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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

# 4-Thiazolidinone and 1-thia-3,4,9-triaza fluorene conjugates: synthesis, characterization and antimicrobial screening

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**Abstract** Some novel 4-thiazolidinone derivatives have been synthesized by the condensation of isatin/5-chloroisatin with thiosemicarbazide to yield thiosemicarbazones, which were then cyclized to form corresponding thia-3,4,9-triaza-fluoren-2-ylamines. These were reacted with substituted aldehydes to give corresponding Schiff bases, which were cyclized using thioglycolic acid in the presence of zinc chloride to obtain the 4-thiazolidinone derivatives. All the synthesized compounds were characterized by spectral (IR, MS and NMR) and elemental analysis. The compounds were screened for their antibacterial activity against Gram-positive bacteria (*B. subtilis*, *S. aureus*, *B. pumilus* and *M. luteus*), Gram-negative bacteria (*P. aeruginosa*, *E. coli* and *P. fluorescens*) and for antifungal activity against *A. niger* and *P. chrysogenum* by agar-diffusion method. The minimum inhibitory concentrations of these compounds were also determined by tube dilution method. The antimicrobial effectiveness of all the compounds was found to be concentration dependent. Two compounds—2-methyl-3-(1-thia-3, 4, 9-triaza-fluoren-2-yl)-thiazolidin-4-one (**7aI**) and 2-naphthalen-1-yl-3-(1-thia-3, 4, 9-tri aza-fluoren-2-yl)-thiazolidin-4-one (**7aII**)—exhibited good antibacterial activity. The antibacterial activity of all the compounds was found to be better than the antifungal activity.

**Keywords** Antimicrobial agents · Isatin · 4-Thiazolidinone · Thiosemicarbazone · Fluorene

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## Introduction

The 4-thiazolidinones are the derivatives of thiazolidine with the carbonyl group at the 4-position, belonging to an important group of heterocyclic compounds containing sulphur and nitrogen in a five membered ring. 4-Thiazolidinone template is one of the privileged structure fragments in modern medicinal chemistry considering its broad pharmacological activity (Verma and Saraf, 2008) and affinity for various biotargets as antimicrobial (Vicini *et al.,* 2006; Bondock *et al.,* 2007; Pooja *et al*., 2011a, b), anti-inflammatory (Ottana *et al.,* 2005), anti-HIV (Rawal *et al.,* 2005, 2007a, b, 2008a, b; Rao *et al.*, 2003, 2004), anti-tuberculosis (Babaoglu *et al.,* 2003), anti-convulsant (Capan *et al.,* 1996; Gursoy *et al.,* 2005; Ergenc *et al.,* 1999), etc. Isatin is an endogenous compound, i.e. derivative of indigo dye isolated in 1988 (Sridhar *et al.,* 2001). The chemistry of isatin and its derivatives is particularly interesting because of their potential application in medicinal chemistry. 2-Amino-11-hydronaphtho[2,1:5,6]pyrano[4,3-*d*]thiazole on treatment with isatin, chloroacetyl chloride and mercaptoacetic acid affords corresponding *N*[naphtha [1,2b] pyrano3,4d]thiazol-8-yl]spiro-[3*H*-indole-(1H,2H)3,4-(2H)-3chloroazetidine-2, 2-diones and *N*[naphtha [1, 2b]pyrano[3,4-d]thiazol-8-yl] spirol-[3*H*-indole-(1H, 2H)-3,2-(4H)-thiazolidine]-2,4-dione with good antimicrobial activity (Pai *et al.*, 2006). Jarrahpour *et al.* (2007) synthesized bis-Schiff bases of isatin by condensation of isatin, benzylisatin and 5-fluoroisatin with primary aromatic amines which possess significant antiviral, antibacterial and antifungal activity. Bhambi *et al.* (2009) synthesized 3′{4(1acetyl-5(4-flurophenyl)-2pyrazoline-3yl) phenyl}1-*N*-ethoxyphthalimido-4′-spiro[indole-3,2′-[1,3] thiazolidene]-2,4′-1*H*-dione, which was formed by reacting 3{4-(1-acetyl-5-(4-chlorophenyl)-2pyrazoline-3-yl)phenyl}-4′*H*-spiro[indole-3,2′-[1,3]thiazolidene]-2,4′-1*H*-dione, in DMF