REVIEW ARTICLE

A Comprehensive Review of the Docking Studies of Chalcone for the Development of Selective MAO-B Inhibitors

Athulya Krishna[1], Sunil Kumar[1], Sachithra Thazhathuveedu Sudevan[1], Ashutosh Kumar Singh[1], Leena K. Pappachen[1,*], T.M. Rangarajan[3], Mohamed A. Abdelgawad[2] and Bijo Mathew[1,*]

[1]*Department of Pharmaceutical Chemistry, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, AIMS Health Sciences Campus, Kochi-682 041, India;* [2]*Department of Pharmaceutical Chemistry, College of Pharmacy, Jouf University, Sakaka, Al Jouf 72341, Saudi Arabia;* [3]*Department of Chemistry, Sri Venketeswara College, University of Delhi, New Delhi-110021, India*

ARTICLE HISTORY

Received: July 01, 2022
Revised: March 24, 2023
Accepted: March 27, 2023

DOI:
10.2174/1871527322666230515155000

Abstract: Monoamine oxidase B is a crucial therapeutic target for neurodegenerative disorders like Alzheimer's and Parkinson's since they assist in disintegrating neurotransmitters such as dopamine in the brain. Pursuing efficacious monoamine oxidase B inhibitors is a hot topic, as contemporary therapeutic interventions have many shortcomings. Currently available FDA-approved monoamine oxidase inhibitors like safinamide, selegiline and rasagiline also have a variety of side effects like depression and insomnia. In the quest for a potent monoamine oxidase B inhibitor, sizeable, diverse chemical entities have been uncovered, including chalcones. Chalcone is a renowned structural framework that has been intensively explored for its monoamine oxidase B inhibitory activity.The structural resemblance of chalcone (1,3-diphenyl-2-propen-1-one) based compounds and 1,4-diphenyl-2-butene, a recognized MAO-B inhibitor, accounts for their MAO-B inhibitory activity. Therefore, multiple revisions to the chalcone scaffold have been attempted by the researchers to scrutinize the implications of substitutions onthe molecule's potency. In this work, we outline the docking investigation results of various chalcone analogues with monoamine oxidase B available in the literature until now to understand the interaction modes and influence of substituents. Here we focused on the interactions between reported chalcone derivatives and the active site of monoamine oxidase B and the influence of substitutions on those interactions. Detailed images illustrating the interactions and impact of the substituents or structural modifications on these interactions were used to support the docking results.

Keywords: Neurodegenerativedisorders, monoamine oxidase B, selective inhibitors, chalcone derivatives, docking interactions, structural modifications.

1. INTRODUCTION

Monoamine oxidase (MAO) is a flavoenzyme found in the periphery of the mitochondrial membrane of both human and animal tissues. The oxidative deamination of xenobiotic and endogenous amines, including neurotransmitters, is a primary function of MAO [1-3]. MAO-A and MAO-B are two protein isozymes isolated and thoroughly investigated [4], showing about 70% sequence identities.They differ significantly in terms of sensitivity to inhibitors and selectivity of the substrates. MAO-A and B inhibitors are currently a hope in clinical trials to treat mental and neurological illnesses. MAO-A is a protein that destroys noradrenaline and serotonin in the central nervous system (CNS), and the inhibitors of MAO-A have been used to treat psychiatric disorders like depression and anxiolytic disorders. MAO-B is a significant metabolic enzyme for phenylethylamine and dopamine in the CNS, and the inhibitors have thus been utilized to medicate neurodegenerative illnesses like Alzheimer's disease (AD) and Parkinson's disease (PD) [5-9]. During catalytic processes, monoamines are degraded to aldehydes, forming hydrogen peroxide (H_2O_2). Reactive oxygen species (ROS) are formed when high levels of H_2O_2 are present, and they are neurotoxic and linked to a variety of neurological diseases. MAO-B expression and activity are dramatically enhanced in the brains of PD and AD patients. MAO-B inhibitors are regarded as prospective treatment medicines for PD and AD because they can increase dopamine levels in the brain while reducing ROS generation [10-12]. Irreversible and reversible MAO-B inhibitors are currently available to treat

*Address correspondence to these authors at the Department of Pharmaceutical Chemistry, Amrita School of Pharmacy, Amrita Vishwa Vidyapeetham, AIMS Health Sciences Campus, Kochi-682 041, India;
E-mails: bijomathew@aims.amrita.edu; bijovilaventgu@gmail.com; leenakpappachen@aims.amrita.edu

1871-5273/XX $65.00+.00