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

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INTRODUCTION

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.

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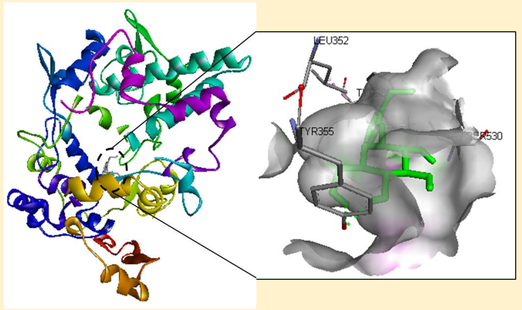
Table: Binding energies and inhibition constants

Compound	COX-1		COX-2	
	Binding energy [kcal/mol]	Ki [μM]	Binding energy [kcal/mol]	Ki [μM]
Salicin	–5.70	66.54	–5.86	50.95
Acetylsalicylic acid	–6.25	26.1	–5.69	67.66



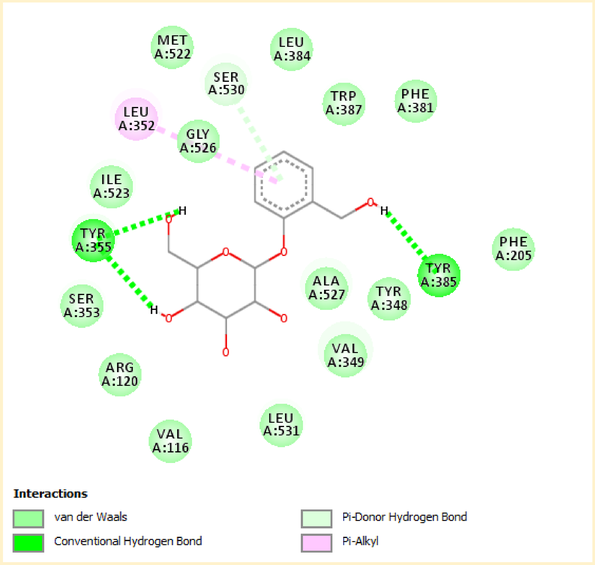
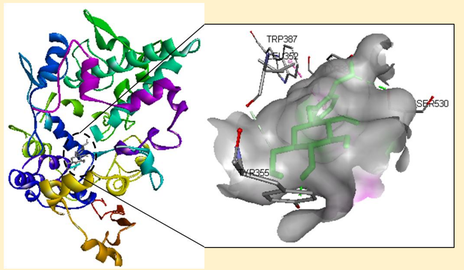


Figure 1. Active site of the COX-1 enzyme with salicin



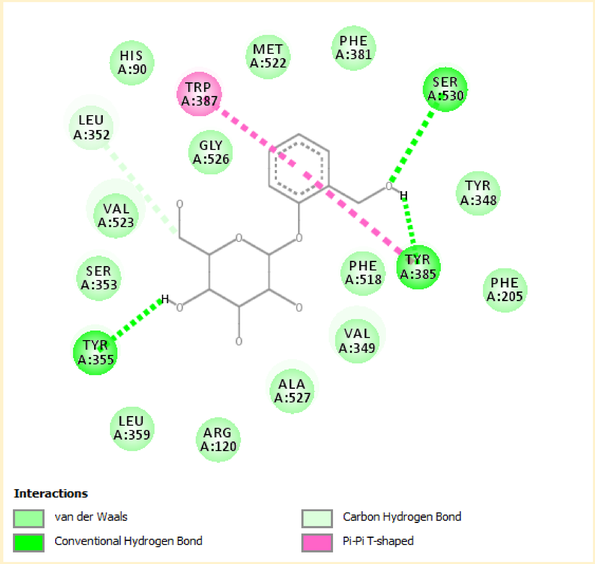


Figure 2. Active site of the COX-2 enzyme with salicin

MATERIAL AND METHODS

Chemical structures of ligands were taken from the PubChem database, while 3D crystallographic structures of COX-1 and COX-2 from Protein Data Bank. Molecular docking was conducted using AutoDock 4.2.3. program, by Lamarckian Genetic Algorithm, with standard docking procedure for rigid receptor and flexible ligand.

Discovery Studio Visualizer 4.5. was used to visualize the results.

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.

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