Saudi Journal of Biological Sciences (2016) 23, 614–620

King Saud University

Saudi Journal of Biological Sciences

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Anti-inflammatory and antimicrobial activities of novel pyrazole analogues

R. Surendra Kumar [a], Ibrahim A. Arif [b], Anis Ahamed [b], Akbar Idhayadhulla [c,*]

[a] Department of Chemistry, Shivani Engineering College, Affiliated to Anna University, Tamil Nadu, India
[b] Prince Sultan Research Chair for Environment and Wildlife, Department of Botany & Microbiology, College of Sciences, King Saud University (KSU), Riyadh, Saudi Arabia
[c] Department of Chemistry, School of Basic Science, VELS University, Chennai 600117, Tamil Nadu, India

Received 4 May 2015; revised 6 July 2015; accepted 22 July 2015
Available online 29 July 2015

KEYWORDS

Ultra sound irradiation;
Pyrazole derivatives;
Mannich bases;
Antimicrobial activity;
Anti-inflammatory activity;
Structure–activity Relationships (SAR)

Abstract A new sequence of pyrazole derivatives (**1**–**6**) was synthesized from condensation technique under utilizing ultrasound irradiation. Synthesized compounds were characterized from IR, ^{1}H NMR, ^{13}C NMR, Mass and elemental analysis. Synthesized compounds (**1**–**6**) were screened for antimicrobial activity. Among the compounds **3** (MIC: 0.25 μg/mL) was exceedingly antibacterially active against gram negative bacteria of *Escherichia coli* and compound **4** (MIC: 0.25 μg/mL) was highly active against gram positive bacteria of *Streptococcus epidermidis* compared with standard Ciprofloxacin. Compound **2** (MIC: 1 μg/mL) was highly antifungal active against *Aspergillus niger* proportionate to Clotrimazole. Synthesized compounds (**1**–**6**) were screened for anti-inflammatory activity and the compound 2-((5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)(4-nitrophenyl) methyl)hydrazinecarboxamide (**4**) was better activity against anti-inflammatory when compared with standard drugs (Diclofenac sodium). Compounds (**2, 3** and **4**) are the most important molecules and hence the need to develop new drugs of antibacterial, antifungal and anti-inflammatory agents.

1. Introduction

The pyrazole moiety is a versatile lead molecule in the pharmaceutical development and has a wide range of biological activities (Goda et al., 2003; El-Emary, 2006; Mansour et al., 2003), antibacterial (Sangapure et al., 2001), antifungal (Gupta et al., 2005; Ashish et al., 2006) and pharmacological activities such as anti-inflammatory (Makhsumov et al., 1986), antitubercular (Chetan and Mulwar, 2000), anticancer (Nimavat and Popat, 2007), analgesic (Udupi et al., 1998), antipyretic (Fabiane et al., 2002), anticonvulsant (Ashok et al., 2001) activities.

Commercially available pyrazole moiety (Fig. 1) such as Celecoxib is potent COX-2 inhibitor (Penning et al., 1997). Some other examples of pyrazole derivatives as NSAID are ramifenazone (Fioravanti et al., 2010), Lonazolac (NSAID)

* Corresponding author. Tel.: +91 9994265115.
E-mail address: a.idhayadhulla@gmail.com (A. Idhayadhulla).
Peer review under responsibility of King Saud University.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.sjbs.2015.07.005
1319-562X

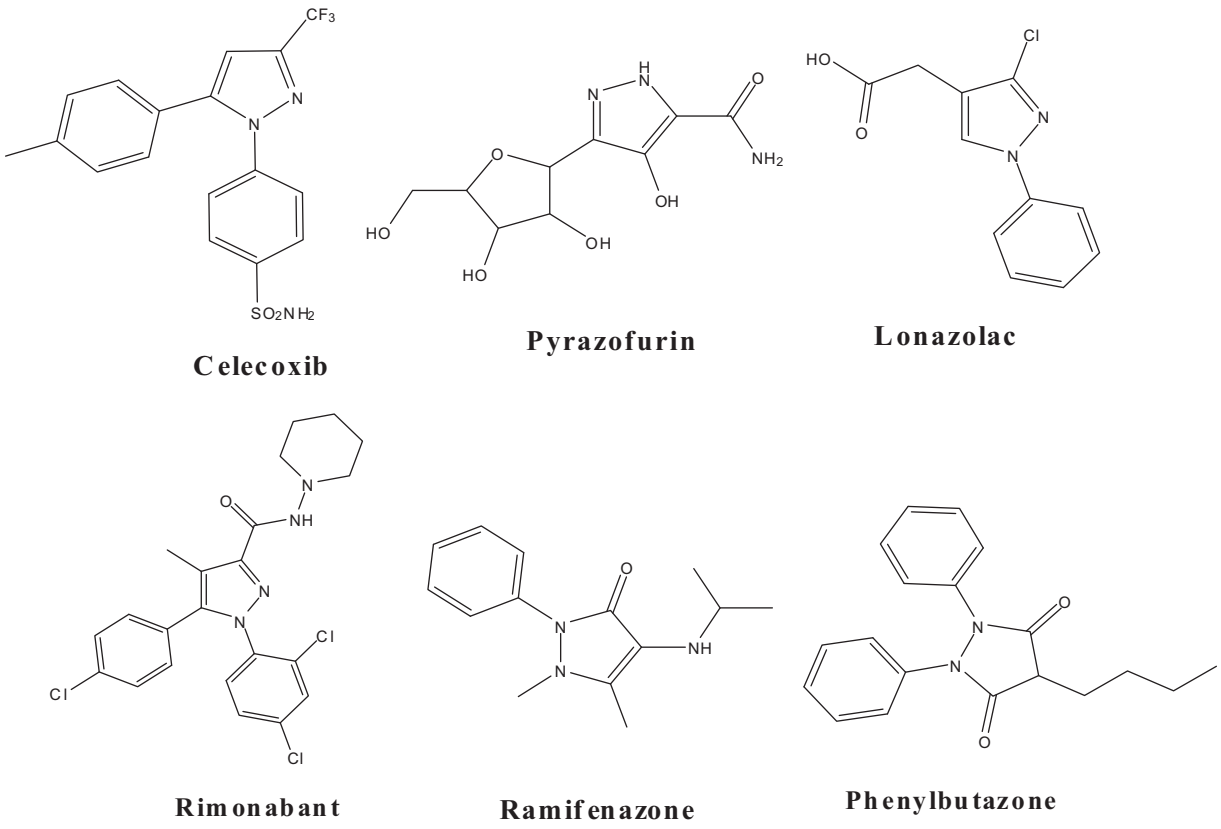

Figure 1 The structures of some drugs bearing the pyrazole moiety.

(Riedel, 1981) and Rimonabant (Isidro and Cordido, 2009). Compound (phenylbutazone) is a non steroidal drug (Reed et al., 1985; Vennerstorm et al., 1987). Pyrazofurin is potential of antiviral activity, HCV virus (Rostom et al., 2003; Riyadh et al., 2010; Popovici-Muller et al., 2009; Farghaly et al., 2011). In the current research, anti-inflammatory drug has been used in most prominent research areas. New anti-inflammatory drugs were previously used in clinical research, some of the drugs are still not efficient and have intolerable side effects.

Based on the above study, we need to develop new drugs against anti-inflammatory and antimicrobial activities. Therefore, we were led to identify new approaches of pyrazole derivatives as well as test the antimicrobial and anti-inflammatory activity.

2. Methods and materials

2.1. Chemicals and reagents

All chemicals were acquired from Sigma–Aldrich Chemical Co (Sigma–Aldrich Corp., St. Louis, MO, USA). The Infrared spectra (KBr), Proton NMR, Carbon NMR, Mass spectra (EI), and Elemental analysis (C, H, N and S) were recorded using Shimadzu 8201PC (4000–400 cm^{-1}), Bruker DRX-400 MHz, Jeol JMS D-300 spectrometer operating, and Elementer analyser model (Varian EL III).

2.1.1. Synthesis of 2-((5-hydroxy-3-methyl-1H-pyrazol-4-yl)(phenyl)methyl)hydrazinecarboxamide (1)

A mixture of 5-hydroxy-3-methyl-1*H*-pyrazoles (0.1 mol), benzaldehyde (0.1 mol) and semicarbazide hydrochloride (0.1 mol) was treated with ultrasound irradiation under ethanol medium. After completion of reaction, the product was isolated and identified by TLC. The identified product was separated from column chromatography and recrystallized by suitable solvent. The above experiential procedure was pursued by remaining compounds **2**–**6**.

IR (cm^{-1}): 3445 (C–OH), 670(–CH–), 1679 (NH CO), 1569 (NH_2). ^{1}H NMR (DMSO-d_6): δ 9.90 (s, 1H, C–OH), 2.71 (d, J = 4.4 Hz, 1H, CH), 2.23(s, 3H,CH_3), 4.45 (dd, J = 5.3 Hz, 1H, –CH–), 7.33–7.49 (m, 5H, Phenyl ring), 2.36 (d, J = 2.0 Hz, 1H, NH), 6.81 (d, J = 1.4 Hz, 1H, NH), 6.25 (s, 2H, NH_2). ^{13}C NMR ($CDCl_3$): δ 167.2(C–OH), 162.6 (C–CH_3), 42.2(C–CH–), 52.3(C–CH–NH), 18.7(C–CH_3), 155.4($CONH_2$), 141.7, 112.0, 129.2, 133.8 (Phenyl ring). Mass (m/z): 261.27 (M^+, 32%), 244.28, 216.38, 200.27 (100%), 185.26, 170.25, 94.15.

2.1.2. 2-[(4-chlorophenyl)(3-hydroxy-5-methyl-4H-pyrazol-4-yl)methyl]hydrazinecarboxamide(2)

IR (cm^{-1}): 3469 (C–OH), 691(–CH–), 1665 (NH CO), 1554(NH_2), 897(C–Cl). ^{1}H NMR (DMSO-d_6): δ 9.96(s, 1H, C–OH), 2.76 (d, J = 4.3 Hz, 1H, CH), 2.29 (s, 3H, CH_3), 4.30(dd, J = 5.2 Hz, 1H, –CH–), 7.21–7.39 (dd, 4H, Phenyl ring), 2.31 (s, J = 2.1 Hz, 1H, NH), 6.73 (s, J = 1.6 Hz, 1H,