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REVIEW

WILEY

Deciphering the detailed structure–activity relationship of coumarins as Monoamine oxidase enzyme inhibitors—An updated review

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Abstract

In the last few years, Monoamine oxidase (MAO) have emerged as a target for the treatment of many neurodegenerative diseases including anxiety, depression, Alzheimer's, and Parkinson's diseases. The MAO inhibitors especially selective and reversible inhibitors of either of the isoenzymes (MAO-A & MAO-B) have been given more attention as both the form have different therapeutic properties and hence can be used for different neurological disorders. The lack of selective and reversible inhibitors available for both the enzymes and severity of the neuronal disorder in society have opened a new door to the researchers to carry out large and dedicated researches in this field. Among the several classes of the molecule as the inhibitors, coumarins hold a rank as a potent scaffold with its ease of synthesis, high therapeutic potential, and reversibility in inhibiting MAOs. The current review is an update of the research in the field that covers the works during the last six years (2014–2020) with a major focus on the SAR of the coumarin derivatives including synthetic, natural, and hybrids of coumarins with FDA-approved drugs.

KEYWORDS

Alzheimer's disease, coumarin, monoamine oxidase, structure–activity relationship

1 | INTRODUCTION

Monoamine oxidases (MAOs) have become a potential target for the treatment and slow down of several neurodegenerative diseases. These are flavoenzymes that are present in the exterior of the mitochondrial membrane (Patil et al., 2013). Members of the monoamine oxidase family of flavoproteins catalyze the breakdown of primary, secondary amines, polyamines, and amino acids, including lysine demethylation in proteins (Gaweska & Fitzpatrick, 2011). MAOs are also found in almost any brain area as well as most of the peripheral organs. MAO exists in two isoforms: MAO-A and MAO-B (Saura et al., 1996). The oxidative deamination of neurochemicals such as dopamine (DA), serotonin, phenylethylamine, adrenaline, and noradrenaline is catalyzed by these enzymes. MAO-A shows an affinity toward substrates serotonin (5-HT), norepinephrine (NE), and dopamine (DA), while MAO-B has it toward phenylethylamine (PEA) and benzylamine (Shih et al., 1999). The degradation of serotonin, norepinephrine, and tyramine by MAO-A is therefore

