**Phenolic Compounds from herbal infusions in the prevention of age-related diseases (atherosclerosis and Alzheimer)**

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### Background

Aqueous extracts from plants have been consumed throughout history for the prevention or amelioration of several diseases namely, atherosclerosis and Alzheimer. Nowadays part of the molecular mechanisms underlying these effects have been disclosed. Phenolic compounds can inhibit enzymes like acetylcholinesterase (AChE) involved in the treatment of Alzheimer Disease (AD) and 3-hydroxy-3-methylglutaryl-CoA reductase (HMGR) used for the reduction of cholesterol in the blood.

### Objectives

1. Identify the bioactive molecules in the infusions with ethnopharmacological applications.
2. Effect on AD through the study of: AChE inhibition; permeation of phenolic compounds through intestinal barrier; the animal brain AChE inhibition.
3. Effect on blood cholesterol level through the study of: blood cholesterol level of people consuming the infusions; effect of phenolics on cholesterol permeation through intestinal barrier; effect of phenolics on cholesterol biosynthesis activity.

### Material and Methods

AChE, HMGR kit, from SIGMA, eluents for HPLC-DAD and LC-MS from Merck, Transwells system from 12-well transwell plate inserts with 10.5 mm diameter, 0.4 mm pore size (BD Falcon\(^{®}\)), plant collected in Portugal are all deposited in FCUL Herbarium, Caco-2 cells (ATCC\#HTB37) from ATCC. Adult male Sprague-Dawley rats (3-4 months old) were obtained from Instituto de Investigação Científica do Bento da Rocha Cabral (Lisbon, Portugal). All the methods are already published.

### Summary

In the present work the effect of infusions containing mainly rosmarinic acid, chlorogenic acid and other flavonoid derivatives were analysed on what concerns their effect on the prevention of age-related diseases like Alzheimer disease (AD) and atherosclerosis. As these ailments are multifactorial-caused, the main selected topics were the inhibitory activity of these compounds or infusions from plants on AChE activity, HMGR, and permeation of cholesterol. The effect of these extracts on the brain AChE activity of laboratory animals was also studied. To evaluate the effect in vivo, blood cholesterol levels were measured and followed for a small number of volunteers who took the herbal teas on a regular basis.

### Conclusions

- The phenolic compounds in this study can permeate the intestinal barrier (RA, CA, Cynarin, luteolin, apigenin and several others).
- RA can reach the brain and act as AChE inhibitor in laboratory animals.
- Different phenolic compounds in these mixtures influence the permeation of each other.
- Cholesterol permeation through intestinal barrier as well as its biosynthesis can be reduced by phenolic compounds.
- These results pave the way to further studies on molecular mechanism of cholesterol transport modulation by phenolic compounds.

### References


### Results

<table>
<thead>
<tr>
<th>Infusion</th>
<th>IC(_50) (mg/mL)</th>
<th>Phenolic</th>
<th>Phenolic Permeation Caco-2 cell barrier (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. cardunculus</em></td>
<td>2.3</td>
<td>CA+cynarin</td>
<td>18+19</td>
</tr>
<tr>
<td><em>P. barbatus</em></td>
<td>1.2</td>
<td>RA+luteolin+apigenin*</td>
<td>43</td>
</tr>
<tr>
<td><em>P. boldus</em></td>
<td>0.9</td>
<td>Flavonoids</td>
<td>28</td>
</tr>
<tr>
<td><em>A. cheyromila</em></td>
<td>0.6</td>
<td>Rutin</td>
<td>5</td>
</tr>
<tr>
<td><em>P. tridentatum</em></td>
<td>1.1</td>
<td>Biochanin A*</td>
<td>19</td>
</tr>
</tbody>
</table>

\*glycosylated derivatives

- Influence of flavonoids on rosmarinic acid permeation through Caco-2 simulated intestinal barrier.
- Reduction in blood cholesterol level of people drinking infusions.
- Cholesterol reducing studies.

### AChE inhibition 1,4 and phenolic Caco-2 cell permeation

**Cholesterol permeation**

<table>
<thead>
<tr>
<th>Infusion</th>
<th>IC(_50) (mg/mL)</th>
<th>standard IC(_50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. cardunculus</em></td>
<td>152.6 mg/mL</td>
<td>Chlorogenic acid 12.9 mM</td>
</tr>
<tr>
<td><em>P. boldus</em></td>
<td>329 mg/mL</td>
<td>Cynarin 9.1 mM</td>
</tr>
<tr>
<td><em>P. tridentatum</em></td>
<td>&gt;100 mg/mL</td>
<td>Statin 138 nM</td>
</tr>
<tr>
<td><em>A. cheyromila</em></td>
<td>0.137 mg/mL</td>
<td>Rutin 16 µM</td>
</tr>
</tbody>
</table>