Biological evaluation of the antimicrobial and antihyperlipidemic activity of novel 3,5-disubstitutedamido -1,2,4-thiadiazole and 2,5-disubstitutedamido -1,3,4-thiadiazole

By

Luma Adel Abd Al-Samad

Supervisor

Dr. Lama Hamadneh

Co-supervisor

Professor Dr. Tariq Al-Qirim

Abstract

The emergence of pathogenic resistance to several antimicrobial agents becomes a major health problem worldwide in hospital and community, leading to sever infections, complications and even increase in mortality rates; developing a new antimicrobial agent with modified mechanism of action is urgently needed to overcome this increase in microbial resistance. In addition, hyperlipidemia a serious condition that is responsible for coronary heart disease; one of the top reasons of early death globally; necessitates the development of new antihyperlipidemic agents with higher potency and lower side effects. In this study, novel derivatives of 2,5-diamino-1,3,4-thiadiazole derivatives (I), 3,5-diamino-1,2,4-thiadiazole derivatives (II) and Schiff base derivatives

(III) were synthesized at Chemistry Department, Faculty of Science, University of Jordan and Hamdi Mango Center for Scientific Research, were screened for their potential antimicrobial activity against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Candida albicans.* Compounds 4, 9, 7 and 11 showed good activity against ATCC and clinical isolates of *E.coli* with best activity seen with compound 9 having MIC value of 100µg/well, while compounds 1, 2 and 3 showed moderate activity towards clinical *E.coli* isolates. Compound 1 showed equal activity against ATCC and clinical strains of *Candida albicans* when compared with fluconazole as reference drug. β-carbonic anhydrase presented a promising target for thiadiazole derivatives as antimicrobial agents. On the other hand, antihyperlipidemic activity for compounds 9, 9a and 9b were screened in hyperlipidemic rat model. It is show that compound 9 have the highest activity in reduction triglyceride level (97%), total cholesterol and low density lipoprotein (LDL) along with increased levels of high density lipoprotein (HDL). Thiadiazole containing Schiff base derivative may exert their lipid lowering activity through activation of peroxisome proliferator activated receptor-α (PPAR-α) that plays a crucial role in lipid and lipoprotein metabolism.