Abstract

One of the ways to alleviate the global problem of antibiotic resistance is, among other things, the synthesis and development of new antimicrobials. All compounds prepared in this work are based on the molecule 4-amino-1-benzylpiperidine or its isomer 4-(piperidin-1-ylmethyl)aniline. The parent molecule was chosen on the based on its previously reported activity. Thirteen imines were prepared using one-step synthesis by reacting the starting amine with the corresponding aldehyde. Two additional syntheses led to the amides by reaction of the starting molecule with the corresponding salicylic acid. The yields of the reactions ranged from 26 to 97 % for the imines and were 25 and 39 % for the amides. All compounds were prepared in sufficient quantity and purity to determine biological activity.

All fifteen compounds were tested for their antibacterial activity against clinically relevant Gram-positive and Gram-negative strains. They were further tested for their antifungal activity, antimycobacterial aktivity, and their ability to inhibit the enzymes acetylcholinesterase and butyrylcholinesterase was also tested. The results of the evaluation showed that the amides were ineffective against microbes, but some imines showed excellent results. In general, the compounds were more active against pathogenic fungi, but the diiodinated and dichlorinated imines also showed a good activity against Gram-positive bacterial strains. The lowest MIC (minimum inhibitory concentration) for both bacteria (15.62 µmol/L) and fungi (1.95 µmol/L) was found for (*E*)-2,4-diiodo-6-{[(4-(piperidine-1-ylmethyl)phenyl]imino}methyl)phenol.

(E)-2,4-Dichloro-6-{[(4-(piperidin-1-ylmethyl)phenyl)imino]methyl}phenol (IC50 = 0.60 µmol/L and SI = 0.06) and (E)-1-(3-nitrophenyl)-N-{[(4-piperidin-1-yl)methyl]phenyl]methanimine (IC50 = 0.23 µmol/L and SI = 0.02) showed the highest selectivity for the enzyme acetylcholine esterase. SI denotes selectivity index, determined by AChE/BChE calculation. The best selectivity to butyrylcholinesterase among the prepared compounds showed (E)-2-{[(1-benzylpiperidin-4-yl)imino]methyl}-4,6-diiodophenol (IC50 = 18.33 µmol/L and SI = 1.33).

Key words

4-amino-1-benzylpiperidine, antimicrobials, cholinesterase, enzyme inhibition, methicillin-resistant staphylococci, new compounds, resistance, salicylic acid, synthesis