



Anti-inflammatory Activity of Olive Oil Polyphenols The Role of Oleacein and Hydroxytyrosol Metabolites

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Several studies show that adherence to the Mediterranean diet reduces the incidence of human chronic diseases, like cardiovascular and neurodegenerative diseases, and it has been suggested that polyphenols in extra virgin olive oil (EVOO), the major source of fats in this diet, may contribute to the health effects.^{1,2} The phenolic composition of EVOO includes the phenolic alcohols hydroxytyrosol and tyrosol and their secoiridoid precursors such as oleocanthal and oleacein.³ However, the major protective polyphenol in EVOO is still not defined. Oleacein, the main antioxidant polyphenol in EVOO, is believed to be one of the main responsible for the reducing cellular damage and inflammation.³

In this work, the anti-inflammatory potential of oleacein, hydroxytyrosol and their main known metabolites was assessed using RAW 264.7 macrophages challenged with lipopolysaccharide (LPS).





- ✓ Cell Viability
- ✓ NO Levels
- ✓ L-Citrulline Levels



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Results



Figure 1 – Effects of increasing the concentration of oleacein, HyTy, AcHyTySS, AcHyTy, HyTyG and HyTySS on cell viability of non-activated RAW 264.7 cells, assessed by MTT reduction, after 24 h of exposure. Results are expressed as the mean ± SEM of four independent assays, each one performed in triplicate. * *p* < 0,05; ** *p* < 0,01; *** *p* < 0,001 compared to respective control.



Figure 2 – Effect of increasing the concentration of oleacein, HyTy, AcHyTySS, AcHyTy, HyTyG and HyTySS on NO and L-citrulline production by LPS-stimulated RAW 264.7 macrophages. Results are expressed as the mean \pm SEM of four independent assays, each performed in triplicate. * *p* < 0,05; ** *p* < 0,01; *** *p* < 0,001 compared to respective control.

Conclusions and Future Perspectives

- ✓ AcHyTy was the only compound that exhibits decreased cell toxicity, significantly reducing the cell viability for concentrations equal or higher than 50 μM.
- The significant reduction of NO and L-citrulline levels induces by oleacein, HyTy, AcHyTySS and AcHyTy in LPS-stimulated macrophages is similar, so these compounds can be considered as potential anti-inflammatory agents.
- ✓ The exposure to HyTyG and HyTySS metabolites do not affect the NO generation by LPS-stimulated macrophages.
- ✓ Our next goals will be 5-lipoxygenase (5-LOX) inhibition assay and phospholipase A2 (PLA2) inhibition assay, two enzymes which act in the arachidonic acid pathway, and lead to the formation of eicosanoids, compounds that play important roles as inflammatory mediators.
- ✓ More than that, we also aim to evaluate the anti-inflammatory potential of other hydroxytyrosol metabolites and EVOO polyphenols.

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References

¹ Carluccio, M.A., et al., *Chapter 27 - Mediterranean Diet Polyphenols*, in *The Mediterranean Diet*, V.R. Preedy and R.R. Watson, Editors. 2015, Academic Press: San Diego. p. 291-300.

² Parkinson, L. & Cicerale, S. The health benefiting mechanisms of virgin olive oil phenolic compounds. *Molecules* 21, 1734 (2016).
³ Paiva-Martins, F. and A. Kiritsakis, *Olive fruit and olive oil composition and their functional compounds*, in *Olives and Olive Oil as Functional Foods: bioactivity, chemistry and processing*, A. Kiritsakis and F. Shahidi, Editors. 2017, John Wiley & Sons. p. 81-115.