Polyphenols-rich extracts derived from two Portuguese fruits (Prunus avium and Opuntia ficus indica) as potential natural anti-inflammatory modulators in Inflammatory Bowel Diseases

S. Nunes1, A.T. Serra1,2, M.R. Bronze1,2,3, A.A. Matias* 1,2,3, Catarina M.M. Duarte1,2

1 ITQB/UNL, Av. da República, Estação Agronómica Nacional, 2780-157 Oeiras, Portugal; 2 IBET, Apartado 12, 2781-901 Oeiras, Portugal; 3 IMED, FFUL, Av. das Forças Armadas, 1649-019, Lisboa, Portugal
*Corresponding author: amatias@itqb.unl.pt

Investigate the preventive anti-inflammatory activity of two polyphenolic-rich extracts (PRES) derived from Opuntia ficus-indica (cactus pear) and Prunus avium (sweet cherry) in an in vitro cell-based model of intestinal inflammation

Introduction

- Inflammatory Bowel Diseases (IBD) are chronic intestinal disorders with high incidence and prevalence in developed countries.
- Pathogenesis of IBD generally includes: Intestinal barrier dysfunction, excessive release of pro-inflammatory mediators and hyperactivation of NF-κB pathway.
- Oxidative stress plays a major role in amplification and perpetuation of inflammatory cascades.
- Conventional therapy involves multiple medications and life-long treatments that are associated with severe side effects and high costs.
- Urgent need to find new and safe compounds to prevent or treat IBD.

Polyphenols as natural anti-inflammatory alternatives in IBD

Preventive Anti-inflammatory Activity

<table>
<thead>
<tr>
<th>PRES Characterization</th>
<th>IBD Cell-model</th>
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<tbody>
<tr>
<td>Preparation of cactus pear’s and cherry’s PRE</td>
<td>Fully differentiated Caco-2 cells were pre-incubated with cherry’s or cactus pear’s PRE (50μg/mL) during 4 hours followed by stimulation with pro-inflammatory cocktail (50ng/mL TNF-α, 25μg/mL IL-1β and 10ng/mL LPS) during 24h.</td>
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Polyphenolic composition

<table>
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<tr>
<th>Cherry PRE</th>
<th>Cactus pear PRE</th>
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<tbody>
<tr>
<td>Total polyphenolic activity</td>
<td>496.6 ± 12.0</td>
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<tr>
<td>Total flavonoids</td>
<td>0.34 ± 0.00</td>
</tr>
</tbody>
</table>

Cherry PRE - Mainly composed by Anthocyanins that are compounds recognized for their anti-inflammatory capacity.

Cactus pear PRE - Mainly composed by bioflavonoids and derivatives that are compounds with anti-inflammatory activity beyond their antioxidant capacity. Also present in its composition a Betaine, namely Indoxylacetate, known for their anti-inflammatory activity.

Barrier Dysfunction

Barrier dysfunction was measured by alterations in fluorescein permeability across Caco-2 monolayer.

Both PRE could protect against barrier dysfunction but in different directions:

- Cherry PRE was more effective in basolateral to apical direction.
- Cactus pear PRE had higher protection in apical to basolateral direction.

IL-8 secretion

- IL-8 is a chemoattractant cytokine that is overexpressed in IBD.
- Cactus pear’s and cherry’s PRE can reduce IL-8 secretion in a similar percentage.

Both extracts could reduce IL-8 secretion

NO secretion

- Nitric oxide (NO) is an important inflammatory mediator in IBD.
- Cactus pear’s and cherry’s PRE were able to reduce NO secretion.

NF-κB activation

- NF-κB activation was measured indirectly by determination of IκBα levels.
- Cactus pear’s and cherry’s PRE could modulate NF-κB activation but cherry’s PRE was more effective.

Both PRE could modulate NF-κB activation

Conclusion

- Cactus pear’s and Cherry’s polyphenolic-rich extracts could modulate inflammatory mediators in an in vitro cell-based model of intestinal inflammation.
- Since oxidative stress is an activator of NF-κB pathway, this is one possible mechanism of action of both extracts.
- Possibly, PRES could control IL-8 and NO secretion through a mechanism depended on NF-κB.
- Both extracts are promising agents in prevention of IBD.

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References