Docking-based virtual screening and pharmacophore analysis of novel GH-20 β-N-acetylglucosaminidase inhibitors

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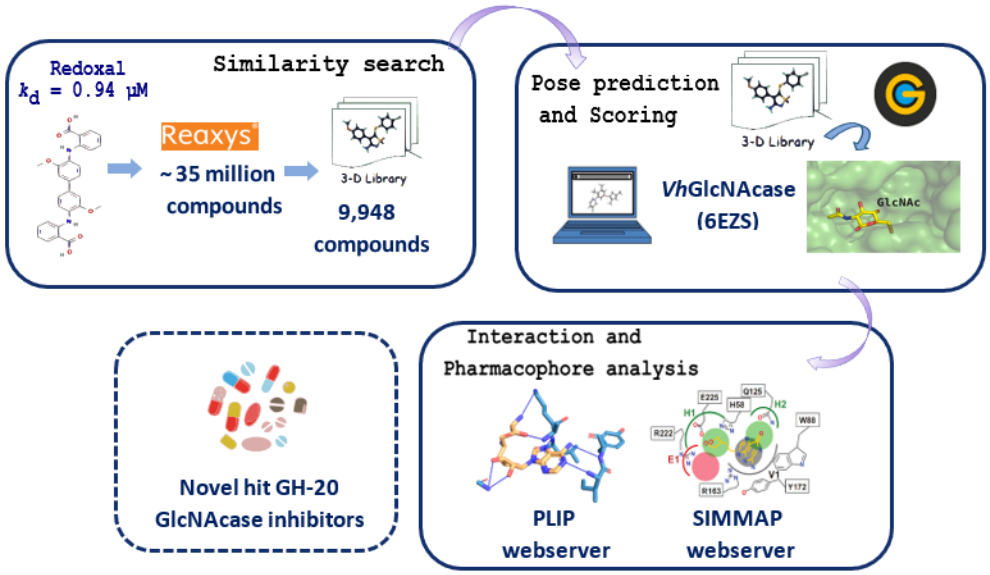
Abstract: GH-20 β-N-Acetylglucosaminidases (GlcNAcase) is a promising target for the development of new drugs active against *Vibrio* infections since the suppression of GH-20 GlcNAcase activity can lead to the inhibition of *Vibrio* spp. growth. In this study, we set up a virtual screening for potential GH-20 GlcNAcase inhibitors from the Reaxys commercial database, using a known active compound (Redoxal) as a ligand search model and GlcNAcase from *V. harveyi* (*Vh*GlcNAcase) as a protein search model. Virtual screening results identified the top ten compounds, with ChemPLP scores between 98.27 and 104.15. All ten compounds had scores greater than those of Redoxal (85.74) and the natural substrate $(GlcNAc)_4$ (85.40). Interactions and pharmacophore analysis indicated that W582 is a key residue that interacts with all the identified molecules, mainly by π-stackings interactions. The inner part of all ten molecules is located at subsite -1, deep in the catalytic pocket of *Vh*GlcNAcase, while the outer part stretches beyond the binding pocket. Hit compounds identified in this study may serve as potential candidates for further development of new, highly potent antimicrobial agents for controlling *Vibrio* spp. infections in both aquaculture and humans.

Graphical abstract:



Keywords: Virtual screening; Molecular docking; β-N-acetylglucosaminidases; *Vh*GlcNAcase; GH-20 GlcNAcases inhibitors; Protein-drug interactions

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