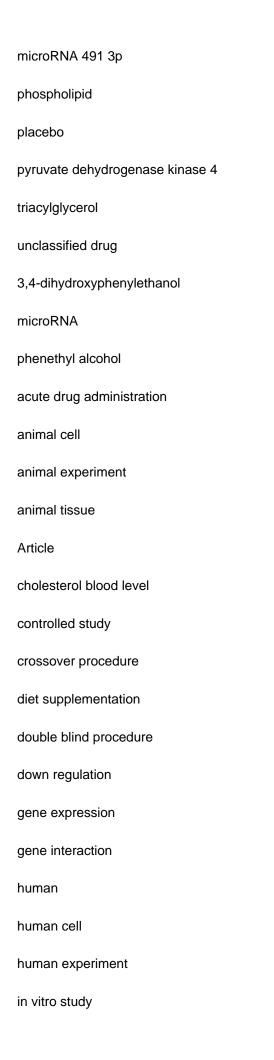
Hydroxytyrosol supplementation modulates the expression of miRNAs in rodents and in humans

Dietary microRNAs (miRNAs) modulation could be important for health and wellbeing. Part of the healthful activities of polyphenols might be due to a modulation of miRNAs' expression. Among the most biologically active polyphenols, hydroxytyrosol (HT) has never been studied for its actions on miRNAs. We investigated whether HT could modulate the expression of miRNAs in vivo. We performed an unbiased intestinal miRNA screening in mice supplemented (for 8 weeks) with nutritionally relevant amounts of HT. HT modulated the expression of several miRNAs. Analysis of other tissues revealed consistent HT-induced modulation of only few miRNAs. Also, HT administration increased triglycerides levels. Acute treatment with HT and in vitro experiments provided mechanistic insights. The HT-induced expression of one miRNA was confirmed in healthy volunteers supplemented with HT in a randomized, double-blind and placebo-controlled trial. HT consumption affects specific miRNAs' expression in rodents and humans. Our findings suggest that

the modulation of miRNAs' action through HT consumption might partially explain its healthful activities and might be pharmanutritionally exploited in current therapies targeting endogenous miRNAs. However, the effects of HT on triglycerides warrant further investigations. © 2016 Elsevier Inc. **Dietary Supplementation** Hydroxytyrosol Intestine Lipids MiRNAs CD36 antigen cholesterol CXCL13 chemokine dual specificity phosphatase 6 glutathione transferase A3 hydroxytyrosol interleukin 33 messenger RNA microRNA microRNA 1247 5p microRNA 135a 1 3p microRNA 1898 microRNA 193a 5p microRNA 196b 3p microRNA 1982 5p microRNA 346 5p microRNA 483 3p



in vivo study
lipid metabolism
male
nonhuman
normal human
oxidative stress
phospholipid blood level
randomized controlled trial
rat
treatment duration
triacylglycerol blood level
upregulation
analogs and derivatives
animal
antibody specificity
C57BL mouse
cell culture
cell line
clinical trial
comparative study
cytology
dietary supplement
intestine mucosa
metabolism
mononuclear cell
organoid

small intestine
tissue culture technique
Animals
Cell Line
Cells, Cultured
Cross-Over Studies
Dietary Supplements
Double-Blind Method
Humans
Intestinal Mucosa
Intestine, Small
Leukocytes, Mononuclear
Male
Mice, Inbred C57BL
MicroRNAs
Organ Specificity
Organoids
Phenylethyl Alcohol
Tissue Culture Techniques