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REVIEW

2nd Cancer Update

Synthesis, antimicrobial and anticancer activities of amido sulfonamido methane linked bis heterocycles

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Abstract A new class of amido sulfonamido methane linked bis heterocycles- bis-oxazoles, thiazoles and imidazoles were prepared and screened for antimicrobial and anticancer activities. The chloro substituted amido sulfonamido bisimidazole exhibited excellent antimicrobial activity and also it was the most potent compound on lung, colon and prostate cancer cell lines.

Contents

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1. Introduction

Sulfonamide drugs are associated with a wide range of biological activities and in fact brought an antibiotic revolution in medicine (Ali et al., 2006; McCarroll et al., 2007; Wilkinson et al., 2007). Many oxazole and/or thiazole containing macrocycles are naturally occurring molecules, *viz*., Bistratamides (You and Kelly, 2005), Didmolamides A and B (You and Kelly, 2005), Lyngbyabellin A (Yokokawa et al., 2001), and Calyculins (Yokokawa et al., 2001; Degnan et al., 1989; Pihko and Koskinen, 1998; Perez and Faulkner, 2003; Rudi et al., 2003; Tan et al., 2003), which show cytotoxic, antimicrobial and multiple drug resistance activities. Several classes of drugs based on imidazole *viz*., 2-nitroimidazole commonly called Azomycin are a natural antibiotic. Some synthetic nitroimidazoles are active against intestinal infections (Breccia et al., 1986). In fact metronidazole is used for intestinal infections and also as a radiosensitizer in X-ray therapy (Middlemiss and Watson, 1994). The incorporation of sulfonamide moiety into heterocyclic rings can produce pharmacologically potent compounds. The present work comprises design and synthesis of new molecules having two pharmacophoric heterocyclic units linked by bis methane amido sulfonamido moiety which are expected to have pharmacological activity. Although chemically unrelated to these compounds, other classes of antibiotics such as the anthracyclines (Miller and Stoodley, 2011) which were originally isolated from strains of *Streptomyces peucetius*, show antibacterial activity (mostly against Gram positive bacteria, for example *Staphylococcus aureus*) and have been in clinical use for the treatment of various forms of cancer for several decades. Triazolopyrazole thiones also exhibit antibacterial, antifungal and promising anticancer activities; the latter compared with the anthracycline doxorubicin.

2. Experimental

2.1. General

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 1:3). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wavenumbers were given in cm^{-1}. The ^{1}H NMR spectra were recorded in DMSO-d_6 on a Bruker spectrospin operating at 400 MHz. The ^{13}C NMR spectra were recorded in DMSO-d_6 on Bruker spectrospin operating at 100 MHz. All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. For anticancer activity the optical density was determined at 450 nm using a microplate reader (BioTek Instruments Inc., Winooski, VT, USA).

2.2. Synthesis of bis(carbethoxymethylsulfonyl)amine (2)

To a solution of ethyl sulfamylacetate (**1**) (0.003 mol) in dichloromethane (10 ml), triethylamine (0.0031 mol), and 4-dimethylaminopyridine (DMAP) (0.0001 mol) were added and stirred at room temperature for 15 min. Then, a solution of ethyl 2-chlorosulfonylacetate (0.0033 mol) in dichlorometh-