Possible toxicity of olive leaf extract in a dietary supplement
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I recently advised on a case involving a 67-year-old woman who suffers from severe hay fever, but experiences side effects associated with anti-histamines which limits her treatment options. She visited a pharmacy and was advised to take a dietary supplement containing extracts of olive (Olea europaea) leaf, horseradish (Armoracia rusticana) root and eyebright (Euphrasia officinalis) for sinus and hay fever relief. She had been taking another dietary supplement containing olive leaf extract (OLE) for approximately 2 years, with no untoward effects, and she continued to take this supplement with the sinus and hay fever relief supplement. Her total OLE dose was equivalent to 5.5 g dry olive leaf/day (ie, dry leaf equivalent).

As with many other dietary supplements, OLE is marketed broadly, including anti-aging, as an immunostimulator, antioxidant, anti-hypertensive, cardio-protective, blood-sugar regulating, and as an antibiotic. While there is some animal (eg, blood-pressure lowering) and clinical (eg, blood-pressure lowering) data to support some of these ‘claims’, the evidence is scant, and sometimes contradictory.

The woman is usually a calm, considerate person, but after taking the sinus and hay fever relief supplement, she felt more easily annoyed and argumentative, and after several weeks of the recommended daily dose, she reported often feeling tearful, angry, easily annoyed, negative, reactive and lacking control. All of these uncharacteristic behavioural traits disappeared several days after stopping taking the sinus and hay fever relief supplement.

These interesting and out of character behavioural responses might be explained by the ingredients of OLE, namely oleuropein and hydroxytyrosol (Figure 1). Oleuropein is thought to agonise the G-protein oestrogen receptor,3 which is unlikely to explain the effects seen in this case. On the other hand, hydroxytyrosol has significant structural analogy with the neurotransmitter dopamine. Dopamine, in conjunction with serotonin, is involved in mood and aggression4 and perturbation of its synaptosomal levels are thought to result in mood changes (eg, in attention-deficit/hyperactivity disorder (ADHD)5). Interestingly, it is possible that esterase-catalysed metabolic cleavage of the oleuropein ester bond (Figure 1) would liberate hydroxytyrosol which might further exacerbate the postulated dopamine-related mood effects of OLE.

OLE, like all other dietary supplements, is regulated as a food rather than a medicine. This means that it has not undergone the rigorous risk/benefit toxicity/efficacy testing to which medicines are subjected with the quid pro quo that it cannot have a medicinal claim. However, OLE, like other dietary supplements, is often sold in pharmacies and therefore most customers would likely regard the product in a medicinal, not food, context.

The woman had tolerated 500 mg/day OLE for at least 2 years, but 38 additional 5 g/day (dry leaf equivalent) in the sinus and hay fever relief supplement caused toxicity. The woman’s weight is approximately 65 kgs, which suggests that an OLE (dry leaf equivalent) dose of 85 mg/kg body weight is toxic.

This case is further evidence that we should require dietary supplements to undergo toxicity and efficacy testing before they are approved for marketing in New Zealand if they are to be used in a medical, rather than a food, setting.
Figure 1: Dopamine (A) and hydroxytyrosol (B) showing their structural analogies, and oleuropin (C) showing its postulated esterase-catalysed metabolism to release hydroxytyrosol.

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