Homology modeling and docking studies of Comamonas testosteroni B-356 biphenyl-2, 3-dioxygenase involved in degradation of polychlorinated biphenyls

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Introduction
Biphenyl dioxygenase is a microbial enzyme which catalyzes the stereospecific dioxygenation of aromatic rings of biphenyl congeners leading to their degradation. Hence, it has attracted the attention of researchers due to its ability to oxidize chlorinated biphenyls, which are one of the serious environmental contaminants. In the present study, the three-dimensional model of α-subunit of Biphenyl dioxygenase (BphA) from Comamonas testosteroni B-356 has been constructed. The resulting model was further validated and used for docking studies with a class of chlorinated biphenyls such as biphenyl, 3, 3'-dichlorobiphenyl and 4, 4'-dichlorobiphenyl. The kinetic parameters of these biphenyl compounds were well matched with the docking results in terms of conformational and distance constraints. The binding properties of these biphenyl compounds along with identification of critical active site residues could be used for further site-directed mutagenesis experiments in order to identify their role in activity and substrate specificity, significantly leading to improved mutants for degradation of these toxic compounds.

Homology modelling of Comamonas testosteroni B-356 biphenyl - 2, 3-dioxygenase

The 3D model of α-subunit of BphA from Comamonas testosteroni B-356 was built by homology modeling using high-resolution crystal structures of Camuine dioxygenase (cumA1A2) from Pseudomonas putida F1 [PDB ID: 1wql] as a template. The automated homology modeling software MODELLER 7.0 on windows operating environment (http://salilab.org) was used to generate five 3D models of α-subunit of BphA.

Docking studies

Docking of α-subunit of BphA with the CBs was carried out with version 4.0 of the program AutoDock (http://autodock.org). This program combines a rapid energy evaluation through pre-calculated grids of affinity potentials with a variety of search algorithms to find suitable binding positions for a ligand on a given protein. The program allows torsional flexibility in the ligand.

Results

Table 1: Coordination geometry of Fe ion along with the oxygen and different PCB congeners in each docking experiment along with their dock score.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Compound</th>
<th>Kcat(1/M.s)</th>
<th>Distance of Fe ion from CB (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Biphenyl</td>
<td>28</td>
<td>4.64</td>
</tr>
<tr>
<td>2</td>
<td>3, 3'-dichlorobiphenyl</td>
<td>190</td>
<td>8.75</td>
</tr>
<tr>
<td>3</td>
<td>4, 4'-dichlorobiphenyl</td>
<td>NR</td>
<td>2.99</td>
</tr>
</tbody>
</table>

*In presence of 4,4’-dichlorobiphenyl, the initial rate of O2 uptake increased linearly with the concentration of O2.*

Conclusion

In the present work the 3D model of BphA was constructed in order to accomplish its molecular modeling and docking studies. The model was validated and further used for docking studies with some well known PCBs. The resulting docking results were analyzed for binding pattern and conformational analysis. It was observed that the proximity of the C2 and C3 positions of the docked PCBs were determined for their oxygen utilization and ultimate catalysis. Hence, this work could be further useful for the mutagenesis studies where mutations created at various positions of the binding site may alter the substrate specificity and potency. Further work is still going on in our laboratory for the same.

References