MS06-2-9 Amino acids mediated active site control in Pseudomonas aeruginosa native Ketopantoate reductase PaKPR PanE2
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Abstract
Pseudomonas aeruginosa possesses two copies of Ketopantoate reductase (KPRs) enzyme that catalyses cofactor dependent conversion of Ketopantoate to Pantoate, one of the steps involved in the biosynthesis of pantothenate and coenzyme A. Although these two copies are similar in function but they widely vary in their sequence with only 30% similarity between them. Evolutionary studies made in our recent work have shown one of the copy was attained via horizontal gene transfer whereas the other one was conserved. A detailed structural and functional characteristics of the acquired copy of PaKPR (PanE1) was also studied. In this current work we have thoroughly studied the differences present between the wild type conserved PaKPR (PanE2) and the acquired one, and tried to figure out whether any structural implications are present for the co existence of the 2 copies of the same functional proteins in the same genome. For successfully addressing these facts, we have solved the crystal structures of this native PaKPR PanE2, cofactor(NADP+) bound panE2 and a ternary complex of panE2+NADP+Pantoate. And we found several changes in the secondary structure organisation while overall shape of the protein was same. However, Cofactor and substrate binding active site is a bit squeezed in the PaKPR panE2 that may cause a problems in entry and exit of the ligands into it. Moreover, crystallographic evidences have shown that F132 and Y148 together act as a gate for the entry and exit of the substrate and product, present at the outside of the active site . Their movements were clearly visible in native and ligand bound states. This control over the movements of the substrate and product can cause a delay is the conversion process.

References
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