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Oral administration of *d*-Limonene controls inflammation in rat colitis and displays anti-inflammatory properties as diet supplementation in humans

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Abstract

Aims

To further explore the anti-inflammatory properties of *d*-Limonene.

Main methods

A rat model was used to compare evolution of TNBS (2,5,6-trinitrobenzene sulfonic acid)-induced colitis after oral feeding with *d*-Limonene compared to ibuprofen. Peripheral levels of TNF-α (Tumor Necrosis Factor alpha) were assessed in all animals. Cell cultures of fibroblasts and enterocytes were used to test the effect of *d*-Limonene respectively on TNFα-induced NF-κB (nuclear factor-kappa B) translocation and epithelial resistance. Finally, plasmatic inflammatory markers were examined in an observational study of diet supplementation with *d*-Limonene-containing orange peel extract (OPE) in humans.

Key findings

Administered per os at a dose of 10 mg/kg p.o., *d*-Limonene induced a significant reduction of intestinal inflammatory scores, comparable to that induced by ibuprofen. Moreover, *d*-Limonene-fed rats had significantly lowered serum concentrations of TNF-α compared to untreated TNBS-colitis rats. The anti-inflammatory effect of *d*-Limonene also involved inhibition of TNFα-induced NF-κB translocation in fibroblast cultures. The application of *d*-Limonene on colonic HT-29/B6 cell monolayers increased epithelial resistance. Finally, inflammatory markers, especially peripheral IL-6, markedly decreased upon OPE supplementation of elderly healthy subjects submitted or not to 56 days of dietary supplementation with OPE.

Significance

In conclusion, *d*-Limonene indeed demonstrates significant anti-inflammatory effects both in vivo and in vitro. Protective effects on the epithelial barrier and decreased cytokines are involved, suggesting a beneficial role of *d*-Limonene as diet supplement in reducing inflammation.

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Keywords

TNF-α; NF-κB; Orange peel extract (OPE)

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