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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Effect of chloro and fluoro groups on the antimicrobial activity of 2,5-disubstituted 4-thiazolidinones: a comparative study

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Abstract The article reports the synthesis of a series comprising of twenty-one 2,5-disubstituted-4-thiazolidinone derivatives, bearing 3-chloro-4-fluorophenyl imino, 4-chlorophenyl imino and 3-chlorophenyl imino groups at position-2 and substituted arylidene groups at position-5. The title compounds were obtained in high yields through Knoevenagel condensation and evaluated for antimicrobial activity against *B. subtilis*, *S. aureus*, *P. aeruginosa*, *E. coli*, and *C. albicans*. Success of the synthesis was confirmed through spectral analysis. The newly synthesized compounds exhibited promising antibacterial activity but no antifungal activity. SAR studies revealed that the presence of a fluoro group in addition to a chloro group had a marked influence on the antibacterial activity.

Keywords 4-Thiazolidinones · Arylidene · Spectral analysis · Imino · Knoevenagel condensation · Antimicrobial

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Introduction

Medicinal chemistry involves the discovery of new chemical entities for the treatment of disease and systematic study of SARs of these compounds. Such studies provide the basis of development of better medicinal agents from lead compounds (Fries, 2008). The nature of these compounds is largely synthetic with some compounds being natural or semi-synthetic. Among the synthetic compounds, only a few qualify to be a "drug." It is an established fact that one drug out of three is a halogenated derivative and halogens are found in drugs belonging to practically all therapeutic classes (Wermuth, 2003). Halogen groups impart different effects on physicochemical and pharmacological activities of drugs.

Antibiotics belong to one of the most prescribed classes of drugs. However, their misuse and evolutionary pressures have led to growing incidences of drug resistant pathogens (Prescott, 2007). This coupled with a decreased pace of discovery of anti-infective agents has aggravated the problem. Thus, there is an urgent need to develop new pharmacophores which not only offer a broad spectrum of activity but also possess a different mechanism of action so as to avoid cross resistance (Chugh, 2008; Williams, 1996).

Heterocyclic compounds present themselves as a group with a plethora of varying biological activities. 4-thiazolidinones are moieties which possess innumerable activities like antimicrobial (Bondock, 2006, 2007; Bonde and Gaikwad 2004; Kavitha *et al.*, 2006; Ronad *et al.*, 2010; Omar *et al.*, 2010; Vicini *et al.*, 2008); anti-convulsant (Shingalapur *et al.*, 2010); anti-diabetic (Faidallah *et al.*, 2011); anti-HIV(Rawal *et al.*, 2005, 2007); cardio-protective (Ozaki and Ohi, 1999); tumor necrosis factor-α antagonist activities (Voss *et al.*, 2003); Ca^{2+} channel blocker (Kato *et al.*, 1999; Hara *et al.*, 1999) and the list is ever