness.

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Side Effects

- Nausea
- Vomiting
- Diarrhea
- Allergic skin rash

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Administrative Information

Aliases

Limonene

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E-mail your questions and comments to aboutherbs@mskcc.org.