Abstract

Mycotic systemic infection is often very severe, whether due to patient immunodeficiency, the side effects of available antifungal agents, or clinical or drug resistance. Emphasis should therefore be placed on the timely determination of the correct diagnosis, appropriate indications of current drugs, and especially the development of new antifungal agents (ATM).

The core of all synthesized compounds is the molecule of itaconic acid (IA) or its anhydride. The starting molecule was chosen based on its broad spectrum of biological activities, including antibacterial and antifungal activities. The aim was to create ten monoamides using a one-step synthesis of IA anhydride with the appropriate chlorinated aniline. These monoamides were then cyclized to form ten imides. The yields of the reactions to form the monoamides were high, with two exceptions (24% and 31%), and were generally above 80%. The yields of the reactions to form the imides were lower, ranging from 29% to 86%.

The antimicrobial activity was tested using the broth microdilution method for all imides and most monoamides. All compounds were ineffective against gram-negative bacteria, and very low activity against gram-positive bacteria was shown by the compounds 1-(2,4,6-trichlorophenyl)-3-methylene-2,5-pyrrolidinedione, 1-(2,6-dichlorophenyl)-3-methylene-2,5-pyrrolidinedione, and 1-(3,4,5-trichlorophenyl)-3-methylene-2,5-pyrrolidinedione. Inhibitory activity against acetyl- and butyrylcholinesterase was tested for all compounds, but the results showed relatively high IC_{50} values (the lowest measured concentration was 67.76 µM). The tested compounds exhibited the highest activity in inhibiting fungi. The best measured MIC values (7.81 µmol/L) were shown by the compounds 1-(2,4,6-trichlorophenyl)-3-methylene-2,5-pyrrolidinedione and 1-(3,4,5-trichlorophenyl)-3-methylene-2,5-pyrrolidinedione against the strain *Trichophyton interdigitale*. All measured biological and biochemical activities depended on both the number of chlorine atoms in the molecule and the position of these atoms (it cannot be said that activity always increased with the growing number of chlorine atoms, nor that a compound with chlorine attached in a certain position was always active).

Keywords

Antimicrobial activity, antifungal agents, antifungal resistance, cholinesterase inhibition, itaconic acid, mycoses