An Investigation of Aldehyde Dehydrogenase Enzyme as a Target for Drug Design and Potential Therapeutic Applications

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Abstract

Aldehyde dehydrogenase (ALDH) is a superfamily of enzymes that play a vital role in various biochemical processes in most eukaryotes, including both human and fungi. In humans, a correlation has been proven between ALDH inhibition and therapeutic enhancement in various diseases. Therefore, targeting fungal ALDH could be of high potential in treating fungal diseases. Diethyl amino benzaldehyde (DEAB), a commonly used ALDH inhibitor, has been found to inhibit yeast ALDH, but with a non-selective and unclear mode of action. Therefore, this study aims at developing analogues for DEAB and investigate their inhibitory activity on both ALDH and yeast. Accordingly, eleven DEAB analogues were synthesized and assayed against yeast ALDH, in addition to six commercial compounds and using DEAB as a control. The results showed promising ALDH inhibition for four synthesized compounds, which was found the best for LIDA1 compound with IC_{50} = 10.7 μM compared to DEAB (IC_{50} = 11.8 μM).

Subsequently, the synthesized compounds were investigated against *C. albicans* and *S. cerevisiae*, and the results indicated an antifungal activity only for LIDA1 at 15 mM, with an inhibition zone of 12.8 mm on *S. cerevisiae*. In conclusion, LIDA1 demonstrated promising inhibition of yeast ALDH at both enzymatic and cellular levels.

Key words: Antifungal, DEAB, Yeast ALDH**.**