Interaction and inhibition of α-glucosidase with selected monoterpenes

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Introduction

• It has been estimated that 425 million people are suffering from diabetes, of which 90% is type 2 diabetes (Choi et al., 2009).

• WHO claims diabetes will be the 7th cause of death by 2030 (Zhang et al., 2019).

• There are synthetic α-glucosidase inhibitors such as acarbose is used as anti-diabetic agents but they have side effects including diarrhea and flatulence (Choi et al, 2009, Van de Laar et al., 2005).

• Hence, there is a need for alternative, preferably phytochemicals.
• There are many reports on monoterpenes as inhibitors of α-glucosidase.

• However, many often the enzyme inhibition studies are conducted for essential oils rather than individual compounds.

• Hence, the present study aims to analyze the inhibitory action, interaction potential, and SAR of some selected monoterpenes against α-glucosidase.
Materials and methods

1. **Extraction of maltase** (from Yeast)
2. **α-glucosidase activity** (DNS assay)
3. **Maltase inhibition assay** (the absorbance is recorded at 540nm, from the slope, the IC50 value is calculated)
4. **Ligand preparation** (LigPrep module of the Schrödinger, structurally optimized and protonation states were assigned)
5. **2D-QSAR modelling** (AutoQSAR tool of Schrödinger)
6. **Molecular Docking** (Human maltase-Glucoamylase protein (PDB: 2QMJ) was used as the target, followed Glide protocol)
Maltose glucoamylase in complex with acarbose (PDB ID 2QMJ; Sim et al., 2008).

From PDB-101
doi: 10.2210/rcsb_pdb/GH/DM/drugs/gi/glucosidase
Results & Discussion

α-glucosidase activity

The extracellular enzyme was reacted with α-PNPG substrate, and the reaction mixture turned yellow indicating α-glucosidase (Palleroni and Lindegren, 1953)
<table>
<thead>
<tr>
<th>Inhibitor</th>
<th>P(IC50)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citronellol</td>
<td>3.363582</td>
</tr>
<tr>
<td>Citronellal</td>
<td>3.318054</td>
</tr>
<tr>
<td>1,8-Cineole</td>
<td>3.354187</td>
</tr>
<tr>
<td>Camphene</td>
<td>3.799067</td>
</tr>
<tr>
<td>Cinnamic acid</td>
<td>4.066057</td>
</tr>
<tr>
<td>Tris</td>
<td>3.489683</td>
</tr>
<tr>
<td>α-pinene</td>
<td>4.982132</td>
</tr>
<tr>
<td>limonene</td>
<td>5.020452</td>
</tr>
<tr>
<td>p-cymene</td>
<td>5.011441</td>
</tr>
<tr>
<td>Carvacrol</td>
<td>4.959398</td>
</tr>
<tr>
<td>Thymol</td>
<td>4.749336</td>
</tr>
<tr>
<td>Carveol</td>
<td>3.28735</td>
</tr>
</tbody>
</table>
2D-QSAR model
Acarbose
Conclusion

• Monoterpenes interacted with maltase/glucoamylase and had an inhibitory effect
• Ligands such as Carvacrol, carveol, citronellal, and citronellol had H-bond mediated interactions
• Whereas, p-cymene and thymol had Pi-Pi stacking with Tyr, Trp & Phe and
• 1, 8- cineole, a-pinene, limonene had non-bonded interactions
• The binding energy of ten monoterpenes with target proteins varied from -4.9 to -1.0 kcal/mol and Acarbose possess lowest binding energy of -9.8 Kcal/mol.
• Hence, the search for novel ligands from natural source will always continue…
References


