Anti-inflammatory properties of the olive (*Olea europaea* L.) leaf extract Xorialyc® for psoriasis treatment

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Introduction

Psoriasis is a common chronic inflammatory disease that affects 2-3% of individuals. Under an inflammatory stimulus, epidermis can convert arachidonic acid to prostaglandin E_2 (PGE_2), a pro-inflammatory mediator which can elevate the cellular levels of cyclic nucleotides promoting psoriasis pathogenesis[1].

Adherence to prescribed drugs might be a problem in some patients due to side effects associated, so finding an alternative natural treatment is of great interest.

Several studies have reported anti-inflammatory effects of olive (*Olea europaea* L.) leaves components preventing some of the pro-inflammatory pathways related to psoriasis[2].

Objectives

Due to the anti-inflammatory properties related to olive (*Olea europaea* L.) leaves, the objective of this work was to characterise the bioactive components of Xorialyc®, a standardized olive leaves extract, and test its anti-inflammatory action compared to other similar extracts.

Materials and Methods

Samples of olive leaf extract marketed under the brand name Xorialyc® were provided by Pharmactive Biotech Products S.L. in powder.

Identification of Luteolin-7-o-glucoside was accomplished by high performance liquid chromatography (HPLC) with the method described by Benavente-García O. et al 2000[3], while the characterization of ortho-diphenol levels was carried out by colorimetric determination based on the method described by Blekas G. et al 2002[4] as catechin monohydrate.

To determine the anti-inflammatory activity, the production of PGE_2 was measured in lipopolysaccharide and interferon γ-stimulated murine macrophages, RAW264.7 cells, in the presence or absence of different doses of Xorialyc®, Diclofenac or other olive leaves extracts, using The Cayman Chemicals PGE_2 Express Elisa kit (Biosapphire, Sydney, Australia). The remaining cells were used to study cell viability by MTT assay.

Results

More than 1 mg/g of L7G was found in Xorialyc® sample at 355 nm, in addition to another complex of flavonoids typical from *Olea europaea* leaves. The total ortho-diphenolic content was higher than 30% of dry basis quantified as catechin monohydrate.

All extracts inhibited the release of PGE_2 in a dose dependent relation, being Xorialyc® the most active olive leaves extract (p-value ≤ 0.05).

Compared with Diclofenac, Xorialyc® induced higher inhibition of PGE_2 release at lower doses (p-value ≤ 0.005), but not at higher ones, where Diclofenac induced more inhibition (p-value ≤ 0.05).

There was no cytotoxicity detected for Xorialyc® at any concentration tested.

Discussion

As is described by Park C. M. and Song Y.S. 2013[2] and Richard N. et al. 2011[5] respectively, Luteolin-7-o-glucoside and some ortho diphenols as hydroxytyrosol can inhibit the activation of the Nuclear Factor κB (NFκB), reducing the activation of the pro-inflammatory pathways as the inducible Nitric Oxide Synthase (iNOS) and Cyclooxygenase 2 (COX-2), and in the end reducing the release of PGE_2 by the murine macrophages. Due to this decreased release of PGE_2, a pro-inflammatory factor increased in psoriasis, Xorialyc® could be used for reducing or prevent the symptoms of the inflammation produced by this disease.

These findings may help in the search of more natural anti-psoriatic treatments as an alternative to the pharmacological ones that, in general, are related to higher side effects.

Conclusions

The high levels of ortho-diphenols and Luteolin-7-o-glucoside at Xorialyc® could be responsible for the higher release inhibition of PGE2 at RAW264.7 cells compared to the other hydroxytyrosol extracts, being at lower doses more active than Diclofenac.

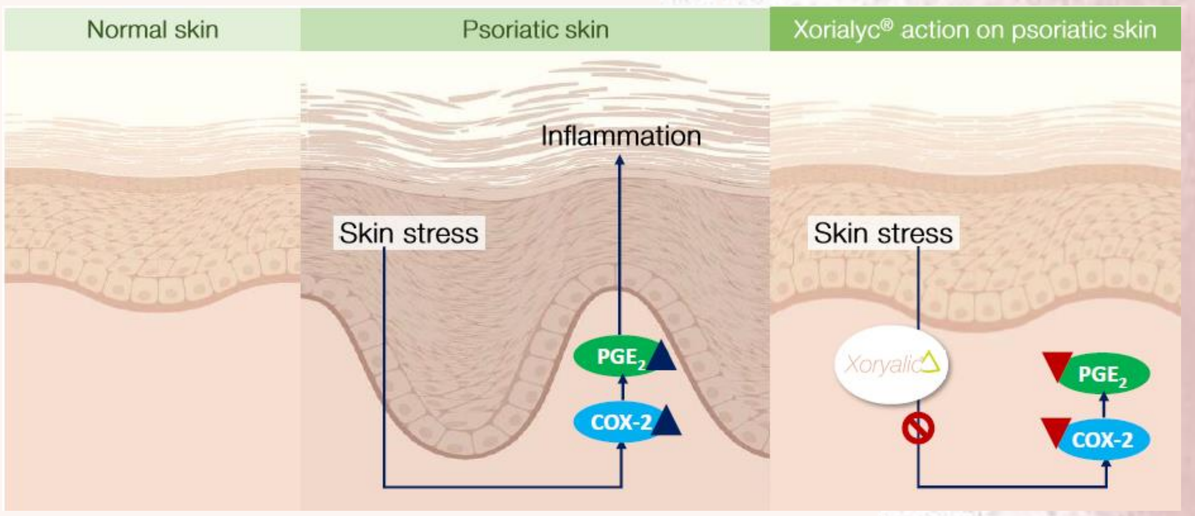

Figure 1. Inflammatory molecular pathway summary from psoriasis and Xorialyc® action mechanism. Due to the bioactive molecules present at Xorialyc®, the pro-inflammatory pathway of NF-κB which activates COX-2 is inhibited.

References

- 1. Hammarström S. et al., 1975. Proc. Nat. Acad. Sci.
- 2. Park C.M. and Song Y.S., 2013. Nutrition Research and Practice.
- 3. Benavente-García O. et al., 2000. Food Chemistry.
- 4. Blekas G. et al., 2002. European Journal of Lipid Science and Technology.
- 5. Richard N., et al., 2011. Planta Medicina-Natural.

Characterization results

More than **1 mg/g of Luteolin-7-o-glucoside** was quantified in Xorialyc® sample at 355 nm. The total **ortho-diphenolic content was higher than 30%** of dry basis quantified as catechin monohydrate.

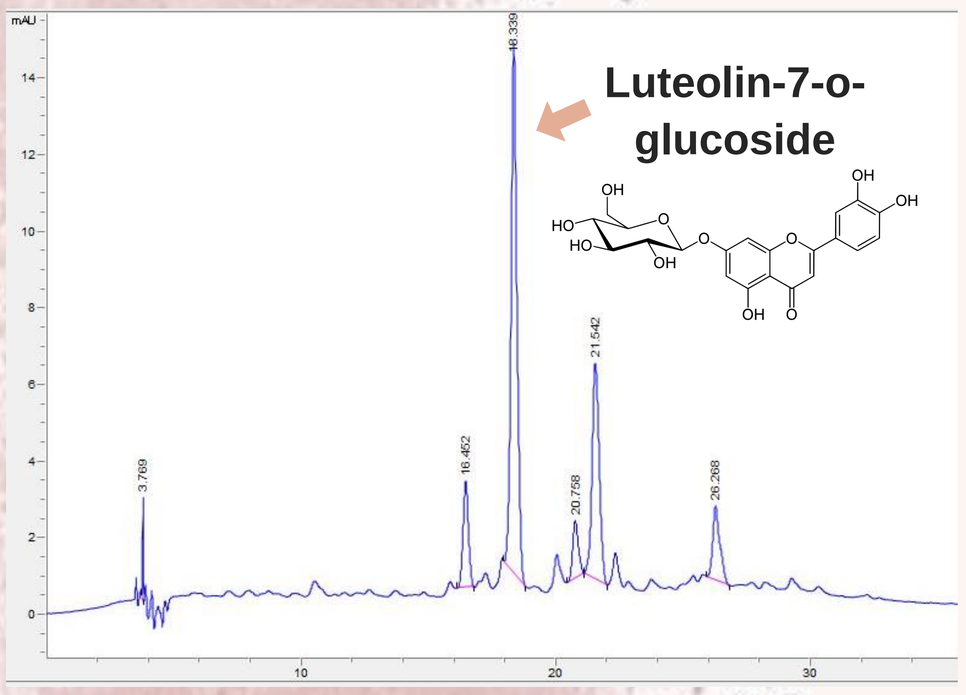

Figure 3. Chromatogram at 355nm of Xorialyc®.

In Vitro study results

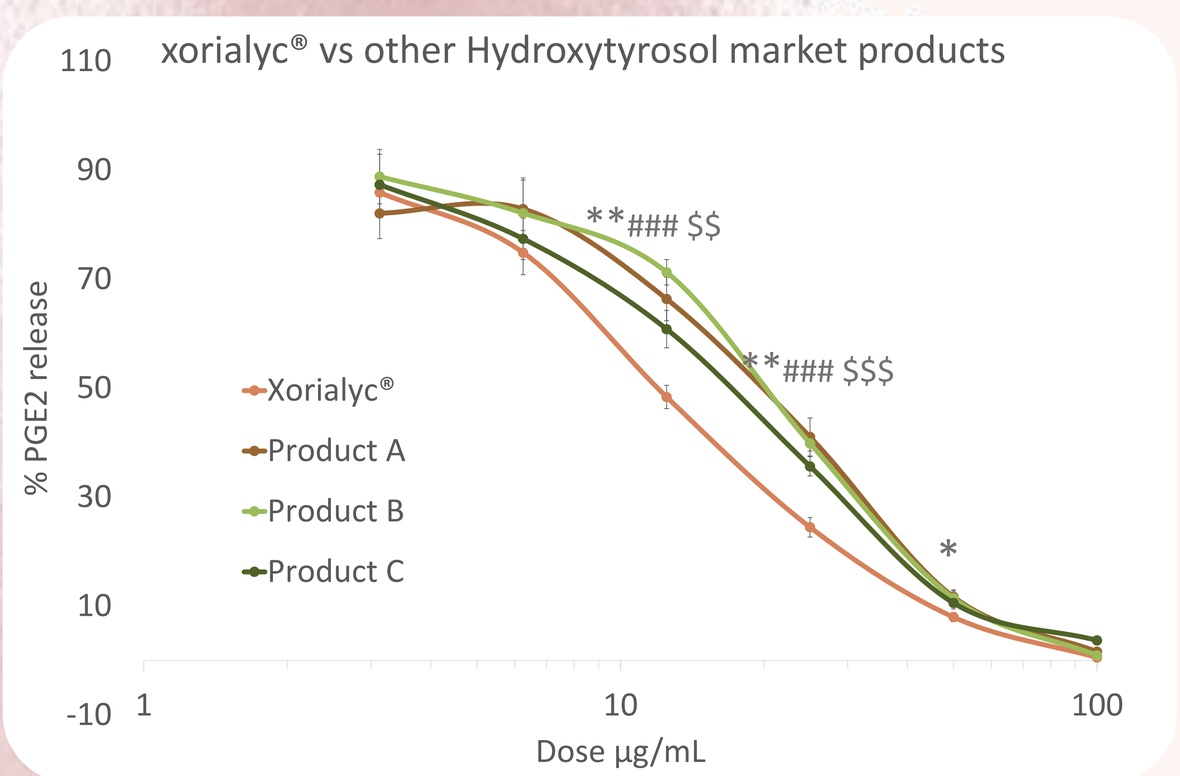

Figure 2. Inhibition of PGE_2 release by different doses of Xorialyc® and other similar olive leaves extracts in RAW264.7 cells. Values are represented as the mean ± SD. P-value of Xorialyc®: * vs Product A ≤ 0.05; ** vs Product A ≤ 0.01; ### vs Product B ≤ 0.001; $$ vs Product C ≤ 0.01; $$$ vs Product C ≤ 0.001.

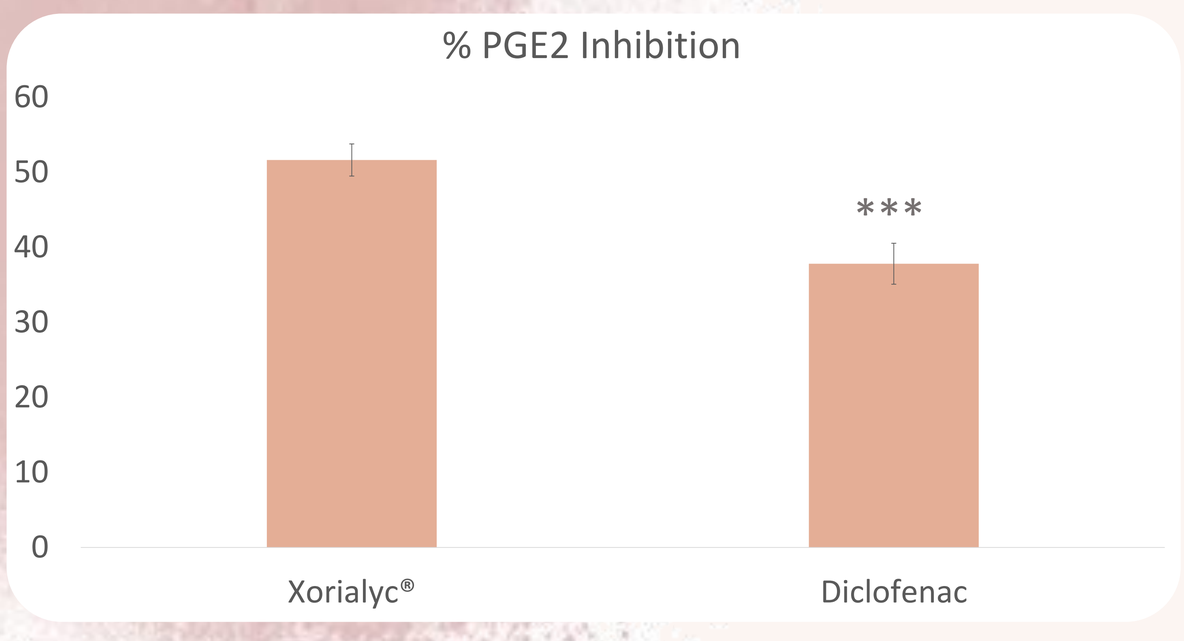

Figure 3. PGE_2 release inhibition of Xorialyc® and Diclofenac in RAW264.7 cells. Values are represented as the mean ± SD. Same dose tested: 12.5 µg/mL. *** P-value ≤ 0.001 vs Xorialyc®.

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