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

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Title

Olive oil polyphenols reuce oxysterols-induced redox imbalance and pro-inflammatory response in interstinal cells

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Keywords

Phenolic extract, olive phenolics, intestinal cells, CaCo-2 enterocytes, cholesterol, oxysterols, inflammation

Summary

Chronic gastrointestinal disorders including inflammatory bowel diseases, are typified the production of pro-inflammatory cytokines and chemokines from the local environment (enterocytes and immune cells), excessive nitric oxide, and oxidative radical formation (*2, 3*). In this context, it is becoming increasingly evident that a pro-inflammatory diet is associated with the onset and progression of inflammatory gastrointestinal disorders (*4*). For example, oxidized products of dietary cholesterol (oxysterols), have been shown to cause damage in the colon (epithelial barrier) due to their pro-inflammatory properties, and have been associated with inflammatory bowel diseases and colon cancer (*5-10*). In this study, the effects of olive phenolics in ameliorating the pro-inflammatory effects of oxysterols in epithelial cells was investigated. The well-known antioxidant and anti-inflammatory effects of olive phenolics provides the basis for this investigation.

Key points and implications

For the experiments in this study, differentiated CaCo-2 enterocytes were treated for various time periods (typically 24 hours), with a mixture of cholesterol analogues (oxysterols, at a final concentration of 60 µM). To study the effects of olive phenolics, a phenolic-enriched extract was prepared from extra virgin olive oil (Bosana cultivar, Villasor, Cagliari, Italy – South Sardinia), and CaCo-2 cells were treated with various concentrations for 30 minutes prior to treatment with the oxysterol mixture. Following cell treatments, various commercially available kits were utilised to measure pro-inflammatory cytokine and chemokine levels, nitric oxide production, hydrogen peroxide production, and intracellular glutathione levels. Further, immunoblotting was performed to investigate cellular inflammatory (p38, MAPK-NF-κB), pathways. As anticipated, oxysterol treatment resulted in a strong MAPK-NF-κB pathway mediated inflammatory

environment including increased production of cytokines, oxidative species, and nitric oxide, and reduced levels of glutathione. The findings indicated that pre-treatment with the phenolic extract attenuated these effects by dampening the inflammatory pathway and returning nitric oxide to control levels. Overall, these findings highlight the molecular mechanisms which may potentially account for the prevention of diet-induced gastrointestinal inflammatory conditions.

Related publications

1. G. Serra *et al.*, Olive oil polyphenols reduce oxysterols -induced redox imbalance and pro-inflammatory response in intestinal cells. *Redox biology* **17**, 348-354 (2018).
2. J. L. Wallace, L. Ma, Inflammatory mediators in gastrointestinal defense and injury. *Experimental biology and medicine* **226**, 1003-1015 (2001).
3. S. Bek *et al.*, Systematic review: genetic biomarkers associated with anti-TNF treatment response in inflammatory bowel diseases. *Alimentary pharmacology & therapeutics* **44**, 554-567 (2016).
4. J. A. Uranga, V. Lopez-Miranda, F. Lombo, R. Abalo, Food, nutrients and nutraceuticals affecting the course of inflammatory bowel disease. *Pharmacological reports : PR* **68**, 816-826 (2016).
5. S. C. Mills, A. C. Windsor, S. C. Knight, The potential interactions between polyunsaturated fatty acids and colonic inflammatory processes. *Clinical and experimental immunology* **142**, 216-228 (2005).
6. F. Biasi *et al.*, Pro-oxidant and proapoptotic effects of cholesterol oxidation products on human colonic epithelial cells: a potential mechanism of inflammatory bowel disease progression. *Free radical biology & medicine* **47**, 1731-1741 (2009).
7. F. Biasi, C. Mascia, G. Poli, The contribution of animal fat oxidation products to colon carcinogenesis, through modulation of TGF-beta1 signaling. *Carcinogenesis* **29**, 890-894 (2008).
8. M. Deiana *et al.*, Derangement of intestinal epithelial cell monolayer by dietary cholesterol oxidation products. *Free radical biology & medicine* **113**, 539-550 (2017).
9. C. Mascia *et al.*, Proinflammatory effect of cholesterol and its oxidation products on CaCo-2 human enterocyte-like cells: effective protection by epigallocatechin-3-gallate. *Free radical biology & medicine* **49**, 2049-2057 (2010).
10. A. Jusakul, P. Yongvanit, W. Loilome, N. Namwat, R. Kuver, Mechanisms of oxysterol-induced carcinogenesis. *Lipids in health and disease* **10**, 44 (2011).