www.sphinxsai.com

International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.3, pp 1413-1425, July-Sept 2010

Synthesis, Charecterization, and Biological Activities of some New Pyrazoline Derivatives, derived from Ethyl-2-(2, 5-dichloroanilido) Acetohydrazide

Raj Narayan Sharma[1]*, K.P. Sharma[2], S.N. Dixit[3]

[1]Department of Chemistry, NRI College of Engineering and Management, Gwalior, M.P., India.

[2,3]Department of Chemistry, SMS Govt. Model Science College, Gwalior – 474002, M.P., India.

Corres.author : rajnarayan1974@gmail.com

Abstract: A series of new 1-[(2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl-N-2, 5-dichloroanilino)-5- phenyl pyrazoline have been synthesized in 51 to 78% yield, by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2,5-dichloroaniline with Ethyl-2-(2, 5-dichloroanilido) acetohydrazide. Pyrazolines are yellow, cream and brown color solids, having high melting points. Identity of these products has been established by elemental analysis and spectral data. Newly synthesized compounds (6a-t) have been tested for their antibacterial activity against gram positive bacteria S. albus , S. aureus and gram negative bacteria E. Coli and Pseudomonas poisonous .The compound (**6a, 6b, 6c, 6f, 6g, 6j, 6m, and 6r**) shown significant activity and the compound (6i, 6k, 6l, 6p, 6t,) have shown moderate activity. The same compounds were tested for their antifungal activity against Candida albicans, Aspergillus Niger and Alternaria alternata at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (**6c, 6j, 6m, and 6r**) shown significant activities and compound (6a, 6b, 6f, and 6g) were found to be moderately active against Candida albicans and Aspergillus Niger. All the other compounds did not show significant activity against the fungi at the concentration used. Some new compounds have been tested for antitubercular activity in-vitro using Mycobacterium tuberculosis**.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with Mycobacterium tuberculosis**,** $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (**6a, 6b, 6c, 6f, 6g, 6j, and 6m**) inhibited the growth of Mycobacterium tuberculosis at 100mg/mL concentration other compounds were found to be inactive.

Keywords: 5-phenyl Pyrazoline, Synthesis, Characterization, and Biological Activities.

Introduction

Considerable attention has been focused on Pyrazolines and substituted Pyrazolines due to their interesting biological activities. They have found to possess anti-fungal[1], anti-depressant [2-7], anti-convulsant [8], anti-inflammatory [9-12], anti-bacterial [13-14], anti-cancer[15-16], anti-oxidant [17-18], anti-pyretic[19], anti-neoplastic activities [20-21], anti-viral [22], anti-amoebic [23-24], Acaricidal agro chemical fungicides or insecticides [25], anti-cholinergic [26-27], anti-diabetic [28], anti-HIV [29-32], anti-malarial [33], Anesthetic [34], Anaxiolytic [35], anti-parasitic[36], anti-allergic[37], anti-microbial [38-40], anti-tuberculosis[41-44],Tyrosinase inhibitor [45], Blue photo luminescence and electro luminescence

[46], Food and chemical toxicology [47], Herbicidal [48-50], Hypoglycemic [51], Hypotensive [52], immuno suppressive [53], anti-tumor[54-55]. Moreover, many selectively chloro-substituted organic compounds show peculiar pharmacological and agrochemical properties. The work reported herein was aimed at the preparation of some new pyrazoline derivatives with anticipated biological activities.

EXPERIMENTAL

General

All chemicals were used of A.R. grade (either of B.D.H. or Excel-R or Extra pure E. Merck quality). The structures of the compounds were determined by elemental analysis, IR and NMR spectral data. All melting points were measured on an electro thermal melting point apparatus and are uncorrected. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3-300 or a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^{1}H –NMR (200 MHz) and ^{13}C-NMR (50 MHz) spectra were recorded in DMSO-d_6 on a Varian Mercury VX 200 NMR using TMS as the internal reference. Mass spectra were measured on a GCMS-QP 1000 EX spectrophotometer at 70 eV. Purity of the compounds is checked on T.L.C. using Silica Gel-G. Elemental analysis is performed on Carlo-Erba1108 analyzer

Synthesis of Ethyl-2-[2, 5-dichloroanilido] Ethanoate [1]:

A mixture of 2, 5-dichloroaniline (10ml) and diethylmalonate (20ml) was refluxed for forty five minutes in a round bottomed flask fitted with an air condenser of such a length (14") that ethanol formed escaped and diethylmalonate flowed back into the flask. Contents were cooled, ethanol (30 ml) was added, when malon-2, 5-dichlorodianilide separated out. It was filtered under suction. The filtrate was poured on to crushed ice (Ca160g) and stirred when ethyl-2-(2, 5-dichloroanilido) ethanoate precipitated as green mass. On recrystallization from aqueous ethanol (50%), ester was obtained as white crystals. Yield; 82%, M.P. 90^0C, M.W. 276.Anal. calculation for C_{11} H_{11} N_1 O_3 Cl_2 : Found ; C 39.20, O 14.25, N 4.14, Cl 21.09, Calcd. C 39.21, O 14.26, N 04.15 IR [KBr] V_{max} cm^{-1} : 1665-1660 [C=O diketone], 1290 [-C-O- Ester], 765-760 [2,5- di substituted benzene], 1260 [C-Cl Stretching], 1590, 1520 , 1440 [C=C Ring stretching], 3150 [N-H Stretching], 3040 [C-H aromatic], 1330-1322[C-H Stretching]. PMR (DMSO): δ 4.42 (2H, s, CO-CH_2-CO), 4.0 (2H, s, NH_2), 7.4-8.6 (3H, m, Ar-H), 9.2 (1H, s, CO-NH D_2O exchangeable), 10.6 [1 H, s, Ar-NH D_2O exchangeable].

Synthesis of Ethyl-2-(2, 5- dichloroanilido) acetohydrazide [2]:

Ethyl-2-(2, 5-dichloroanilido) ethanoate (9.54 gm; 0.03 mol), ethanol (10 ml) and hydrazine hydrate (15 ml; 80%) were mixed together and stirred for thirty five minutes. Ethyl-2-(2, 5-dichloroanilido) acetohydrazide was filtered under suction and recrystallised from ethanol in white crystals. Yield; 78%, MP = 172°C, MW 262: Analytical calculation for C_9 H_9 N_3 O_2 Cl_2 : Calculated ; N 09.02 ,C 41.32, O 10.33, Cl 15.28, Found; N 09.01, C 41.30, O 10.31, Cl 15.27 IR [KBr] V_{max} cm^{-1}**:** 3160 [N-H Stretching], 3048 [C-H aromatic], 1670 [C=O diketone], 1440 [C-Cl aromatic], 1595, 1520, 1445 [C=C ring stretching]. NMR Spectra (δ DMSO): 2.44 (2H, s, CH_2), 3.2 (3H, s, CH_3), 4.22-4.32 (1H, t, N-H), 7.2-7.6 (3H, m, ArH).

Mono Cyanoethylation of 2, 5-dichloroaniline [3]:

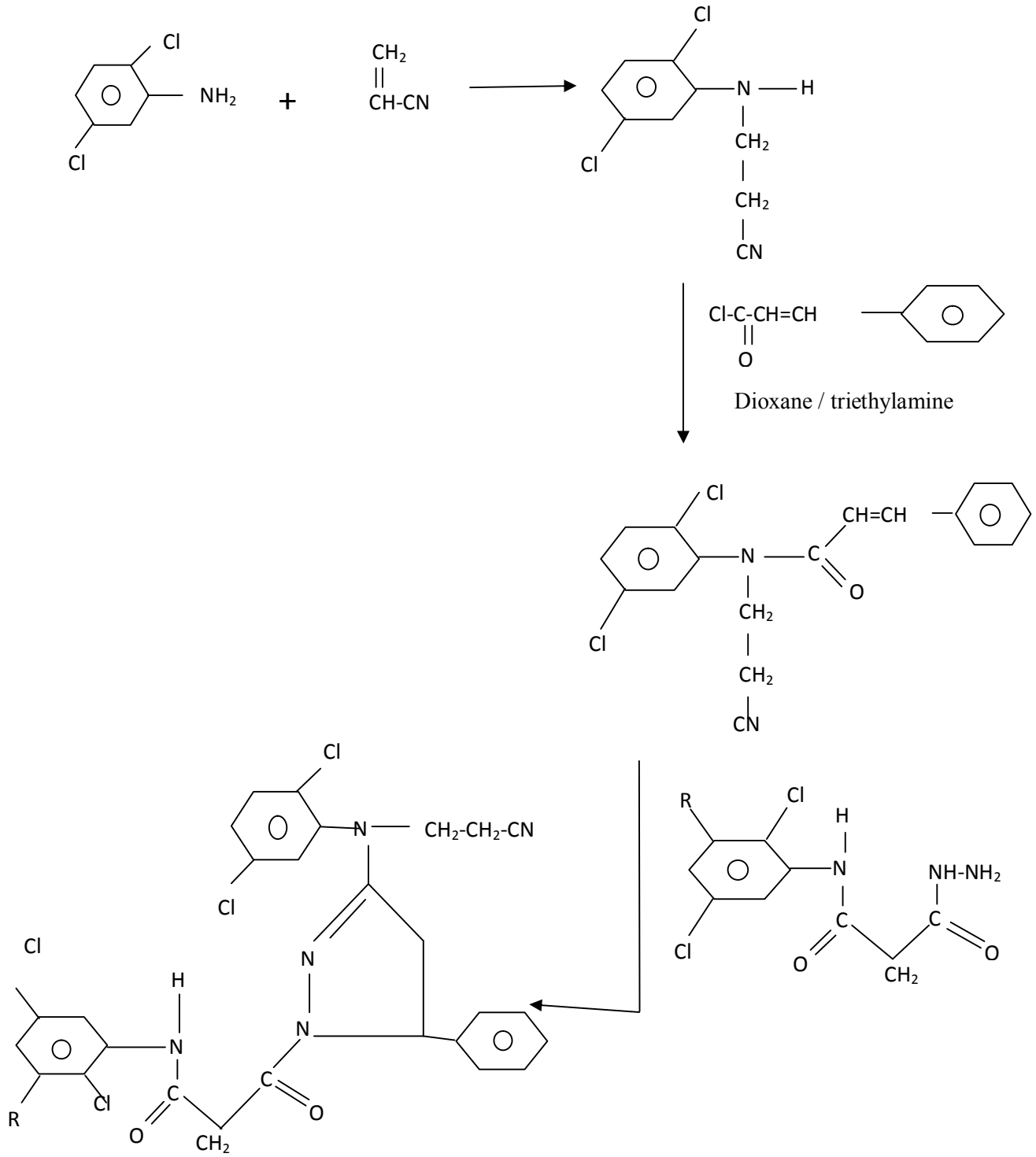
A 250 ml three necked flask equipped with a stirrer, reflux condenser and thermometer was charged with 2, 5-dichloro aniline (0.1mol, 16.2g), acrylonitrile (0.1mol, 10.6 g) and Cupric acetate monohydrate (1.02g, 4% by weight of the amine). The mixture was stirred and refluxed on boiling water bath for three hours. The dark mixture was then transferred to a 250 ml distilling flask fitted with a 15.2 cm modified vigorous column and the unchanged acrylonitrile was first collect at 100 mm (water pump). The distillation was continued and the unchanged 2, 5-dichloro aniline B.P. 254^0C/0.5mm was recovered. The N-Cyanoethyl-2, 5-dichloroaniline was obtained as light yellow colored viscous liquid at 177-178^0C/mm which solidified after keeping overnight. Yield: 15.7g (95%)., M.P. 84^0C

Preparation of Cinnamoyl Chloride [4]:

Cinnamic acid (10 g, 0.067mol) and thionyl Chloride (12.0 ml) were taken in a round bottomed flask fitted with a reflux condenser carrying a calcium chloride guard tube. The contents were refluxed on a water bath for two and half hours in a fume cupboard until the evolution of HCl gas ceased from the guard tube. After cooling liquid was carefully transferred to a Claisen flask and distilled under reduced pressure when unreacted thionyl chloride distilled over first. Cinnamoyl chloride was collected at 165-166^0C/ 18-20mm pressure.

SCHEME-I

(The reaction scheme for the complete synthesis of compounds)



Some characteristics of the synthesized compounds are shown in table-I. Analytical and spectral data (U.V., I.R., ^{1}H –NMR, FAB^{+}-MS) confirmed the structures of the new compounds.

Synthesis of N-Cinnamoyl –N-2'-Cyanoethyl -2, 5-dichloroaniline [5]:

Solution of cinnamoyl chloride (3.5 g, 0.02 mol), dioxane (2ml), N-2'-cyanoethyl -2, 5-dichloro aniline (7.90g, 0.02 mol) and triethylamine (2.1 g) were placed in a round bottomed flask having a Liebig condenser carrying calcium chloride guard tube. The contents were heated for two hours on a boiling water bath. On keeping over night triethylamine hydrochloride separated as solid. It was filtered and contents concentrated when crystals separated out. Two crystallization from ethanol gave shining white needles. Yield: 58 %, M.P.: 160^0C, Anal. Calculated for C_{18} H_{14} Cl_2 N_2 O; M.W. 345; N: 4.5, Cl: 11.3 ; found N: 4.3 , Cl : 11.2 % , IR[KBr] V_{max} Cm^{-1} : 3280-3060 (C-H stretching , aromatic), 2960 and 2890 (C-H Stretching, aliphatic (asymmetric) and C-H stretching , aliphatic (symmetric), 2230(C-N stretching), 1660(C=C stretching , benzene ring), 1650 C=O (stretching, tertiary amide), 1620, 1580, 1460, (C=C ring stretching), 1060, 760, (2, 5-disubstituted benzene).

Synthesis of 1-(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6]:

A mixture of N-cinnamoyl-N-2'-cyanoethyl -2, 5-dichloroaniline (0.345 g; 0.001 mol), Ethyl-2-(2, 5-dichloroanilido) acetohydrazide (0.262g; 0.001 mol), dioxane (3 ml), and glacial acetic acid (2 drops) was refluxed for five hours. The solid which separated during the course of heating was filtered under suction and purified by washing thrice with hot ethanol, when the pyrazoline was obtained as yellow needles. Yield: 68%, M.P.: 255^0C, M.W.: 589, Anal. Calculated for C_{27} H_{21} Cl_4 N_5 O_2 Cl: 15.9; N: 7.8, found Cl: 15.7, N: 7.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 212.2 (4.92), 318.6 (4.78). IR[KBr] V_{max} Cm^{-1} **:** 3300-2840 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2230 (C N stretching), 1650 [C=O and N-H (amide)] , 1588 (C=N stretching), 1580, 1470, 1420 (C=C ring stretching , aromatic), 1040, 820, (C-Cl stretching , 2, 5 -disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.22-2.46 (2H, s, CH_2), 3.4-3.9 (3H, s, CH_3), 4.12-4.40(1H, s, NH), 6.95-7.40 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.65 H_Z, C_4- H_A of pyrazoline ring). 3.92 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.60 Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.13 Hz COCH geminal proton), 5.58 (1H, dd J_{MX} 12.80 H_Z , J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: ∂/ppm 179.58 (C=O), 159.78 (C=N), 141.05, 137.65, 134.45, 131.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2, ester), 61.83 (C-5, pyrazoline), 46.95 (C-4, pyrazoline), 18.86 (CH_3). –MS-FAB$^+$: m/z: 589 [M]. Synthetic sequence for new pyrazolines has been outlined in scheme-I.

1-[(2, 5-dichloroanilinomalonyl)] -3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6a]:

Yield: 68%, M.P.: 255^0C, M.W.: 589, Anal. Calculated for C_{27} H_{21} Cl_4 N_5 O_2 Cl: 15.9; N: 7.8, found Cl: 15.7, N: 7.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 212.2 (4.92), 318.6 (4.78). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2840 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2230 (C N stretching), 1650 [C=O and N-H (amide)] , 1588 (C=N stretching), 1580, 1470, 1420 (C=C ring stretching , aromatic), 1040, 820, (C-Cl stretching , 2,5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.22-2.46 (2H, s, CH_2), 3.4-3.9 (3H, s, CH_3), 4.12-4.40(1H, s, NH), 6.95-7.40 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.65 H_Z, C_4- H_A of pyrazoline ring). 3.92 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.60 Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.13 Hz COCH geminal proton), 5.58 (1H, dd J_{MX} 12.80 H_Z , J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 179.58 (C=O), 159.78 (C=N), 141.05, 137.65, 134.45, 131.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2,* ester), 61.83 (C-5, pyrazoline), 46.95 (C-4, pyrazoline), 18.86 (CH_3). –MS-FAB$^+$: m/z: 589 [M].

1-[(o-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 b].

Yield: 51%, M.P.: 278^0C, M.W.: 604, Anal. Calculated for C_{28} H_{23} Cl_4 N_5 O_2, N: 5.6; found N: 5.8, Cl: 11.3; found Cl: 11.2 %. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 214.6(4.90), 319.4 (4.82). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2890 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2242 (C N stretching), 1660 [C=O and N-H (amide)] , 1590 (C=N stretching), 1585, 1478, 1430 (C=C ring stretching , aromatic), 1045, 822, (C-Cl stretching , 2,5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.23-2.48 (2H, s, CH_2), 4.16-4.30(1H, s, NH), 6.90-7.45 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 16 H_Z, J_{AX} = 4.60H_Z, C_4- H_A of pyrazoline ring). 3.98 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.43 Hz COCH geminal proton), 5.70 (1H, dd J_{MX} 12.40 H_Z , J_{AX} = 4.50 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 181.58 (C=O), 158.74 (C=N), 143.07, 136.54, 133.40, 130.74 (4C, ArC's), 131.47, 130.36, 126.62, 124.70, 114.31 (5C, Ar CH's), 63.66 (CH_2,* ester), 60.81 (C-5, pyrazoline), 46.91 (C-4, pyrazoline), 18.82 (CH_3). –MS-FAB$^+$: m/z: 604 [M].

1-[(m-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 c].

Yield: 58%, M.P.: 270^{0}C, M.W.: 604, Anal. Calculated for $C_{28}H_{23}Cl_4N_5O_2$ Cl: 13.2; N: 6.5, found Cl: 13.0, N: 6.3%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 212.2 (4.92), 318.6 (4.78). *IR[KBr]* V_{max} Cm^{-1} **:** 3300-2950 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2240(C N stretching), 1670 [C=O and N-H (amide)] , 1575 (C=N stretching), 1560, 1430, 1410 (C=C ring stretching , aromatic), 1050, 815, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.32-2.56 (2H, s, CH_2), 4.35-4.55(1H, s, NH), 6.40-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 3.88 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.55 Hz, C_4-H_M of pyrazoline ring) , 4.68 (1H, d, J = 16.16 Hz COCH geminal proton), 5.66 (1H, dd J_{MX} 12.60 H_Z , J_{AX} = 4.40 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 167.56 (C=O), 154.61 (C=N), 143.01, 136.62, 133.43, 130.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.77, 112.28 (5C, Ar CH's), 62.67 (CH_2,* ester), 61.83 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 18.84 (CH_3). –MS-FAB$^+$: m/z: 604 [M].

1-[(p-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 d].

Yield: 69%, M.P.: 252^{0}C, M.W.: 604, Anal. Calculated for $C_{28}H_{23}Cl_4N_5O_2$ Cl: 15.5; N: 7.6, found Cl: 15.1, N: 7.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 227.3 (4.96), 319.6 (4.70). *IR[KBr]* V_{max} Cm^{-1} **:** 3300-3040 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2250(C N stretching), 1620 [C=O and N-H (amide)] , 1570 (C=N stretching), 1550, 1460, 1430 (C=C ring stretching , aromatic), 1040, 825, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.14-2.41 (2H, s, CH_2), 4.28-4.35(1H, s, NH), 6.80-7.60(13H, m, ArH). 3.28 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.61 H_Z, C_4- H_A of pyrazoline ring). 3.87 (1H, dd J_{MA} = 17.79 Hz, J_{MX} = 13.58Hz, C_4-H_M of pyrazoline ring) , 4.68 (1H, d, J = 16.45 Hz COCH geminal proton), 6.11 (1H, dd J_{MX} 13.30 H_Z , J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 174.55 (C=O), 157.77 (C=N), 139.15, 135.65, 133.44, 131.80 (4C, ArC's), 131.42, 129.85, 126.62, 124.64, 111.17(5C, Ar CH's), 64.61 (CH_2,* ester), 62.81 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 17.93 (CH_3). –MS-FAB$^+$: m/z: 604 [M].

1-[(o-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 e].

Yield: 60%, M.P.: 269^{0}C, M.W.: 623.5, Anal. Calculated for $C_{27}H_{20}Cl_5N_5O_2$, Cl: 15.7; N: 6.2, found Cl: 15.4, N: 6.0%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 215.5 (5.10), 319.2 (5.16). *IR[KBr]* V_{max} Cm^{-1} **:** 3300-3110[broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2290(C N stretching), 1680 [C=O and N-H (amide)] , 1540 (C=N stretching), 1530, 1490, 1440 (C=C ring stretching , aromatic), 1080, 890, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 3.10-3.18 (2H, s, CH_2), 4.19-4.55(1H, s, NH), 6.87-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.62 H_Z, C_4- H_A of pyrazoline ring). 4.05 (1H, dd J_{MA} = 18.10 Hz, J_{MX} = 13.90 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.19 Hz COCH geminal proton), 5.45 (1H, dd J_{MX} 13.15 H_Z , J_{AX} = 5.10 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 164.79 (C=O), 154.72 (C=N), 147.22, 143.60, 138.44, 132.83 (4C, ArC's), 130.79, 128.85, 123.63, 121.72, 115.26(5C, Ar CH's), 64.60 (CH_2,* ester), 60.92 (C-5, pyrazoline), 47.15 (C-4, pyrazoline), 19.10(CH_3). –MS-FAB$^+$: m/z: 623[M], 624 [M+1].

1-[(m-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 f].

Yield: 59%, M.P.: 261^{0}C, M.W.: 623.5, Anal. Calculated for $C_{27}H_{20}Cl_5N_5O_2$, Cl: 17.4; N: 6.8, found Cl: 17.2, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 214.6 (4.97), 322.4 (4.81). *IR[KBr]* V_{max} Cm^{-1} **:** 3300-3120 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2240(C N stretching), 1658 [C=O and N-H (amide)] , 1605 (C=N stretching), 1570, 1460, 1430 (C=C ring stretching , aromatic), 1070, 830, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.58-2.87 (2H, s, CH_2), 4.35-4.62(1H, s, NH), 7.10-7.55 (13H, m, ArH). 3.34 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.70 H_Z, C_4- H_A of pyrazoline ring). 4.15 (1H, dd J_{MA} = 17.90Hz, J_{MX} = 13.20 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.44 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 13.30 H_Z , J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 178.57 (C=O), 155.65 (C=N), 144.11, 138.64, 135.44, 132.82 (4C, ArC's), 131.88, 130.15, 126.60, 123.80, 116.26(5C, Ar CH's), 61.66 (CH_2,* ester), 59.95(C-5, pyrazoline), 47.93 (C-4, pyrazoline), 18.95(CH_3). –MS-FAB$^+$: m/z: 623 [M], 624 [M+1].

1-[(p-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 g].

Yield: 65%, M.P.: 269^{0}C, M.W.: 623.5, Anal. Calculated for $C_{27}H_{20}Cl_5N_5O_2$ Cl: 18.2; N: 7.2, found Cl: 18.0, N: 6.9%. U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 216.3 (5.20), 340.6 (4.88). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2960 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2290(C N stretching), 1680 [C=O and N-H (amide)] , 1620 (C=N stretching), 1575, 1465, 1415 (C=C ring stretching , aromatic), 1035, 825, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.86-3.10 (2H, s, CH_2), 4.19-4.45(1H, s, NH), 6.90-7.42 (13H, m, ArH). 3.28 (1H, dd, J_{AM} = 17H_Z, J_{AX} = 4.68 H_Z, C_4- H_A of pyrazoline ring). 3.70 (1H, dd J_{MA} = 17.81 Hz, J_{MX} = 13.30 Hz, C_4-H_M of pyrazoline ring) , 4.20 (1H, d, J = 16.48 Hz COCH geminal proton), 5.22(1H, dd J_{MX} 12.89 H_Z , J_{AX} = 4.57 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 169.52 (C=O), 157.78 (C=N), 152.20, 148.65, 142.44, 138.85 (4C, ArC's), 134.48, 132.53, 129.68, 123.77, 126.27 (5C, Ar CH's), 64.67 (CH_2,* ester), 62.60 (C-5, pyrazoline), 47.25 (C-4, pyrazoline), 18.35 (CH_3). –MS-FAB$^+$: m/z: 623 [M], 624 [M+1].

1-[(o-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 h].

Yield: 69%, M.P.: 246^{0}C, M.W.: 620, Anal. Calculated for $C_{28}H_{23}Cl_4N_5O_3$, Cl: 15.6; N: 7.8, found Cl: 15.7, N: 7.6%. U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 215.3 (5.04), 318.4(4.79). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2880 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2270(C N stretching), 1640 [C=O and N-H (amide)] , 1575 (C=N stretching), 1570, 1455, 1440 (C=C ring stretching , aromatic), 1050, 810, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.38-2.51 (2H, s, CH_2), 4.29-4.50(1H, s, NH), 6.90-7.20 (13H, m, ArH). 3.27 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 3.98 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.82 (1H, d, J = 16.23 Hz COCH geminal proton), 5.51 (1H, dd J_{MX} 11.90 H_Z , J_{AX} = 4.40 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 173.52 (C=O), 158.70 (C=N), 144.10, 138.62, 135.65, 130.85 (4C, ArC's), 133.38, 131.40, 129.46, 123.80, 116.18 (5C, Ar CH's), 63.66 (CH_2,* ester), 63.68(C-5, pyrazoline), 45.92(C-4, pyrazoline), 19.15(CH_3). –MS-FAB$^+$: m/z: 620 [M].

1-[(m-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 i].

Yield: 73%, M.P.: 258^{0}C, M.W.: 620, Anal. Calculated for $C_{28}H_{23}Cl_4N_5O_3$, Cl: 16.9; N: 8.4, found Cl: 16.6, N: 8.1%. U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 218.1 (4.95), 317.9 (4.68). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2910 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2240(C N stretching), 1660 [C=O and N-H (amide)] , 1590 (C=N stretching), 1585, 1480, 1410 (C=C ring stretching , aromatic), 1060, 825, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.12-2.49 (2H, s, CH_2), 4.14-4.45(1H, s, NH), 7.10 -7.40 (13H, m, ArH). 3.22 (1H, dd, J_{AM} = 19H_Z, J_{AX} = 4.59 H_Z, C_4- H_A of pyrazoline ring). 4.10(1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.65 Hz, C_4-H_M of pyrazoline ring) , 4.74 (1H, d, J = 16.10 Hz COCH geminal proton), 5.70 (1H, dd J_{MX} 12.40 H_Z , J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 178.56 (C=O), 153.77 (C=N), 142.05, 139.40, 132.45, 130.80(4C, ArC's), 131.45, 129.80, 127.84, 125.70, 113.18 (5C, Ar CH's), 61.67 (CH_2,* ester), 62.82 (C-5, pyrazoline), 46.65 (C-4, pyrazoline), 18.42 (CH_3). –MS-FAB$^+$: m/z: 620[M].

1-[(p-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 j].

Yield: 78%, M.P.: 269^{0}C, M.W.: 620, Anal. Calculated for $C_{28}H_{23}Cl_4N_5O_3$ Cl: 17.6; N: 8.7, found Cl: 17.3, N: 8.4%. U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 216.4 (4.93), 318.7 (4.76). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2890 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2230(C N stretching), 1680 [C=O and N-H (amide)] , 1610 (C=N stretching), 1590, 1520, 1460 (C=C ring stretching , aromatic), 1030, 840, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.56 (2H, s, CH_2), 4.10-4.80(1H, s, NH), 6.85-7.10 (13H, m, ArH). 3.18 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.62 H_Z, C_4- H_A of pyrazoline ring). 3.97 (1H, dd J_{MA} = 18.20 Hz, J_{MX} = 13.50Hz, C_4-H_M of pyrazoline ring) , 4.80 (1H, d, J = 16.18 Hz COCH geminal proton), 5.60 (1H, dd J_{MX} 12.70 H_Z , J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 174.55 (C=O), 158.71 (C=N), 143.10, 138.60, 137.45, 133.85 (4C, ArC's), 132.48, 130.55, 128.66, 125.75, 114.68 (5C, Ar CH's), 62.80 (CH_2,* ester), 63.20 (C-5, pyrazoline), 46.80 (C-4, pyrazoline), 18.86 (CH_3). –MS-FAB$^+$: m/z: 620 [M].

1-[(p-floro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 k].

Yield: 55%, M.P.: 236^{0}C, M.W.: 608, Anal. Calculated for $C_{27}H_{20}Cl_4F_1N_5O_2$, Cl: 12.6; N: 6.2, found Cl: 12.5, N: 5.9%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 222.5 (4.98), 317.9 (4.73). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2860 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2250(C N stretching), 1660 [C=O and N-H (amide)] , 1575 (C=N stretching), 1570, 1460, 1430 (C=C ring stretching , aromatic), 1070, 860, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.18-2.34 (2H, s, CH_2), 4.16-4.70(1H, s, NH), 6.70-7.10 (13H, m, ArH). 3.16 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.93 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.70 Hz, C_4-H_M of pyrazoline ring) , 4.90 (1H, d, J = 16.40 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 12.90 H_Z, J_{AX} = 4.55 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 176.47 (C=O), 156.78 (C=N), 142.05, 137.62, 135.45, 132.84 (4C, ArC's), 130.28, 129.50, 126.60, 122.70, 111.88 (5C, Ar CH's), 63.10 (CH_2,* ester), 62.40 (C-5, pyrazoline), 47.10 (C-4, pyrazoline), 18.95 (CH_3). –MS-FAB$^+$: m/z: 608[M].

1-[(o-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 l].

Yield: 63%, M.P.: 260^{0}C, M.W.: 669, Anal. Calculated for $C_{27}H_{20}Cl_4N_5O_2Br$ Cl: 13.6; N: 6.8, found Cl: 13.5, N: 6.4%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 210.2 (4.93), 318.7 (4.85). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2880 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2230(C N stretching), 1620 [C=O and N-H (amide)] , 1555 (C=N stretching), 1605, 1510, 1490 (C=C ring stretching , aromatic), 1060, 840, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.54 (2H, s, CH_2), 4.25-4.45(1H, s, NH), 6.80-7.30 (13H, m, ArH). 3.25 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 4.04 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.50 Hz, C_4-H_M of pyrazoline ring) , 4.80 (1H, d, J = 16.66 Hz COCH geminal proton), 5.68 (1H, dd J_{MX} 13.10 H_Z, J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 178.70 (C=O), 158.72 (C=N), 141.10, 138.40, 136.49, 130.85 (4C, ArC's), 131.48, 130.32, 127.66, 124.77, 113.38 (5C, Ar CH's), 62.60 (CH_2,* ester), 61.84 (C-5, pyrazoline), 45.92 (C-4, pyrazoline), 19.06 (CH_3). –MS-FAB$^+$: m/z: 669 [M].

1 -[(o-ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 m].

Yield: 67%, M.P.: 265^{0}C, M.W.: 634, Anal. Calculated for $C_{29}H_{25}Cl_4N_5O_3$, Cl: 15.5; N: 7.6, found Cl: 15.2, N: 7.5%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 212.5 (4.98), 318.4 (4.88). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2920 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2260(C N stretching), 1640 [C=O and N-H (amide)] , 1580 (C=N stretching), 1590, 1480, 1460 (C=C ring stretching , aromatic), 1050, 860, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.30-2.44 (2H, s, CH_2), 4.14-4.40(1H, s, NH), 6.80-7.20 (13H, m, ArH). 3.17 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.65 Hz, C_4-H_M of pyrazoline ring) , 4.55 (1H, d, J = 16.35 Hz COCH geminal proton), 5.50(1H, dd J_{MX} 12.90 H_Z, J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 176.58 (C=O), 156.74 (C=N), 140.05, 136.65, 135.45, 132.90 (4C, ArC's), 131.46, 130.52, 129.66, 126.72, 112.44 (5C, Ar CH's), 62.90 (CH_2,* ester), 61.88 (C-5, pyrazoline), 46.35 (C-4, pyrazoline), 18.80 (CH_3). –MS-FAB$^+$: m/z: 634 [M].

1-[(m- ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 n].

Yield: 63%, M.P.: 250^{0}C (d), M.W.: 634, Anal. Calculated for $C_{29}H_{25}Cl_4N_5O_3$ Cl: 14.6; N: 7.2, found Cl: 14.3, N: 7.0%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 210.2 (4.89), 318.5 (4.72). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2890 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2240(C N stretching), 1670 [C=O and N-H (amide)] , 1570 (C=N stretching), 1580, 1460, 1430 (C=C ring stretching , aromatic), 1055, 830, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.14-2.26 (2H, s, CH_2), 4.18-4.30(1H, s, NH), 7.0-7.30 (13H, m, ArH). 3.15(1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.55 Hz, C_4-H_M of pyrazoline ring) , 4.75(1H, d, J = 16.12 Hz COCH geminal proton), 5.55(1H, dd J_{MX} 12.70 H_Z, J_{AX} = 4.50 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 174.54 (C=O), 153.78 (C=N), 143.10, 140.64, 137.45, 136.85 (4C, ArC's), 133.48, 131.55, 127.66, 124.57, 112.28 (5C, Ar CH's), 64.65 (CH_2,* ester), 62.85 (C-5, pyrazoline), 46.45 (C-4, pyrazoline), 18.95 (CH_3). –MS-FAB$^+$: m/z: 634 [M].

1-[(p-ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 o].

Yield: 59%, M.P.: 248^{0}C, M.W.: 634, Anal. Calculated for $C_{29}H_{25}Cl_4N_5O_3$ Cl: 13.7; N: 6.7, found Cl: 13.4, N: 6.5%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 218.2 (4.88), 318.6 (4.72). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2930 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2250(C N stretching), 1640 [C=O and N-H (amide)] , 1555 (C=N stretching), 1590, 1450, 1430 (C=C ring stretching , aromatic), 1045, 840, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.46 (2H, s, CH_2), 4.10-4.45(1H, s, NH), 6.90-7.30 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 19 H_Z, J_{AX} = 4.80 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.60 Hz, J_{MX} = 13.65Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.20 Hz COCH geminal proton), 5.65(1H, dd J_{MX} 12.60 H_Z , J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 181.52 (C=O), 162.78 (C=N), 142.20, 138.65, 137.42, 133.84(4C, ArC's), 129.88, 128.50, 127.60, 126.75, 110.38 (5C, Ar CH's), 63.67 (CH_2,* ester), 61.83 (C-5, pyrazoline), 46.65 (C-4, pyrazoline), 18.99 (CH_3). –MS-FAB$^+$: m/z: 634 [M].

1-[(m-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 s].

Yield: 66%, M.P.: 243^{0}C, M.W.: 669, Anal. Calculated for $C_{27}H_{20}Cl_4N_5O_2Br$ Cl: 13.4; N: 6.8, found Cl: 13.2, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 214.3 (4.90), 318.4 (4.70). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2890 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2240 (C N stretching), 1660 [C=O and N-H (amide)] , 1570 (C=N stretching), 1570, 1490, 1470 (C=C ring stretching , aromatic), 1050, 830, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.28-2.52 (2H, s, CH_2), 4.13-4.30(1H, s, NH), 6.90-7.55 (13H, m, ArH). 3.15 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.70 H_Z, C_4- H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.50 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.10 Hz COCH geminal proton), 5.80 (1H, dd J_{MX} 12.90 H_Z , J_{AX} = 4.70 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 178.57 (C=O), 157.77 (C=N), 140.15, 136.64, 134.40, 130.80 (4C, ArC's), 130.18, 128.75, 127.66, 125.78, 113.19(5C, Ar CH's), 61.62(CH_2,* ester), 61.70 (C-5, pyrazoline), 46.90 (C-4, pyrazoline), 18.75 (CH_3). –MS-FAB$^+$: m/z: 669 [M].

1-[(p-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline [6 t].

Yield: 55%, M.P.: 258^{0}C, M.W.: 669, Anal. Calculated for $C_{27}H_{20}Cl_4N_5O_2Br$, Cl: 11.9; N: 5.9, found Cl: 11.7, N: 5.6%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ nm), log ε]: 210.2 (4.94), 318.7 (4.76). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-2850 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2250(C N stretching), 1650 [C=O and N-H (amide)] , 1580 (C=N stretching), 1560, 1480, 1440 (C=C ring stretching , aromatic), 1040, 840, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.44 (2H, s, CH_2), 4.15-4.45(1H, s, NH), 6.90-7.45 (13H, m, ArH). 3.20(1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.85 Hz, J_{MX} = 13.65Hz, C_4-H_M of pyrazoline ring) , 4.75 (1H, d, J = 16.15 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 12.85H_Z , J_{AX} = 4.64 Hz, C_5-H_X of pyrazoline ring). ^{13}C-NMR: *∂/ppm 180.55 (C=O), 161.78 (C=N), 142.15, 138.65, 136.45, 133.80 (4C, ArC's), 131.46, 128.50, 127.65, 125.70, 114.27 (5C, Ar CH's), 62.68 (CH_2,* ester), 60.88(C-5, pyrazoline), 47.20 (C-4, pyrazoline), 18.95 (CH_3). –MS-FAB$^+$: m/z: 669 [M]. Most of the pyrazolines are high melting point and light yellow or cream colored solids. The data of new products are furnished in table- I.

Table-I : [1- (Unsubstituted / Substituted 2, 5-dichloroanilinomalonyl) -3-(N-2'-cyanoethyl-N-2, 5-dichloroanilino)-5-phenyl pyrazolines].

CS. No.	R	Color	M.P. (˚C)	Yield (%)	M.W.	Molecular Formula
6a.	H	Yellow	255	68	589	$C_{27}H_{21}Cl_4N_5O_2$
6b.	CH_3(o)	Cream	278	51	604	$C_{28}H_{23}Cl_4N_5O_2$
6c.	CH_3(m)	Light Yellow	270	58	604	$C_{28}H_{23}Cl_4N_5O_2$
6d.	CH_3(p)	Light Yellow	252	69	604	$C_{28}H_{23}Cl_4N_5O_2$
6e.	Cl(o)	white	269	60	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6f.	Cl(m)	Light Yellow	261	59	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6g.	Cl(p)	Cream	269	65	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6h.	O-CH_3(o)	Yellow	246	69	620	$C_{28}H_{23}Cl_4N_5O_3$
6i.	O-CH_3(m)	White	258	73	620	$C_{28}H_{23}Cl_4N_5O_3$
6j.	O-CH_3(p)	Cream	269	78	620	$C_{28}H_{23}Cl_4N_5O_3$
6k.	F(p)	Yellow	236	55	608	$C_{27}H_{20}Cl_4F_1N_5O_2$
6l.	Br(o)	Dark brown	260	63	669	$C_{27}H_{20}Cl_4N_5O_2Br$
6m.	O-C_2H_5 (o)	L. Brown	265	67	634	$C_{29}H_{25}Cl_4N_5O_3$
6n.	O-C_2H_5 (m)	Brown	250	63	634	$C_{29}H_{25}Cl_4N_5O_3$
6o.	O-C_2H_5 (p)	Brown	248	59	634	$C_{29}H_{25}Cl_4N_5O_3$
6p.	CO_2H (o)	Brown	243	66	634	$C_{28}H_{21}Cl_4N_5O_4$
6q.	CO_2H (m)	Brown	258	55	634	$C_{28}H_{21}Cl_4N_5O_4$
6r.	CO_2H (p)	L. brown	267	61	634	$C_{28}H_{21}Cl_4N_5O_4$
6s.	Br(m)	Brown	243	66	669	$C_{27}H_{20}Cl_4N_5O_2Br$
6t.	Br(p)	Brown	258	55	669	$C_{27}H_{20}Cl_4N_5O_2Br$

All compounds gave satisfactory elemental analysis.

Biological Evaluation

Anti-bacterial activity

Newly synthesized compounds (6a-t) have been tested for their antibacterial activity against gram positive bacteria S. albus, S. aureus and gram negative bacteria E.Coli and Pseudomonas poisonous by agar plate disc diffusion method at 30 µg/mL concentration. Ampicillin and Tetracycline used as a reference compound. The compound (**6a, 6b, 6c, 6f, 6g, 6j, 6m, and 6r**) shown significant activity and the compound (6i, 6k, 6l, 6p, 6t,) have shown moderate activity.

Anti-fungal activity:

The same compounds were tested for their antifungal activity against Candida albicans, Aspergillus Niger and Alternaria alternata at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (**6c, 6j, 6m, and 6r**) shown significant activities and compound (6a, 6b, 6f, and 6g) were found to be moderately active against Candida albicans and Aspergillus Niger. All the other compounds did not show significant activity against the fungi at the concentration used.

Tuberculostatic Activity:

Some new compounds have been tested for antitubercular activity in-vitro using Mycobacterium tuberculosis**.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with Mycobacterium tuberculosis**,** $H_{27,}$ R_V strains, incubated at 37^0C and observed, weekly for the growth of organism for eight weeks. The compound (**6a, 6b, 6c, 6f, 6g, 6j, and 6m**) inhibited the growth of Mycobacterium tuberculosis at 100mg/mL concentration other compounds were found to be inactive. Results are assembled in table-II.

Table-II: Tuberculostatic Activity of new pyrazolines:

S.No.	***Compounds***	***Growth at conc. [mg/mL]***	
		10	***100***
6a.	*1-[(2, 5-dichloroanilinomalonyl)] -3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	*0*
6b.	*1-[(o-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	*0*
6c.	*1-[(m-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	0
6d.	*1-[(p-methyl) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6e.	*1-[(o-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6f.	*1-[(m-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	0
6g.	*1-[(p-chloro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	*0*
6h.	*1-[(o-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6i.	*1-[(m-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	*0*
6j.	*1-[(p-methoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6k.	*1-[(p-floro) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline.*	+	+
6l.	*1-[(o-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6m.	*1-[(o-ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	*0*
6n.	*1-[(m- ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6o.	*1-[(p-ethoxy) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6s.	*1-[(m-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+
6t.	*1-[(p-bromo) 2, 5-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazoline*	+	+

'+' and '0' indicate presence and inhibition of growth respectively.

Results and Discussion

Newly synthesized 1-[(2, 5-dichloroanilinomalonyl)] -3-(N-2'-cyanoethyl -N-2, 5-dichloroanilino)-5- phenyl pyrazolines have been synthesized by the reaction of N-cinnamoyl-N-2'-cyanoethyl -2, 5-dichloro aniline with Ethyl-2-(2, 5-dichloroanilido) acetohydrazide. Pyrazolines are yellow, cream and brown color solids, having high melting points. Identity of these products has been established by elemental analysis and spectral data. Newly synthesized compounds (6a-t) have been tested for their antibacterial activity against gram positive bacteria S. albus , S. aureus and gram negative bacteria E. Coli and Pseudomonas poisonous .The compound (**6a, 6b, 6c, 6f, 6g, 6j, 6m, and 6r)** shown significant activity and the compound (6i, 6k, 6l, 6p, 6t,) have shown moderate activity. The same compounds were tested for their antifungal activity against Candida albicans, Aspergillus Niger and Alternaria alternata at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (**6c, 6j, 6m, and 6r**) shown significant activities and compound (6a, 6b, 6f, and 6g) were found to be moderately active against Candida albicans and Aspergillus Niger. All the other compounds did not show significant activity against the fungi at the concentration used. Some new compounds have been tested for antitubercular activity in-vitro using Mycobacterium tuberculosis**.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with Mycobacterium tuberculosis**,** $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (**6a, 6b, 6c, 6f, 6g, 6j, and 6m**) inhibited the growth of Mycobacterium tuberculosis at 100mg/mL concentration other compounds were found to be inactive.

Conclusion

Newly synthesized compounds (6a-t) have been tested for their **antibacterial activity** against gram positive bacteria S. albus , S. aureus and gram negative bacteria E. Coli and Pseudomonas poisonous .The compound (**6a, 6b, 6c, 6f, 6g, 6j, 6m, and 6r**) shown significant activity and the compound (6i, 6k, 6l, 6p, 6t,) have shown moderate activity. The same compounds were tested for their **antifungal activity** against Candida albicans, Aspergillus Niger and Alternaria alternata at concentration of 30 mg/mL using sabouraud dextrose agar media. The compound (**6c, 6j, 6m, and 6r)** shown significant activities and compound (6a, 6b, 6f, and 6g) were found to be moderately active against Candida albicans and Aspergillus Niger. All the other compounds did not show significant activity against the fungi at the concentration used. Some new compounds have been tested for **antitubercular** activity in-vitro using Mycobacterium tuberculosis**.** The compounds were incorporated into Lowenstein Jensen egg medium having concentrations of 10 and 100 mg/mL and were inoculated with Mycobacterium tuberculosis**,** $H_{27,}$ Rv strains, incubated at 37^0C and observed, the compound (**6a, 6b, 6c, 6f, 6g, 6j, and 6m**) inhibited the growth of Mycobacterium tuberculosis at 100mg/mL concentration other compounds were found to be inactive.

Acknowledgement

The authors are thankful to Director, C. D. R. I. Lucknow (U. P.), for elemental analysis, Director, Tuberculosis Research Centre, Amargadh (Gujrat), for testing tuberculostatic activity and Director, D. R. D. E. Gwalior (M.P.), for spectral studies, and Director, Cancer Hospital and Research Institute, G.R. Medical College and Birla Institute of Medical Research, Gwalior (M. P.), for Biological activities. We are also grateful to principal SMS Government Model Science College, Gwalior (M.P), for providing research facilities.

References

1. Korgaokar, S. S.; Patil, P. H.; Shah, M. J; Parekh, H. H. *Indian J. Pharm. Sci.* ***58*****,**222-225 (**1996)**.
2. J. C. Jung, E. B. Watkins and M. A. Avery, Heterocycles **65,** 77–94,(**2005**).
3. E. Palaska, M. Aytemir, T. Uzbay and D. Erol, Eur. *J. Med. Chem.* **36,** 539–543, (**2001**).
4. Julian, L. *Med. Hypotheses* ***69***, 684-689, (**2007**).
5. Rajendra, P. Y.; Lakshmana, R. A.; Prasoona, L.; Murali, K.; Ravi, K. P. *Bioorg. Med. Chem. Lett*. ***15***, 5030-5034, (**2005).**
6. Ruhogluo, O.; Ozdemir, Z.; Calis, U.; Gumusel, B.; Bilgin, AA. *Arzneimittelforschung* ***55***, 431-436,***(*****2005)**.
7. Ozdemir, Z.; Kandilici, HB; Gumusel, B.; Calis, U.; Bilgin, AA. *Eur. J. Med. Chem*. ***42*****,** 373-379,**(2007).**
8. Ashok Kumar, Sharma S, Bajaj K, Bansal D, Sharma S, Saxena KK, Lata S, Gupta B and

Srivastava VK, Ind. J. Chem., **44B**, **1979-1984,** (**2003**).

9. Udupi, R. H., Narayanrao, S. and Bhat, A. R. Indian J. Heterocyclic Chemistry, **7**, 217-220,**(1998**).

10. Amir M, Kumar S. Indian J. Chem **44B**: 2532-2537, (**2005**).

11. Udupi, R. H.; Kushnoor, A.S.; Bhat, A. R. *Indian J.Heterocycl. Chem*. ***8***, 63-66, (**1998**).

12. Amir, M., Kumar, H., Khan, S. A. *Bioorg. Med. Chem. Lett. **18***, 918-922, (**2008).**

13. unawar A. Munawar, Muhammad Azad , Makshoof Athar and Paul W.Groundwater; Chemical Papers, Vol. **62**, **3,** 288-293, (**2008**).

14. Sadaf Sadiq Khan and Aurangzeb Hasan; Heterocycl. Commun. **13,** 131-138, **(2007**).

15. Islam MR, Muhsin M. Bangladesh J. Pharmacol. **2**, 7-12, (**2007).**

16. Hull, M.A.; Ko, S.C.W.; Hawcroft, G. *Mol. Canc. Ther. **3,*** 1031-1039, (**2004**).

17. T. S. Jeong, K. S. Kim, J. R. Kim, K. H. Cho, S. Lee and W. S. Lee, *Bioorg. Med. Chem. Lett*. **14 ,** 2719–2723, (**2004**), DOI: 10.1016/j.bmcl.**2004.03.072.**

18. T. Saibara, K. Toda, A. Wakatsuki, Y. Ogawa, M. Ono and S. Onishi, *Toxicol. Lett.* 143 , 51–54, (**2003**). DOI: 10.1016/S0378-4274(03)00113-9.

19. El-Zohry MF, Younes MI, Metwally SA. Synthesis 972, (**1984)**.

20. R. Lin, G. Chiu, Y. Yu, P. J. Connolly, S. Li, Y. Lu, M. Adams, A. R. Fuentes-Pesquera, S. L. Emanuel and L. M. Greenberger, *Bioorg. Med. Chem. Lett.* **17,** 4557–4561; (**2007**) DOI: 10.1016/j. bmcl.**2007**.05.092.

21. S. Rollas, N. Gulerman and H. Erdeniz, *Farmaco* **57,** 171–174, (**2002**).

22. Olsen, D. B., A. B. Eldrup, L. Bartholomew, B. Bhat, M. R. Bosserman, A. Ceccacci, L. F. Colwell, J. F. Fay, O. A. Flores, K. L. Getty, J. A. Grobler, R. L. LaFemina, E. J. Markel, G. Migliaccio, M. Prhavc, M. W. Stahlhut, J. E. Tomassini, M. MacCoss, D. J.Hazuda and S. S. Carroll. Antimicrob. Agents Chemother. **48:**3944–3953, (**2004)**.

23. Abid M, Azam A. *Bioorg Med Chem Lett* **16**, 2812-6, (**2006)**.

24. Asha Budakoti, Abdul Roouf Bhat; Amir Azam; Eur. J. Med. Chem. Vol. 44, Issue- **3,** 1317-1325, (**2009).**

25. Inoue Y, Kobayashi T, Masu A, Asahina K. *Jpn Kokai Tokkyo Koho*.1991; JP03197467 [*Chem Abstr.* **115**, 280054p, (**1991**).

26. A.A. Bekhit, H.M.A. Ashour, A.A. Guemei, Arch. Pharm. **338,** 167, **(2005**).

27. M. Bagheri, M. Shekarchi, M. Jorjani, M.H. Ghahremani, M. A. Shafiee, Arch. Pharm. **337,** 25,**(2004**).

28. J. H. Ahn, H. M. Kim, S. H. Jung, S. K. Kang, K. R. Kim, S. D. Rhee, S. D. Yong, H. G. Cheon and S. S. Kim, *Bioorg. Med. Chem. Lett*. **14 ,** 4461–4465, (**2004**).

29. Joel O, Jean-Yves P, Patricia M, Pascal C, Fretier P, Philippe J, Dereuddre-Bosquet N, Dominique D, and Jean-Louis I, J. *Med. Chem.* **42**, 4733-4740, (**1999).**

30. Maria L, Barreca, Jan B, Alba C, Erik DC, Laura DL, Hans DH, Monforte AM, Monfort P, Christophe P, RaoA and Maria Z, Design, *J. Med. Chem* **45**, 5410- 5413, (**2002).**

31. S. D. Bhardwaj, V. S. Jolly, *Orient. J. Chem.* **12** (**1996**) 185; *Chem. Abstr.* **126,** 1442174, (**1997**).

32. Genin MJ, Biles C, Keiser BJ et al, *J Med Chem*, **43**, 1034-40, (**2000b**).

33. G. V. Subbraju, A. Ranga Nayakulu, D. Parameshwara, *Indian J. Heterocycl. Chem.* **4** 87, (**1994**).

34. Krishna R B, Panade R, Bhaithwal S P and Parmar S S, *Eur Med J Chem.*, 15567, (**1980).**

35. Wagner E., Becan L. and Nowakowska E.; Bio. Org. Med. Chem.; **12,** 265, (**2004).**

36. Troeberg, L.; Chen, X.; Flaherty, T. M.; Morty, R. E.; Cheng, M.; Hua, H.; Springer, C.; Mc Kerrow, J. H.; Kenyon, G. L.; Lonsdale-Eccles, J. D.; Coetzer, T. H. T.; Cohen, F. E. Chalcone, *Mol. Med. (N.Y.) **6***, 660-669, (**2000)**, [*Chem. Abstr.* **2001**, ***134***, 246896x].

37. B. Roman, *Pharmazie* **45,** 214, (**1990).**

38. Azarifar, D.; Shaebanzadeh, M.; *Molecules **7***, 885-895, (**2002**).

39. Shekarchia M, Pirali-Hamedania B L, Navidpourb N, Adiba and Shafieeb A, *J Iranian Chem Soc.,* **5,** 150-158, (**2008).**

40. Francesc Puig-Basagoiti; Mark Tilgner, Brett M. Forshey, Seen M. Philpott, Noel G. Espina, Devid E. Wentworth, Scott J. Goebel, Paul S. Masters, Barry Falgout, Ping Ren, David M. Ferguson, and Pei-Yong Shi; vol. **50,** No. 4, p.1320-1329, April-(**2006).**

41. Yale, H. L.; Losee, K.; Martins, J.; Holsing, M.; Perry, F. M.; Bernstein, J. Chemotherapy of Experimental Tuberculosis. VIII. *J. Am. Chem. Soc.* **1953**,***75***, 1933-1942. *Molecules*, ***8*** 754, **(2003).**

42. Corbett, E.L., Watt, C.J., Walker, N., Maher, D., Williams, B.G. Raviglione, M.C.,

and Dye,C, Arch Intern Med **163**, 1009-1021, (**2003**).

43. M.A. Ali, M. Shaharyar, A. A. Siddiqui, Eur. J. Med. Chem. **42,** 268- 275, **(2007**).

44. M. Shaharyar, A.A.Siddiqui, M.A. Ali, D. Shriram, P.Yogeeshwari, Bioorg. Med. Chem. Lett.**16,** 3947- 3949, **(2006**).

45. J. N. Domínguez, C. León, J. Rodrigues, N. Gamboa de Domínguez, J. Gut, J. Philip, P. J. Rosenthal, *Farmaco*, **60,** 307-10, (**2005).**

46. Zhang, X.H.; Wu, S.K.; Gao, Z.Q.; Lee, C.S.; Lee, S.T.; Kwong, H.L. *Thin Solid Films*. ***371***, 40-46, (**2000).**

47. Suwalsky M, Orellana P, Avello M, Villena F. Food and Chemical Toxicology. **45,** 130-135, (**2007).**

48. Tice CM, Bryman LM, Roemmele RC. *Eur Pat Appl*. **1994**;EP 733622 [*Chem Abstr*. **125**, 275903s, (**1996**).

49. Verma B L and Singhal M, *Indian J Heterocycl Chem*., **14,** 343-346, (**2007).**

50. Desai NC, Nayan Bhatt, Mukesh Kumar. Indian J. Heterocyclic Chem. **17**, 277-278, (**2008).**

51. M. A. El-Hashasn, F. M. A. Sulaiman, L. M. Souka, A. S. Salman, *Rev. Roum. Chim.* **40,** 59, (**1995**).

52. G. Turan-Zitouni, P. Chevallet, F.S. Kilic¸, K. Erol, Eur. J. Med. Chem. **35,** 635e641, **(2000).**

53. M. S. Karthikeyan, B. S. Holla, N. S. Kumari, *Eur. J. Med. Chem.* **42,** 30, (**2007**).

54. Habib NS, Soliman R, Ismail K, Hassan AM, Sarg MT, Pyrimidines. Part II: *Boll Chim Farm*, **142**, 396-405, (**2003**).

55. Greenlee, R.-T.; Hill-Marmon, M.-B.; Murray, T.; Thun, M., *Cancer J. Clin*. ***51***, 15-36, (**2001**).

*****