

Identification and Characterization of Inhibitors of Epoxide Hydrolase from *Trichoderma reesei*

Authors : Gabriel S. De Oliveira, Patricia P. Adriani, Christophe Moriseau, Bruce D. Hammock, Felipe S. Chambergo

Abstract : Epoxide hydrolases (EHs) are enzymes that are present in all living organisms and catalyze the hydrolysis of epoxides to the corresponding vicinal diols. EHs have high biotechnological interest for the drug design and chemistry transformation for industries. In this study, we describe the identification of substrates and inhibitors of epoxide hydrolase enzyme from the filamentous fungus *Trichoderma reesei* (TrEH), and these inhibitors showed the fungal growth inhibitory activity. We have used the cloned enzyme and expressed in *E. coli* to develop the screening in the library of fluorescent substrates with the objective of finding the best substrate to be used in the identification of good inhibitors for the enzyme TrEH. The substrate (3-phenyloxiranyl)-acetic acid cyano-(6-methoxy-naphthalen-2-yl)-methyl ester showed the highest specific activity and was chosen for the next steps of the study. The inhibitors screening was performed in the library with more than three thousand molecules and we could identify the 6 best inhibitors. The IC₅₀ of these molecules were determined in nM and all the best inhibitors have urea or amide in their structure, because it has been recognized that these groups fit well in the hydrolase catalytic pocket of the epoxide hydrolases. Then the growth of *T. reesei* in PDA medium containing these TrEH inhibitors was tested, and fungal growth inhibition activity was demonstrated with more than 60% of inhibition of fungus growth in the assay with the TrEH inhibitor with the lowest IC₅₀. Understanding how this EH enzyme from *T. reesei* responds to inhibitors may contribute for the study of fungal metabolism and drug design against pathogenic fungi.

Keywords : epoxide hydrolases, fungal growth inhibition, inhibitor, *Trichoderma reesei*

Conference Title : ICBBBS 2018 : International Conference on Biotechnology, Biomechanics and Synthetic Biology

Conference Location : Sydney, Australia

Conference Dates : January 29-30, 2018