Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2015, 7(2):112-116
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis and antimicrobial activity of novel 1-thiocarbamoyl-2-pyrazoline derivatives

N. Rama Rao[1], M. V. Basaveswara Rao[2] and K. Lakshmi[1]*

[1]*Chalapathi Institute of Pharmaceutical Sciences, Guntur (A.P.) India*
[2]*Krishna University, Dr. MRAR PG Centre, Nuzvid (A.P.) India*

ABSTRACT

To the continuation of our research work in the present study, eighteen novel quinazolinonyl-1- thiocarbamoyl-2-pyrazolines (3a-r) were synthesized from the cyclization of different thioxoquinazolinonyl chalcones with thiosemicarbazide. The structures of the newly synthesized compounds were confirmed by IR, ^{1}H NMR and Mass spectroscopic analysis and all were tested for their antimicrobial potential. Most of the synthesized compounds showed significant antimicrobial activities when compared to control and standard drugs.

Keywords: 2-Thioxo-4(3*H*) quinazolinones, 1-Thiocarbamoyl-2-pyrazolines, Ciprofloxacin, Fluconazole and Antimicrobial.

INTRODUCTION

Pyrazole and triazole compounds can provide privileged scaffolds for generation of drug like compounds to drug discovery. COX-II inhibitor Celecoxib success in the year 1997 in the treatment of rheumatoid arthritis and osteoarthritis pointed out the importance of azoles in drug discovery [1]. Pyrazoles are five membered heterocycles with two nitrogens. 2-Pyrazolines are widely studied by medicinal chemists and are considered as cyclic hydrazine moiety [2]. Pyrazoline derivatives possess variety of biological action such as antimicrobial, anti- mycobacterial, anti-depressant, analgesic, anti-inflammatory, insecticidal and herbicidal activities [3-8]. Besides pyrazolines thioxoquinazolinones are another important nitrogenous heterocycles with broad spectrum of biological activities [9-15]. In the light of above observations the present study focuses on the synthesis of novel 1-thiocarbamoyl-2-pyrazoline derivatives bearing thioxo quinazolinone ring. First thioxo quinazolinonyl chalcones were synthesized and then they were cyclized with thiosemicarbazide to synthesize novel 1-thiocarbamoyl-2-pyrazoline derivatives. The titled compounds after spectral characterization were subjected for anti microbial screenings.

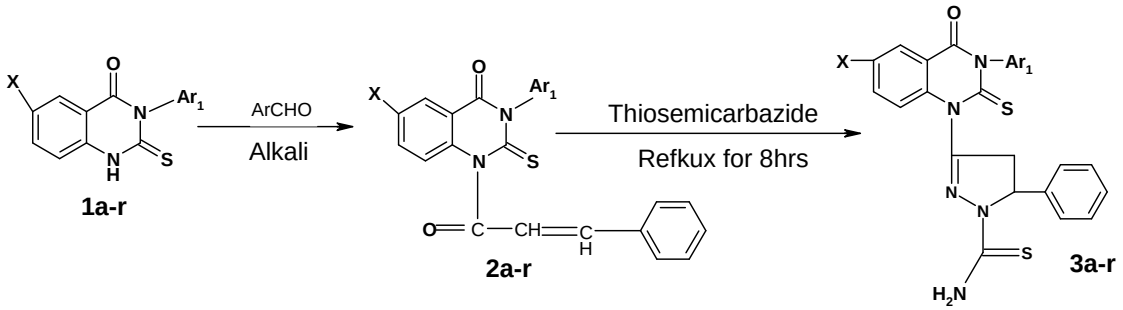
MATERIALS AND METHODS

Melting points of the synthesized compounds were determined by an open-end capillary tube method by electrically heated melting point apparatus. The respective values were expressed in $^{\circ}$C and were uncorrected. Reaction progress and compounds purity was ascertained by Thin Layer Chromatography (TLC). The % elemental analysis data of synthesized compounds obtained from Carlo Erba-1108 elemental analyzer has been found to be in agreement with the molecular formula of the assigned structures. Functional group analysis of all the synthesized compounds was obtained by Fourier Transformer-Infrared Spectrophotometer (Perkin Elmer 1600 series) using KBr-Pellet method. The proton NMR and molecular mass data was obtained by ^{1}H FT-NMR (BRUCKER MX 400 MHz) spectrophotometer analysis using TMS as internal standard and Liquid Chromatography- Mass Spectrophotometer (Agilent 1100 series).

General procedure:

Synthesis of 1-thiocarbamoyl-2-pyrazoline derivatives 3a-r:

Thioxoquinazolinones 1a-r, thioxoquinazolinonyl chalcones 2a-r were synthesized according to the literature method [16]. To a solution of 0.01 moles of quinazolinonylchalcone and 0.01 moles of thiosemicarbazide in 25 ml of ethanol, 5 ml of 0.02 molar NaOH solution was added and has been refluxed for 8 hrs. The mixture was allowed to cool and was poured into crushed ice. The solid thus obtained was filtered, washed with water and recrystallized from absolute ethanol. The synthetic scheme was given in Scheme 1.



Ar_1 = Phenyl, *p*-Chlorophenyl, *p*-Bromophenyl, *m*-Chlorophenyl, *p*-Fluorophenyl, *p*-tolyl

x = H, Br and I

Scheme-1: Synthesis of 1-thiocarbamoyl-2-pyrazoline derivatives

Antimicrobial activities:

All the eighteen synthesized compounds 3a-r were screened for their *in vitro* antibacterial potential against two non-pathogenic and four pathogenic bacteria. The synthesized compounds were also tested for their antifungal activity against five organisms using disc diffusion method [17]. The zone of inhibition was measured in mm after incubation using digital antibiotic zone reader. The activity of the synthesized compounds was compared with standard drug Ciprofloxacin and Fluconazole. The antibacterial and antifungal data was given in Table 1.

Spectral characterization of synthesized compounds:

1-Thiocarbamoyl-5-phenyl-3-[3'-phenyl-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3a, brown solid, m.p. 164-66 °C, yield 72.0%; IR (cm^{-1}): 693.93 (C^5-H), 1022.67 (C^5-N), 1446.24 (C^4-H), 1565.48 (C=N), 3237.85 (N-H), 1226.93 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.01 (1H, dd, HA), 3.24 (1H, dd, HB), 3.86 (1H, dd, HX), 8.16 (2H, s, $-NH_2$), 6.82-7.43 (14H, m, Ar-H); MS (m/z): 457(M^+). Anal calcd for: ($C_{24}H_{19}N_5S_2O$) C: 62.99, H: 4.15, N: 15.31; found: C: 62.98, H: 4.14, N: 15.32.

1-Thiocarbamoyl-5-phenyl-3-[3'-(4"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]- 2-pyrazoline. 3b, brown solid, m.p. 100-02 °C, yield 73.5%; IR (cm^{-1}): 696.60 (C^5-H), 1092.62 (C^5-N), 1449.24 (C^4-H), 1534.82 (C=N), 3228.66 (N-H), 1259.53 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.12 (1H, dd, HA), 3.38 (1H, dd, HB), 3.75 (1H, dd, HX), 8.28 (2H, s, $-NH_2$), 6.88-7.45 (13H, m, Ar-H). MS (m/z): 492(M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OCl$) C: 58.53, H: 3.66, N: 14.23; found: C: 58.46, H: 3.65, N: 14.20.

1-Thiocarbamoyl-5-phenyl-3-[3'-(4"-bromophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3c, cream color solid, m.p. 190-92 °C, yield 61.6%; IR (cm^{-1}): 691.53 (C^5-H), 1008.10 (C^5-N), 1483.67 (C^4-H), 1539.70 (C=N), 3294.78 (N-H), 1254.01 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.08 (1H, dd, HA), 3.36 (1H, dd, HB), 3.86 (1H, dd, HX), 8.71 (2H, s, $-NH_2$), 6.78-8.53 (13H, m, Ar-H). MS (m/z): 536(M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OBr$) C: 53.72, H: 3.36, N: 13.06; found: C: 53.71, H: 3.37, N: 13.01.

1-Thiocarbamoyl-5-phenyl-3-[3'-(3"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3d, dark brown solid**,** m.p. 180-82 °C, yield 64.7%; IR (cm^{-1}): 694.54 (C^5-H), 1109.32 (C^5-N), 1456.82 (C^4-H), 1551.63 (C=N), 3247.54 (N-H), 1263.12 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 2.98 (1H, dd, HA), 3.25 (1H, dd, HB), 3.96 (1H, dd, HX), 8.43 (2H, s, $-NH_2$), 6.59-7.56 (13H, m, Ar-H). MS (m/z): 492 (M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OCl$) C: 58.53, H: 3.66, N: 14.23; found: C: 58.54, H: 3.62, N: 14.23.

1-Thiocarbamoyl-5-phenyl-3-[3'-(4"-fluorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3e, cream color solid, m.p. 114-16 °C, yield 76.7%; IR (cm^{-1}): 686.39 (C^5-H), 1051.16 (C^5-N), 1461.56 (C^4-H), 1509.59 (C=N), 3211.01 (N-H), 1216.64 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ=3.06 (1H, dd, HA), 3.42 (1H, dd, HB), 3.99 (1H, dd, HX), 8.46 (2H, s, $-NH_2$), 6.86-8.53 (13H, m, Ar-H). MS (m/z): 475 (M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OF$) C: 60.62, H: 3.79, N: 14.73; found: C: 60.59, H: 3.75, N: 14.72.

1-Thiocarbamoyl-5-phenyl-3-[3'-(4"-tolyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3f, orange color solid, m.p. 102-04 °C, yield 65.6%; IR (cm^{-1}): 688.07 (C^5-H), 1056.15 (C^5-N), 1443.92 (C^4-H), 1561.30 (C=N), 2978.60 (N-H), 1251.97 (C=S); ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ=3.01 (1H, dd, HA), 3.31 (1H, dd, HB), 4.80 (1H, dd, HX), 8.61 (2H, s, $-NH_2$), 6.90-7.85 (13H, m, Ar-H), 2.28 (3H, s, $-CH_3$). MS (m/z): 471 (M^+). Anal calcd for: ($C_{25}H_{21}N_5S_2O$) C: 63.67, H: 4.46, N: 14.85; found: C: 63.68, H: 4.41, N: 14.73.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-phenyl-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3g, black solid, m.p. 242-44 °C, yield 73.5%; IR (cm^{-1}): 688.93 (C^5-H), 1062.54 (C^5-N), 1409.40 (C^4-H), 1526.45 (C=N), 2979.04 (N-H), 1232.94 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.00 (1H, dd, HA), 3.46 (1H, dd, HB), 3.84 (1H, dd, HX), 8.39 (2H, s, $-NH_2$), 6.56-7.91 (13H, m, Ar-H). MS (m/z): 536 (M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OBr$) C: 53.72, H: 3.36, N: 13.06; found: C: 53.69, H: 3.32, N: 13.01.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-(4"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3h, brick red solid, m.p. 254-56 °C, yield 69.2%; IR (cm^{-1}): 701.72 (C^5-H), 1078.93 (C^5-N), 1448.91 (C^4-H), 1533.79 (C=N), 3185.70 (N-H), 1308.89 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 2.78 (1H, dd, HA), 3.32 (1H, dd, HB), 3.95 (1H, dd, HX), 8.46 (2H, s, $-NH_2$), 6.54-7.83 (12H, m, Ar-H). MS (m/z): 570 (M^+). Anal calcd for: ($C_{24}H_{17}N_5S_2OBrCl$) C: 50.48, H: 2.98, N: 12.27; found: C: 50.41, H: 2.97, N: 12.26.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-(4"-bromophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3i, brown solid, m.p. 190-92 °C, yield 63.6%; IR (cm^{-1}): 697.01 (C^5-H), 1084.23 (C^5-N), 1429.21 (C^4-H), 1542.95 (C=N), 3395.09 (N-H), 1296.64 (C=S), ; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 2.86 (1H, dd, HA), 3.14 (1H, dd, HB), 4.18 (1H, dd, HX), 8.83 (2H, s, $-NH_2$), 6.51-8.66 (12H, m, Ar-H).MS (m/z): 615 (M^+). Anal calcd for: $C_{24}H_{17}N_5S_2OBr_2$) C: 46.83, H: 2.76, N: 11.38; found: C: 46.81, H: 2.75, N: 11.36.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-(3"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3j, brown solid, m.p. 176-78 °C, yield 70.4%; IR (cm^{-1}): 681.80 (C^5-H), 1070.71 (C^5-N), 1449.78 (C^4-H), 1555.49 (C=N), 3394.82 (N-H), 1246.63 (C=S), ; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 2.84 (1H, dd, HA), 3.02 (1H, dd, HB), 4.00 (1H, dd, HX), 8.16 (2H, s, $-NH_2$), 6.16-7.37 (12H, m, Ar-H). MS (m/z): 570 (M^+). Anal calcd for: ($C_{24}H_{17}N_5S_2OBrCl$) C: 50.48, H: 2.98, N: 12.27; found: C: 50.45, H: 2.91, N: 12.22.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-(4"-fluorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3k, brown solid, m.p. 110-12 °C, yield 68.6%; IR (cm^{-1}): 720.56 (C^5-H), 1057.29 (C^5-N), 1456.26 (C^4-H), 1506.48 (C=N), 3394.65 (N-H), 1219.75 (C=S), ; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 2.88 (1H, dd, HA), 3.14 (1H, dd, HB), 3.86 (1H, dd, HX), 8.75 (2H, s, $-NH_2$), 6.56-8.16 (12H, m, Ar-H). MS (m/z): 554 (M^+). Anal calcd for: ($C_{24}H_{17}N_5S_2OBrF$) C: 51.98, H: 3.07, N: 12.63; found: C: 51.96, H: 3.01, N: 12.63.

1-Thiocarbamoyl-5-phenyl-3-[6'-bromo-3'-(4"-tolyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3l, light orange solid, m.p. 183-85 °C, yield 66.2%; IR (cm^{-1}): 685.40 (C^5-H), 1054.93 (C^5-N), 1444.51 (C^4-H), 1558.54 (C=N), 3305.01 (N-H), 1251.20 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.00 (1H, dd, HA), 3.38 (1H, dd, HB), 3.94 (1H, dd, HX), 8.37 (2H, s, $-NH_2$), 6.64-7.86 (12H, m, Ar-H), 2.28 (3H, s, $-CH_3$). MS (m/z): 555 (M^+). Anal calcd for: ($C_{25}H_{20}N_5S_2OBr$) C: 54.54, H: 3.63, N: 12.73; found: C: 54.52, H: 3.65, N: 12.69.

1-Thiocarbamoyl-5-phenyl-3-[6'-iodo-3'-phenyl-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3m, grey color solid, m.p. 280-82 °C, yield 59.8%; IR (cm^{-1}): 692.66 (C^5-H), 1067.45 (C^5-N), 1384.75 (C^4-H), 1516.13 (C=N), 3241.85 (N-H), 1214.40 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.06 (1H, dd, HA), 3.27 (1H, dd, HB), 4.03 (1H, dd, HX), 8.49 (2H, s, $-NH_2$), 6.56-7.95 (13H, m, Ar-H). MS (m/z): 583 (M^+). Anal calcd for: ($C_{24}H_{18}N_5S_2OI$) C: 49.39, H: 3.03, N: 12.00; found: C: 49.37, H: 3.02, N: 12.00.

1-Thiocarbamoyl-5-phenyl-3-[6'-iodo-3'-(4"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3n, green solid, m.p. 176-78 °C, yield 60.2%; IR (cm^{-1}): 700.76 (C^5-H), 1067.36 (C^5-N), 1386.11 (C^4-H), 1516.13 (C=N), 3394.26 (N-H), 1218.83 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.06 (1H, dd, HA), 3.18 (1H, dd, HB), 3.92 (1H, dd, HX), 8.46 (2H, s, $-NH_2$), 6.28-7.98 (12H, m, Ar-H); MS (m/z): 583 (M^+). Anal calcd for: ($C_{24}H_{17}N_5S_2OICl$) C: 46.64, H: 2.75, N: 11.34; found: C: 46.62, H: 2.70, N: 11.31.

1-Thiocarbamoyl-5-phenyl-3-[6'-iodo-3'-(4"-bromophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3o, Light green solid, m.p. 170-72 °C, yield 68.7%; IR (cm^{-1}): 709.92 (C^5-H), 1067.42 (C^5-N), 1386.89 (C^4-H), 1517 (C=N), 3239.62 (N-H), 1214.29 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.04 (1H, dd, HA), 3.16 (1H, dd, HB), 3.92 (1H, dd, HX), 8.43 (2H, s, $-NH_2$), 6.52-8.66 (12H, m, Ar-H). MS (m/z): 662 (M^+). Anal calcd for: ($C_{24}H_{17}N_5S_2OI$) C: 43.50, H: 2.57, N: 10.57; found: C: 43.50, H: 2.51, N: 10.54.

1-Thiocarbamoyl-5-phenyl-3-[6'-iodo-3'-(3"-chlorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline 3p, black solid, m.p. 168-70 °C, yield 58.4%; IR (cm^{-1}): 707.33 (C^5-H), 1075.71 (C^5-N), 1483.85 (C^4-H), 1520.39 (C=N), 2978.63 (N-H), 1209.10 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.01 (1H, dd, HA), 3.34 (1H, dd, HB), 3.85 (1H, dd, HX), 8.38 (2H, s, $-NH_2$), 6.39-7.92 (12H, m, Ar-H); MS (m/z): 617 (M^+). Anal calcd for: ($C_{24}H_{17}N_5OS_2ICl$) C: 46.64, H: 2.75, N: 11.34; found: C: 46.63, H: 2.74, N: 11.32.

1-Thiocarbamoyl-5-phenyl-3-[6'-iodo-3'-(4"-fluorophenyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3q, green solid, m.p.104-06 °C, yield 80.1% ; IR (cm^{-1}): 699.68 (C^5-H), 1056.80 (C^5-N), 1404.40 (C^4-H), 1504.39 (C=N), 3394.61 (N-H), 1215.02 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.01 (1H, dd, HA), 3.36 (1H, dd, HB), 3.75 (1H, dd, HX), 8.43 (2H, s, $-NH_2$), 6.18-8.52 (12H, m, Ar-H). MS (m/z): (M^+). Anal calcd for: ($C_{24}H_{17}N_5OS_2IF$) C: 47.92, H: 2.83, N: 11.65; found: C: 47.89, H: 2.80, N: 11.64.

1-Thiocarbamoyl -5-phenyl-3-[6'-iodo-3'-(4"-tolyl)-2'-thioxo-4'(3'*H*)-quinazolinon-1'-yl]-2-pyrazoline. 3r, green solid, m.p. 112-14 °C, yield 78.5% ; IR (cm^{-1}): 707.81 (C^5-H), 1060.61 (C^5-N), 1387.71 (C^4-H), 1511.72 (C=N), 3227.41 (N-H), 1219.97 (C=S),; ^{1}H-NMR (400 MHz, DMSO-d6, TMS) δ= 3.16 (1H, dd, HA), 3.38 (1H, dd, HB), 3.76 (1H, dd, HX), 8.51 (2H, s, $-NH_2$), 6.49-8.00 (12H, m, Ar-H), 2.31 (3H, s, $-CH_3$). MS (m/z): 597 (M^+). Anal calcd for: ($C_{25}H_{20}N_5OS_2I$) C: 50.24, H: 3.35, N: 11.72; found: C: 50.06, H: 3.29, N: 11.59.

RESULTS AND DISCUSSION

5-Phenyl-3-[3'-(un) substituted phenyl-6'-(un) substituted-2'-thioxo-4' (3'*H*)-quinazolinon-1'-yl]-1-thiocarbamoyl-2-pyrazolines 3a-r were prepared by refluxing 3-phenyl-1-[3'-(un) substituted phenyl-6-'(un) substituted-2'-thioxo- 4' (3'*H*)-quinazolinon-1'-yl]-2-propen-1-one(s) with thiosemicarbazide in the presence of sodium hydroxide. Disappearance of peak corresponds to α, β-unsaturated keto functional group of chalcones at 1670 cm^{-1} and appearance of peaks at 709.92 cm^{-1}, 1067.42 cm^{-1}, 1386.89 cm^{-1}, 1517 cm^{-1} and 3239.62 cm^{-1} confirmed the 1-thiocarbamoyl-2-pyrazoline nucleus. Appearance of singlet at δ 8.46 ppm indicated the two protons of thiocarbamoyl group (NH_2-C=S) at 1st position of 1-thiocarbamoyl-2-pyrazoline ring [18].

Table-1: Antimicrobial data of the synthesized compounds

Comp. Code	Activity against bacterial strains						Activity against fungal strains				
	B. s	***B. c***	***S. a***	***S. e***	***P. a***	***E. c***	***C. g***	***C. a***	***A. n***	***A. f***	***S. c***
3a	+	+++	++	++	+	++	+++	++	x	x	++
3b	+++	+++	++++	+++	+++	++	++	++	++	++	++
3c	++	+++	+	++	++	++	++	++	++	++	++
3d	+++	++	++	+++	+++	+++	++	+	x	+++	x
3e	+++	++	+++	++	+++	++	+++	++	+++	++	+++
3f	+++	++	+++	+++	+++	+++	+++	++	++	++	++
3g	++	+++	+++	+++	+++	+++	++	++	++	+++	+
3h	+++	++++	+++	+++	++	+++	++	+++	++++	++++	+++
3i	+++	+++	+++	++	++++	+++	++++	++	++	++++	++
3j	++++	++++	+++	+++	+++	+++	++++	++	x	x	x
3k	++++	++++	+++	++	+++	++	++++	++++	++	++++	+++
3l	+++	++++	+++	+++	+++	++	++++	+++	+++	++++	+++
3m	+++	+++	++	+++	+++	+++	+++	++	+++	++	+
3n	++++	+++	++++	+++	+++	++	++	++	++++	++++	++
3o	x	+++	x	++	x	++	+++	+++	x	++	x
3p	++++	++++	+++	++	+++	+++	++	+	x	x	x
3q	++++	x	x	x	x	x	+++	+++	++	+++	++
3r	++	++++	x	x	x	x	++	++	x	x	+
Cipro.	++++	++++	++++	++++	++++	++++	-	-	-	-	-
Flu.	-	-	-	-	-	-	++++	++++	++++	++++	++++

Note: *1) B.s: Bacillus subtilis, B.c: Bacillus cereus, S.a: Staphylococcus aureus, S.e: Staphylococcus epidermidis, P.s: Pseudomonas aeruginosa, E.c: Escherichia coli*

2) C.g: Candida glabrata, C.a: Candida albicans, A.n: Aspergillus niger, A.f: Aspergillus foetidus, S.c: Saccharomyces cerevisiae

3) Antibacterial data of all the synthesized compounds were divided into four sensitive types on the basis of their zone of inhibitions (mm); <7 mm are less active, between 8-10 mm are weakly active, between 11-13 mm are moderately active, >14 mm are highly active

4) Antifungal data of all synthesized compounds were divided into various sensitive types on the basis of their zone of inhibitions (mm); <8 mm are less active, between 9-12 mm are weakly active, between 13-16 mm are moderately active, >17 mm are highly active

5) x indicates no zone of inhibition

Antimicrobial activity:

All synthesized compounds shown moderate antimicrobial activity against selected microorganisms. Compound 3l was more active than standard Ciprofloxacin on *B. cereus*, and was moderately active against all microorganisms. Compounds 3n, 3h and 3l were the most potent compounds and exhibited highest inhibition zone against *A. niger* while compounds 3h, 3i and 3n were the most potent compounds against *A. foetidus.* Compounds 3h and 3k were

the most potent compounds and exhibited highest zone against *S. cerevisiae* while compound 3k was the most potent compound against *C. glabrata*.

CONCLUSION

Eighteen novel1-thiocarbamoyl-2-pyrazoline derivatives with quinazolinone ring were synthesized by cyclization of substituted thioxoquinazolinonyl chalcones with thiosemicarbazide. It is one of the easiest ways for synthesizing 1-thiocarbamoyl-2-pyrazolines with good yields. All synthesized compounds were subjected for *in vitro* antimicrobial activity. Compounds 3h, 3k and 3l showed potent antimicrobial activity among all synthesized compounds against tested bacterial and fungal strains.

Acknowledgments
Author is very much thankful to management and principal of Chalapathi Institute of Pharmaceutical Sciences for providing the necessary research facilities.

REFERENCES

[1] M.M. Mohy El-Din, A.M. Senbel, A.A. Bistawroos, A. El-Mallah, N.A. Nour El-Din, A.A. Bekhit, H.A. Abd El Razik, *Basic Clin. Pharmacol. Toxicol*., **2011,** 108(4), 263-73.
[2] Md. Azizur Rahman, A.A. Siddiqui**.** *Int. J. Pharm. Sci. Drug Res.*, **2010,** 2(3), 165-175.
[3] K. Mogilaiah, B. Sakram, *Indian J. Heterocycl. Chem.*, **2004,** 13(4), 289-92.
[4] A. Ozdemir, Z.T. Gulhan, Z.A. Kaplancikli, *Turk. J. Chem.*, **2008**, 32(5), 529-38.
[5] Y.R. Prasad, A.L. Rao, L. Prasoona, K. Murali, P.R. Kumar, *Bioorg. Med. Chem. Lett.*, **2005,** 15(22), 5030-34.
[6] M. Amir, H. Kumar, S.A. Khan, *Bioorg. Med. Chem. Lett.*, **2008**, 18(3), 918-22.
[7] I.G. Rathish, K. Javed, S. Ahmad, S. Bano, M.S. Alam, K.K. Pillai, S. Singh, V. Bagchi, *Bioorg. Med. Chem. Lett.*, **2009**, 19(1), 255-58.
[8] K.S. Silver, D.M. Soderlund, *Pestic. Biochem. Phys.*, **2005**, 81(2), 136-43.
[9] R. Subramaniam, G. Rao, *J. Comput. Meth. Mol. Des.*, **2013**, 3(3), 1-9.
[10] V. Alagarsamy, K. Kavitha, M.P. Kumar, V.R. Solomon, J. Kumar, D.S. Kumar, *Acta Pharma.*, **2009**, 59(1)**,** 97-106.
[11] R.S. Kombu, R.P. Mailavaram, H. Devalapally, P.M. Chinnappa, R.K. Devarakonda, R. R.R. Akkinepally, *Open Med. Chem. J.*, **2007**, 2, 101-11.
[12] Y. Wang, N. Serradell, E. Rosa, R. Castaner, *Drugs Future*, **2008**, 33(6), 473-77.
[13] A. Tiwari, *Curr. Opin. Invest. Drugs*, **2009,** 10(10), 1091-104.
[14] H.J. Hess, T.H. Cronin, Scriabine, *J. Med. Chem.*, **1968,** 11(1), 130-36.
[15] Y. Govindaraj, Sathyamoorthy, V. Karthikeyan, M. Vijayalakshmi, V. Agrahari, S. Gupta, R.K. Nema, *Academic J. Cancer Res.*, **2009,** 2(2), 73-7.
[16] K. Lakshmi, N. Rama Rao and M.V. Basaveswara Rao, *Rasayan J. Chem.*, **2014**, 7(1), 44-54.
[17] B.A. Forbes, D.F. Sahm, S.A. Weisseld, E.A. Trevino: Bailey and Scotts's Diagnostic Microbiology, Mosby Co., St. Louis Missouri, pp. 171 (**1990**).
[18] Z.H. Ismaeil, F.M.A. Soliman, S.H. Abd-El Monem, *J Am. Sci.*, **2011,** 7(10), 756-767.