MOLECULAR DOCKING STUDIES OF SALICIN, A MAJOR CONSTITUENT OF WILLOW BARK, AS COX-1 AND COX-2 INHIBITOR

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Salicin is considered the major active compound of willow bark, responsible for its anti-inflammatory, analgesic and antipyretic properties. Inhibition of cyclooxygenase (COX) is one of the possible mechanisms involved in its anti-inflammatory action. The aim of this study was to elucidate the interaction and binding affinity of salicin toward COX-1 and COX-2 using molecular docking.

RESULTS

Salicin had similar affinity toward COX-1 and COX-2. In comparison with acetylsalicylic acid, salicin had similar affinity toward COX-2, but lower toward COX-1. Salicin showed hydrogen bonding and hydrophobic interactions with important amino acid residues of the active sites of COX-1 and COX-2. Interactions of salicin with most of residues at the active site of COX-2 have also been reported for compounds showing strong inhibition of COX-2 and correspond to the active binding site of non-steroidal anti-inflammatory drugs.

Table: Binding energies and inhibition constants

<table>
<thead>
<tr>
<th>Compound</th>
<th>Binding energy [kcal/mol]</th>
<th>COX-1 Ki [µM]</th>
<th>Binding energy [kcal/mol]</th>
<th>COX-2 Ki [µM]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salicin</td>
<td>–5.70</td>
<td>66.54</td>
<td>–5.86</td>
<td>50.95</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>–6.25</td>
<td>26.1</td>
<td>–5.69</td>
<td>67.66</td>
</tr>
</tbody>
</table>

Figure 1. Active site of the COX-1 enzyme with salicin

Figure 2. Active site of the COX-2 enzyme with salicin

CONCLUSION

Lower affinity of salicin toward COX-1 might partially explain why willow bark extract does not damage the gastrointestinal mucosa in contrast to acetylsalicylic acid. Salicin exhibited a number of strong hydrogen bonds and hydrophobic interactions with significant amino acid residues of the active site of COX-2 which could explain anti-inflammatory potency of this compound.