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### Grape seed and red wine polyphenol extracts inhibit cellular cholesterol uptake, cell proliferation and 5-lipoxygenase activity

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**Background** – Accumulating evidence suggests that polyphenolic phytochemicals, ubiquitous in plants, possess a diverse array of actions and may be beneficial in the prevention of inflammatory-mediated diseases such as cardiovascular disease and cancer.

**Objective** – This study aimed to determine whether the reported cardiovascular health benefits of polyphenolic extracts from grape seed products or red wine would also include inhibition of cholesterol uptake, cell proliferation and inhibit a known specific target of the inflammatory process i.e. 5-lipoxygenase (5-LOX).

**Design** – HT29, Caco2, HepG2 or HuTu80 cells were incubated in medium containing [<sup>3</sup>H]cholesterol or the fluorescent cholesterol analogue, NBD-cholesterol, in the absence or presence of a grape seed extract (GSE) or red wine polyphenolic compounds (RWPC, Provinol™) as well as several other commercially available grape seed extracts. The effects of these compounds were determined on cellular cholesterol uptake as well as cell proliferation, apoptosis and 5-LOX activity compared with vehicle controls.

**Outcomes** – RWPC and GSE inhibited cellular [<sup>3</sup>H]cholesterol (or NBD-cholesterol) uptake (P<0.001). The estimated IC<sub>50</sub> values were 60 µg/mL and 83 µg/mL, respectively. RWPC and GSE dose-dependently inhibited HT29 colon adenocarcinoma cell proliferation (P<0.001) which was accompanied by an increase in apoptosis (P<0.001). Additionally, RWPC and GSE inhibited 5-LOX activity with the IC<sub>50</sub> values being 35 µg/mL and 13 µg/mL, respectively. Two of three other commercially available grape seed extracts also significantly inhibited 5-LOX activity, whereas the antioxidant vitamins (C and E) were without effect on any of the parameters tested.

**Conclusion** – The pleiotropic effects of RWPC and GSE observed in this *in vitro* study demonstrate that these compounds have actions that are independent of their potent antioxidant activity. Whilst the exact mechanism(s) are unclear, the observed effects may also contribute to the reported benefits of dietary polyphenolics in preventing the development of chronic degenerative diseases.

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## P50

### The DINO trial: A randomised trial comparing two dietary doses of docosahexaenoic acid. Fatty acid composition of human milk and status of preterm infants

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**Background** – Many preterm infants are fed a combination of human milk (HM) and formula in the neonatal period. An adequate supply of docosahexaenoic acid (DHA) has been shown to be important in development.

**Objective** – This trial aimed to evaluate the effect of increasing the DHA content of both HM and infant formula on the long-chain polyunsaturated fatty acid (LCPUFA) status of preterm infants.

**Design** – Infants born <33 weeks gestation were enrolled in a blinded randomized trial of DHA supplementation. Mothers providing HM consumed capsules containing 3 g of soy oil (control group, no DHA) or tuna oil (900mg DHA). Infants requiring complementary milk were fed a preterm formula designed to match the low- or high-DHA composition of HM. Infants were fed the diets from 5 days of commencing enteral feeds until their estimated due date (EDD). HM samples were collected every 2 weeks while hospitalized then daily for 7 days leading to EDD. Infant erythrocyte phospholipid LCPUFA was assessed from a blood sample collected at EDD.

**Outcomes** – Median HM DHA increased rapidly to 1% total fats in the high-DHA group (n=69) compared with 0.2% in the control group (n=74) and levels were stable throughout the trial. HM arachidonic acid (AA) was not different between groups (~0.5% of total fatty acids) but steadily declined over the course of the trial. Infant erythrocyte DHA was higher (high-DHA group 6.8±1.2, control 5.2±0.7, p<0.0005) and AA was lower in the high-DHA group compared with control (high-DHA group 14.9±1.3, control 16.0±1.2, p<0.0005). Small differences in HM and infant erythrocyte LCPUFA were observed between exclusively and partially BF infants.

**Conclusion** – Supplementing the diets of mothers with tuna oil is a practicable means of raising the DHA content of HM and improving the DHA status of preterm infants when expressed breast milk is part of the feeding regime

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