# *IN SILICO* ENGINEERED SmSDR ENZYME FOR THE PREPARATION OF ENANTIOPURE *R*-PHENYLEPHRINE

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It is a well-established fact that *in silico* enzyme engineering approaches such as molecular modeling, docking, simulation, provide molecular level understanding of the function of biocatalyst and specifically the role of mutational sites. These standalone protocols deliver the understanding of either Michaelis complex formation or the transition state formation or entry/exit path of the substrate. However, an intelligent workflow of these protocols can be applied for not only engineering of enzymes but to design them *in silico*. Quantumzyme has developed QZyme Workbench™, an integrated workflow using open source computational methods and proprietary scripts for scanning all the events involved in the biocatalytic process. The aim of this workbench is to conduct *in silico* protein design and is routinely leveraged to engineer enzyme for achieving desirable functions.

In the current study, we implemented our workbench to engineer a short chain dehydrogenase/reductase (SmSDR) enzyme to prepare *R*-Phenylephrine (*R*-PE) via stereoselective reduction of 1-(3-hydroxyphenyl)-2-(methylamino) ethanone. *R*-PE is one of the commonly used pharmaceutical analogs of Adrenalins. In order to avoid extreme conditions required for chemical methods, an optimal solution is to introduce an enzyme which exhibits high activity, and enantioselectivity to accomplish the asymmetric reduction step to yield enantiopure *R*-PE. Several such engineered enzymes are available for the synthesis of different biologically active compounds. In the present work, we have engineered a variant of SDRs enzyme to have high activity and enantio-specificity, focusing on the Michaelis complex formation using QM/MM method.

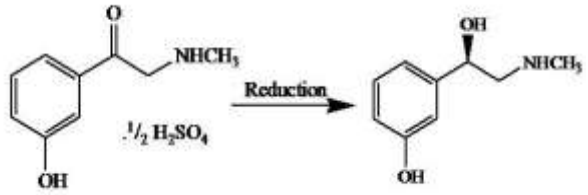


*Figure 1 – Enzymatic reduction scheme of HPMAE to R-PE*

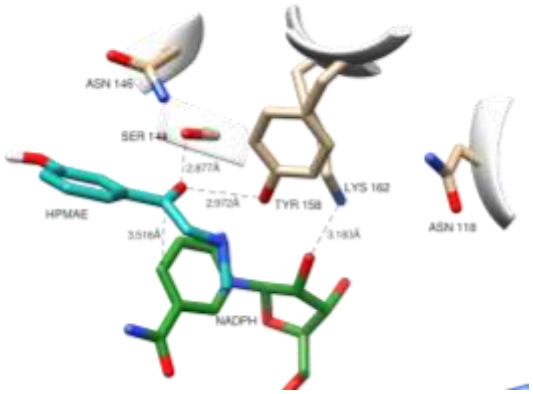


*Figure 2 – Active site of SmSDR for the enzymatic reduction of HPMAE to R-PE*