ABSTRACT

The topic of this thesis is the synthesis of oxadiazole derivatives and their precursors as potential therapeutics for neurodegenerative diseases, and their evaluation primarily as potential inhibitors of cholinesterases (CHE).

The theoretical part of this thesis focuses on Alzheimer's disease, particularly its pathophysiology, diagnosis, and treatment. It also discusses CHE inhibitors that are already clinically used, as well as new structures with potential for future clinical use. Additionally, it addresses the oxadiazole fragment, its chemical and biological properties.

In the experimental work, derivatives of 1,3,4- and 1,2,4-oxadiazoles were synthesized, which differed not only in the type of oxadiazole but also in their substitution. These substances were prepared by the cyclization of precursors, which were also prepared and tested. For 1,3,4-oxadiazoles, besides their inhibitory activity against acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), their potential antimycobacterial, antibacterial, and antifungal activities were tested. For 1,2,4-oxadiazoles, so far, only their inhibitory activity against AChE and BuChE has been tested.

A total of twenty-two substances were synthesized, and the yields of these syntheses ranged from 21-97%. The compound with the lowest IC_{50} value for AChE was 2-(3-nitrophenyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole, specifically measured at 6.68 μM. The lowest IC_{50} for BuChE was measured for the compound 5-(3,5-dinitrophenyl)-3-(pyridin-3-yl)-1,2,4-oxadiazole, at 45.09 μM. The compound with the lowest minimum inhibitory concentration (MIC) values for mycobacteria, bacteria, and fungi was 2-(2,4-dinitrophenyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole, with MIC values from 2 μM for mycobacteria, 7.81 μM for bacteria, and 125 μM for fungi, while most of the remaining compounds were antimicrobial inactive.

KEYWORDS

Acetylcholinesterase, Alzheimer's disease, butyrylcholinesterase, hydrazinecarboxamides, chemical synthesis, cholinesterase inhibition, oxadiazoles.