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*Abstract*

# Microwave-Assisted Synthesis and Butyrylcholinesterase Inhibitory Activity of New Azobenzene Derivatives †

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**Abstract:** Cholinesterase inhibitors (ChEis) play an important role in enhancing cholinergic synaptic activity and, consequently, have therapeutic applications in the treatment of neurodegenerative diseases like Alzheimer's disease (AD). The inhibition of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) avoids the degradation of the neurotransmitter acetylcholine and constitutes a pharmacotherapeutic strategy that has shown important efficacy reducing AD symptoms. Based on previous results obtained by our group and with the purpose of obtaining diverse and more effective compounds, a series of new azobenzene derivatives were designed and synthesized. Additionally, considering the powerful AChE inhibition displayed by this type of compounds it was decided in this work to expand the research by testing BChE inhibitory activity. Nine azobenzene derivatives, with different spacer lengths (4–8 carbons) and terminal tertiary amines, were synthesized by microwave-assisted synthesis and tested for biological activity in vitro. The synthesis was carried out using a microwave oven (in two steps) with a reaction time of around 20 min and moderate to good yields. In addition, cytotoxic properties of the compounds in SH-SY5Y human neuroblastoma cells will be tested. The inhibitory activity of BChE was determined using Ellman's method. All the compounds synthesized were active against BChE, the one with a six carbon atom spacer and ethylbenzylamine moiety ($IC_{50}$: 6.621 μM ± 0.001) being the most effective. From these results we could establish that the optimum length for the spacer was six carbons and that diamines were less active than monoamines.

**Keywords:** azobenzene; Alzheimer's disease; butyrylcholinesterase; microwave; cytotoxic



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