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Chemical Papers 68 (3) 392–400 (2014)
DOI: 10.2478/s11696-013-0452-3

ORIGINAL PAPER

Design and synthesis of novel thiopheno-4-thiazolidinylindoles as potent antioxidant and antimicrobial agents

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Received 22 December 2012; Revised 25 May 2013; Accepted 1 June 2013

A novel and convenient synthesis of thiopheno-4-thiazolidinyl indole analogues is presented (*IVa–IVi*), with the aim of obtaining biologically active compounds. 3,5-disubstituted indol-2-carboxyhydrazides (*Ia–If*) were allowed to react with 3-acetyl-2,5-dichlorothiophene (*II*) to yield the corresponding 3,5-disubstituted indol-2-carbohydrazides (*IIIa–IIIf*). The pre-formed indolecarbohydrazides (*IIIa–IIIf*) were allowed to react with 2-mercaptoacetic acid or 2-mercaptopropanoic acid to produce thiopheno-4-thiazolidinylindoles (*IVa–IVi*). This reaction protocol affords a simple, eco-friendly, non-hazardous, easier preparation and high yields. The antioxidant (free radical scavenging, total antioxidant capacity and ferric-reducing antioxidant power) and antimicrobial activities of the synthesised compounds were evaluated. The structures and purity of the products were confirmed by their IR, ^{1}H NMR, ^{13}C NMR and mass spectral and analytical data. Most of the compounds tested showed very significant scavenging, antioxidant and antimicrobial activities. Compounds containing electron donor group (CH_3) at the fifth position of indole exhibit an excellent ferric-reducing activity. The present study suggests that compounds *IIIa–IIIb*, *IIIf*, *IVa–IVc*, *IVf–IVi*, may serve as promising lead scaffolds for antioxidant and antimicrobial agents.

Keywords: indole carboxyhydrazide, indole carbohydrazide, thiopheno thiazolidinylindoles, dichlorothiophene, antioxidant activity, antimicrobial activity

Introduction

Free radicals are products of normal cellular metabolism (Park et al., 2004). The predominant cellular free radicals are superoxide (O_2^-), hydroxyl (OH) species (Jenner & Olanow, 1996; Simonian & Coyle, 1996), hydrogen peroxide (H_2O_2) and peroxynitrite ($ONOO^-$). Although some of them are not free radicals itself, various chemical reactions can lead to the formation of free radicals. These molecules are denoted as Reactive Oxygen Species (ROS) (Simonian & Coyle, 1996; Valko et al., 2006). Maintaining a balance between the free radicals and antioxidants in the normal metabolism is very important in achieving optimal physiological conditions (Saenjum et al., 2010). The excessive production of ROS or a decrease in antioxidants may lead to the development of a number of diseases such as cancer, rheumatoid arthritis, and ageing (Kataoka et al., 1997; Squadrito & Pryor, 1998). ROS can cause damage to DNA, commonly accepted as a major cause of cancer (Ames, 1983). Resistance against microbial infection remains a serious problem (Francis et al., 2005; Vicini et al., 2006), hence the development of novel antimicrobial agents in addition to the existing ones can overcome this problem (Bonde & Gaikwad, 2004; Khan et al., 2009).

Indole scaffolds are medicinally important components, denoted as privileged structures. Substituted indole derivatives are present in several natural products and medicinal compounds with varied therapeu-

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