ABSTRACT

Antibiotic resistance represents a significant threat to humanity. To combat this trend, the development of new effective substances can be employed to potentially reverse its progression. Due to the broad range of biological activities exhibited by steroid structures, estrone was chosen as the starting material and was modified through various reactions. In total, fifteen new compounds were synthesized, which were tested for their antibacterial, antifungal, and antimycobacterial activities, and additionally for cholinesterases inhibition.

The modification of estrone primarily involved two different approaches, resulting in the formation of hydrazones and esters. Twelve compounds were prepared through these steps. For the remaining three derivatives, changes in the starting materials or procedures were necessary. In the case of four compounds, it was necessary to synthesize one of the reactants. The yields ranged from 62% to 95% for hydrazones and from 8% to 54% for esters. The antibacterial activity was tested against four selected Gram-positive and Gram-negative strains. Antifungal activity was evaluated against four yeasts and filamentous fungi. Antimycobacterial activity was tested against five mycobacterial strains. All these methods utilized the microdilution broth method.

The tested molecules showed no activity in the antibacterial and antifungal assays. Activity was only observed in the antimycobacterial evaluation, where ten out of the twelve tested compounds exhibited activity against at least one mycobacterial strain. The compound 4-chlorobenzohydrazone of estrone (encoded as PaP-7) showed the greatest activity or the lowest minimum inhibitory concentration (MIC) against *Mycobacterium kansasii*.

Inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) was also assessed. All derivatives were active, with IC50 values ranging from 31.88 to 166.19 µM. All compounds were dual inhibitors of both enzymes, with the 4-chlorophenyl ester of estrone showing the best activity against both AChE and BChE.

Although the synthesized compounds did not demonstrate sufficient activity against bacteria and fungi, they could be useful in the fight against mycobacteria and as potential inhibitors of cholinesterases.

Keywords: antimicrobial compounds, antimycobacterial activity, cholinesterases, enzyme inhibition, steroids, synthesis