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OliveNet™ Journal Club
Expert review of literature related to olives and olive oil
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Title

Oleuropein and hydroxytyrosol rich extracts from olive leaves attenuate liver injury and lipid metabolism disturbance in bisphenol A-treated rats

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Mahmoudi et al

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Keywords

Oleuropein, hydroxytyrosol, phenolic compounds, liver injury, metabolism, triglycerides, cholesterol, inflammation

Summary

Exposure to endocrine-disrupting chemicals, such as bisphenol A, which are found in food packaging and insecticides, is very widespread (*2*). Epidemiological evidence has highlighted that these chemicals are associated with metabolic disorders including obesity and diabetes (*3-5*). The most widely produced and well-investigated endocrine disrupting compound is bisphenol A, which is widely used in epoxy resins and plastic packaging (*6*). Chemically, it is analogous to estrogen and has been shown to be associated with a wide variety of diseases including cancer, cardiovascular disease, and type 2 diabetes (*7*). Oxidative stress, induction of apoptosis, and hepatotoxicity are underlying mechanisms by which bisphenol A causes pathological conditions (*8-10*). The anti-inflammatory and antioxidant effects of key olive phenolics such as oleuropein and hydroxytyrosol are well known. Of particular interest with respect to this study is the finding that olive leaf extracts can prevent fluoxetine-induced liver damage by mechanisms involving reductions in oxidative stress, inflammation, and apoptosis (*11*). In this study the effects of olive leaf extracts on bisphenol A-induced toxicity in rats was investigated.

Key points and implications

For this study extracts enriched for oleuropein or hydroxytyrosol were prepared, and the composition was confirmed by HPLC analysis. Rats (5-week old, four groups of eight animals per group), were divided into: 1) control group, 2) bisphenol A group (10 mg per kg per day in drinking water), 3) bisphenol A-oleuropein group (16 mg per kg oleuropein by gavage), and 4) bisphenol A-hydroxytyrosol group (16 mg per kg hydroxytyrosol by gavage); the experiment was conducted over a period of 60 days. During and following the experiment, classical histopathological, biochemical and protein-based parameters were monitored to evaluate the effects of the olive phenolics on bisphenol A-induced toxicity. In summary, the key findings indicate that

bisphenol-A has severe effects body weight, adipose tissue mass, and increased plasma levels of cholesterol and triglycerides, liver function enzymes, and pro-inflammatory markers. The oleuropein and hydroxytyrosol enriched phenolic extracts both had remarkable effects, including: 1) reducing body weight and adipose tissue mass, 2) decreasing plasma levels of liver enzymes (a mechanism which the authors ascribe possibly to enhanced catalase and superoxide dismutase activities), and 3) dampening inflammatory pathways (NF-κB, TNF-α). Overall, these findings highlight the potential beneficial effects of olive phenolic extracts in preventing hepatotoxicity and metabolic effects from noxious environmental compounds, in this case bisphenol A.

Related publications

1. A. Mahmoudi *et al.*, Oleuropein and hydroxytyrosol rich extracts from olive leaves attenuate liver injury and lipid metabolism disturbance in bisphenol A-treated rats. *Food & function*, (2018).
2. A. M. Calafat, X. Ye, L. Y. Wong, J. A. Reidy, L. L. Needham, Exposure of the U.S. population to bisphenol A and 4-tertiary-octylphenol: 2003-2004. *Environmental health perspectives* **116**, 39-44 (2008).
3. J. Ukropec *et al.*, High prevalence of prediabetes and diabetes in a population exposed to high levels of an organochlorine cocktail. *Diabetologia* **53**, 899-906 (2010).
4. D. Melzer, N. E. Rice, C. Lewis, W. E. Henley, T. S. Galloway, Association of urinary bisphenol a concentration with heart disease: evidence from NHANES 2003/06. *PloS one* **5**, e8673 (2010).
5. H. Uemura *et al.*, Associations of environmental exposure to dioxins with prevalent diabetes among general inhabitants in Japan. *Environmental research* **108**, 63-68 (2008).
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7. J. Mendiola *et al.*, Are environmental levels of bisphenol a associated with reproductive function in fertile men? *Environmental health perspectives* **118**, 1286-1291 (2010).
8. Y. B. Wetherill *et al.*, In vitro molecular mechanisms of bisphenol A action. *Reproductive toxicology* **24**, 178-198 (2007).
9. V. Bindhumol, K. C. Chitra, P. P. Mathur, Bisphenol A induces reactive oxygen species generation in the liver of male rats. *Toxicology* **188**, 117-124 (2003).
10. M. K. Moon *et al.*, Bisphenol A impairs mitochondrial function in the liver at doses below the no observed adverse effect level. *Journal of Korean medical science* **27**, 644-652 (2012).
11. H. A. Elgebaly *et al.*, Olive oil and leaf extract prevent fluoxetine-induced hepatotoxicity by attenuating oxidative stress, inflammation and apoptosis. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie* **98**, 446-453 (2018).