The structure and function of a highly proficient enzyme: 
orotidine 5'-monophosphate decarboxylase

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The conversion of orotidine 5'-monophosphate (OMP) into uridine 5'-monophosphate (UMP) by decarboxylation, comprises the final and last step in the de novo biosynthesis of UMP. This reaction is catalyzed by orotidine 5'-monophosphate decarboxylase (ODCase), which is an extremely proficient catalyst. It enhances the rate of the uncatalyzed reaction by a factor 10⁷, without any use of cofactors.

We have determined the crystal structure for the B. subtilis ODCase as apoenzyme and complexed with BMP (1-(5'-phospho-β-D-ribofuranosyl) barbituric acid, one of the most efficient inhibitors of the enzyme. The crystals of the apoenzyme were twinned and the crystals of the selenomethionine substituted protein displayed a change in space group and additional pseudosymmetry. Therefore structure determination was not completely trivial.

The structure revealed a unique arrangement of completely conserved lysine and aspartate residues, which led us to propose of model for the reaction mechanism that involves proton transfer prior to decarboxylation (1). The structure for the B. subtilis enzyme was determined almost simultaneously as the structures for ODCases from three other organisms (2-4). All four structures contain an identical picture of the active site.

The structural results will be discussed in relation to the other approaches we have been employed to elucidate the mechanism of ODCase. One involves characterization of several mutants of ODCase and the other theoretical calculations performed at different levels for selected model system.

Reference