

Search

for

Limits

Preview/Index

History

Clipboard

Details

Display

Show

All: 1

Review: 0



About Entrez

Text Version

## Entrez PubMed

Overview

Help | FAQ

Tutorial

New/Noteworthy

E-Utilities

## PubMed Services

Journals Database

MeSH Database

Single Citation Matcher

Batch Citation Matcher

Clinical Queries

Special Queries

LinkOut

My NCBI (Cubby)

## Related Resources

Order Documents

NLM Catalog

NLM Gateway

TOXNET

Consumer Health

Clinical Alerts

ClinicalTrials.gov

PubMed Central

1: Eur J Cancer Prev. 2002 Aug;11 Suppl 2:S48-57.

[Related Articles, Links](#)


## Antioxidant and antitumor effects of hydroxymatairesinol (HM-3000, HMR), a lignan isolated from the knots of spruce.

**Kangas L, Saarinen N, Mutanen M, Ahotupa M, Hirsinummi R, Unkila M, Perala M, Soininen P, Laatikainen R, Korte H, Santti R.**

Hormos Nutraceutical Ltd, Turku, Finland.

The antioxidant properties of hydroxymatairesinol (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxy radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor lignan with antioxidant and antitumor properties.

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