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Synthesis, characterization, and biological activities of new 1-[(2,5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2,5-dichloroanilino)]-5-phenyl pyrazoline derivatives

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ABSTRACT : A series of new 1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline have been synthesized in 43 to 72% yield, by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2, 5-dichloroaniline with Ethyl-2-[(N-acety) 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 (7a-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 *(7a, 7b, 7c, 7f, 7g, 7j, 7m, and 7r)* shown significant activity and the compound *(7i, 7k, 7l, 7p, 7t)* 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 *(7c, 7j, 7m and 7r)* shown significant activities and compound *(7a, 7b, 7f, and 7g*) 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°C and observed, the compound (*7a, 7b, 7c, 7f, 7g, 7j and 7m*) 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-2,5dichlorodianilide 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: 81%, M. P.: 88°C, M. W.: 276. Anal. Calculation for $C_{11} H_{11} N_1 O_3 Cl_2$: Found: C 39.20, H: 03.24, O: 14.25, N: 4.14, Cl: 21.09, Calcd. C: 39.21, H: 03.26, O: 14.26, N: 04.15, Cl: 21.16. *IR [KBr]* V_{max} Cm^{-1} : 1665-1660 [C=O diketone], 1290 [-C-O- Ester], 760-755 [2,5 disubstituted benzene], 1250 [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 [1H, s, Ar-NH D_2O exchangeable].

Synthesis of Ethyl-2-[(N-acetyl) 2, 5-dichloroanilido] ethanoate [2]

Acetyl chloride (4.74 gm; 0.06 mol), dioxane (6 ml), Ethyl-2-(2,5-dichloroanilido) ethanoate (16.56 gm; 0.06 mol) and Triethylamine (5.7 gm; 0.06 mol) were placed in a round bottomed flask carrying reflux condensor having calcium chloride guard tube. The contents were heated on a boiling water bath for two hours and kept over night when triethylamine hydrochloride separated. It was filtered under suction and the filtrate was poured on to crushed ice (Ca180 g) and stirred when ethyl-2-[(N-acetyl) 2, 5-dichloroanilido] ethanoate separated or solid. It was filtered under suction, dried and purified by recrystallisation from aqueous methanol (1:1) in white crystals. Yield = 75.4 %, MP = 90°C Anal. calculation for $C_{13}H_{13}O_4N_1Cl_2$: [FW = 318], Calculated: N 02.95, C 45.64, H 03.38, O 13.50, Cl 15.00, Found : N 02.94, C 45.62, H 03.37, O 13.52, Cl 15.02. IR [KBr] V_{max} cm^{-1} **:** 1720 [C=O diketone], 1300 [-C-O- Ester], 762[2,5-disubstituted benzene], 1090 [C-Cl Stretching], 1590, 1520, 1440 [C=C Ring stretching], 3160 [N-H Stretching], 3040[C-H aromatic], 1330-1322 [C-H Stretching]. PMR (DMSO): δ 4.44 [2H, s, CO-CH_2-CO], 4.1 [2H, s, NH_2], 7.2-8.5 [3H, m, Ar-H], 9.4 [1H, s, CO-NH D_2O exchangeable], 10.8 [1H, s, Ar-NH D_2O exchangeable].

Synthesis of Ethyl-2-[(N-acetyl) 2, 5-dichloroanilido] acetohydrazide [3]

Ethyl-2-[(N-acetyl) 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-[(N-acetyl) 2, 5-dichloroanilido] acetohydrazide was filtered under suction and recrystallised from ethanol in white crystals. Yield; 79%, MP = 177°C, MW 304: Anal. calculation for $C_{11}H_{11}N_3O_3Cl_2$: Calculated ; N 09.04, C 41.32, H 03.01, O 10.33, Cl 15.28, Found; N 09.01, C 41.30, H 03.00, O 10.31, Cl 15.27.IR [KBr] V_{max} cm^{-1} **:** 3160 [N-H Stretching], 3048 [C-H aromatic], 1660 [C=O diketone], 1432 [C-Cl aromatic], 1595,1520, 1445 [C=C ring stretching]. PMR (DMSO): δ 4.44 (2H, s, CO-CH_2-CO), 4.1 (2H, s, NH_2), 7.2-8.5 (3H, m, Ar-H), 9.4 (1H, s, CO-NH D_2O exchangeable), 10.7 (1H, s, Ar-NH D_2O exchangeable).

Mono cyanoethylation of 2, 5-dichloroaniline [4]

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. 252°C/0.5mm was recovered. The N-Cyanoethyl-2, 5-dichloroaniline was obtained as light yellow colored viscous liquid at 175-176°C/mm which solidified after keeping overnight. Yield: 15.7g (97%), M.P. 82°C.

Preparation of Cinnamoyl Chloride [5]:

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°C/ 18-20mm pressure.

Synthesis of N-Cinnamoyl –N-2'-Cyanoethyl -2, 5-dichloroaniline [6]:

Solution of cinnamoyl chloride (3.5g, 0.02 mol), dioxane (2ml), N-2'-cyanoethyl-2, 5-dichloro aniline (7.90g, 0.02 mol) and triethylamine (2.1g) 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 overnight triethylamine hydrochloride separated as solid. It was filtered and contents concentrated when crystals separated out. Two crystallization from ethanol gave shining white needles. Yield: 55 %, M.P.: 156°C, Anal. Calculated for $C_{18}H_{14}Cl_2N_2O$; M.W. 345; N: 4.5, Cl: 11.3; found N: 4.3, Cl : 11.2 %, IR[KBr] V_{max} Cm^{-1} : 3280-3050 (C-H stretching, aromatic), 2955 and 2890 (C-H Stretching, aliphatic (asymmetric) and C-H stretching, aliphatic (symmetric), 2215 (C-N stretching), 1655(C=C stretching, benzene ring), 1645 C=O (stretching, tertiary amide), 1615, 1575, 1455, (C=C ring stretching), 1050, 750, (2, 5-disubstituted benzene).

Synthesis of 1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7]:

A mixture of N-cinnamoyl-N-2'-cyanoethyl-2, 5-dichloroaniline (0.345 g; 0.001 mol), Ethyl-2-[(N-acetyl) 2, 5-dichloroanilido] acetohydrazide (0.304g; 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: 61%, M.P.: 258°C, M.W.: 631, Anal. Calculated for $C_{29}H_{23}Cl_4N_5O_3Cl$: 13.7; N: 6.8, found Cl: 13.6, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.3 (4.94), 318.9 (4.78). *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], 2240 (C N stretching), 1660 [C=O and N-H (amide)], 1590 (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: 631[M]. Synthetic sequence for new pyrazolines has been outlined in Fig.1.

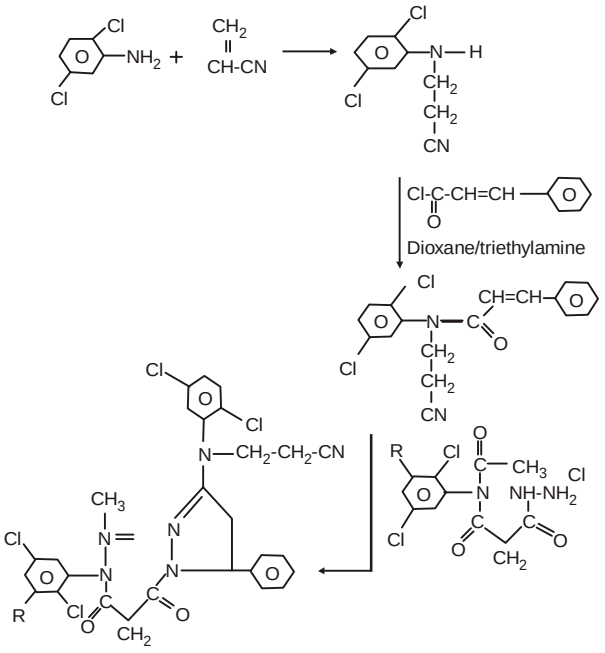

Fig.1. The reaction scheme for the complete sythesis of compounds.

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

1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7a]:

Yield: 62%, M.P.: 262°C, M.W.: 631, Anal. Calculated for $C_{29}H_{23}Cl_4N_5O_3$ Cl: 13.7; N: 6.8, found Cl: 13.6, N: 6.6%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.3 (4.94), 318.9 (4.78). *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], 2240 (C=N stretching), 1660[C=O and N-H (amide)], 1590 (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: 631 [M].

1-[(o-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7b]:

Yield: 43%, M.P.: 269°C, M.W.: 646, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_{3,}$ N: 4.4; found N: 4.1, Cl: 9.0; found Cl: 9.1 %. 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), 1650 [C=O and N-H (amide)], 1580 (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: 646 [M].

1-[(m-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7c]:

Yield: 52%, M.P.: 260°C, M.W.: 646, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_{3,}$ Cl: 11.7; N: 5.7, found Cl: 11.5, N: 5.3%. 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: 646 [M].

1-[(p-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7d]:

Yield: 57%, M.P.: 247°C, M.W.: 666.5, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_3$ Cl: 12.4; N: 6.1, found Cl: 12.1, N: 5.9%. U.V. [($\lambda^{Et\ OH}_{Max}$ 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: 666 [M].

1-[(o-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7e]:

Yield: 48%, M.P.: 264°C, M.W.: 666.5, Anal. Calculated for $C_{29}H_{22}Cl_5N_5O_3$, Cl: 13.0; N: 5.1, found Cl: 13.1, N: 4.9%. U.V. [($\lambda^{Et\ OH}_{Max}$ 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: 666 [M], 667[M+1].

1- [(m-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7f]:

Yield: 61%, M.P.: 268°C, M.W.: 666.5, Anal. Calculated for $C_{29}H_{22}Cl_5N_5O_3$, Cl: 16.0; N: 6.3, found Cl: 16.2, N: 6.1%. U.V. [($\lambda^{Et\ OH}_{Max}$ 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: 666 [M], 667 [M+1].

1- [(p-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7g]:

Yield: 63%, M.P.: 263°C, M.W.: 666.5, Anal. Calculated for $C_{29}H_{22}Cl_5N_5O_3$, Cl: 17.0; N: 6.7, found Cl: 17.2, N: 6.5%. 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} = 17$H_{Z,}$ 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: 666 [M], 667[M+1].

1- [(o-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7h]:

Yield: 66%, M.P.: 251°C, M.W.: 662, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_{4,}$ Cl: 14.4; N: 7.1, found Cl: 14.2, N: 7.0%. 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: 662 [M].

1- [(m-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7i]:

Yield: 70%, M.P.: 255°C, M.W.: 662, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_4$, Cl: 15.2; N: 7.5, found Cl: 15.3, N: 7.2%. 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} = 19$H_{Z,}$ 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: 662 [M].

1-[(p-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7j]:

Yield: 72%, M.P.: 263°C, M.W.: 662, Anal. Calculated for $C_{30}H_{25}Cl_4N_5O_{4,}$ Cl: 15.7; N: 7.7, found Cl: 15.3, N: 7.7%. 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: 662 [M].

1-[(p-floro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7k]:

Yield: 51%, M.P.: 248°C, M.W.: 650, Anal. Calculated for $C_{29}H_{22}Cl_4F_1N_5O_{3,}$ Cl: 11.4; N: 5.6, found Cl: 11.2, N: 5.4%. U.V. [($\lambda^{Et\ OH}_{M\ ax}$ 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: 650 [M].

1- [(o-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7l]:

Yield: 59%, M.P.: 257°C, M.W.: 711, Anal. Calculated for $C_{29}H_{22}Cl_4N_5O_3Br$ Cl: 11.8; N: 5.8, found Cl: 11.5, N: 5.4%. 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: 711 [M].

1- [(o-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7m]:

Yield: 63%, M.P.: 266°C, M.W.: 676, Anal. Calculated for $C_{31}H_{27}Cl_4N_5O_4$, Cl: 13.2; N: 6.5, found Cl: 13.2, N: 6.3%. 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: 676 [M].

1- [(m-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7n]:

Yield: 64%, M.P.: 252°C (d), M.W.: 676, Anal. Calculated for $C_{31}H_{27}Cl_4N_5O_4$ Cl: 13.7; N: 6.7, found Cl: 13.3, N: 6.2%. 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: 676 [M].

1-[(p-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7o]:

Yield: 60%, M.P.: 249°C, M.W.: 676, Anal. Calculated for $C_{31}H_{27}Cl_4N_5O_4$ Cl: 12.8; N: 6.3, found Cl: 12.4, N: 6.1%. 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: 676 [M].

1- [(m-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7s]:

Yield: 57%, M.P.: 250°C, M.W.: 711, Anal. Calculated for $C_{29}H_{22}Cl_4N_5O_3Br$ Cl: 11.4; N: 5.6, found Cl: 11.2, N: 5.2%. 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: 711 [M].

1- [(p-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline [7t]:

Yield: 48%, M.P.: 258°C, M.W.: 711, Anal. Calculated for $C_{29}H_{22}Cl_4N_5O_3Br$, Cl: 9.8; N: 4.8, found Cl: 9.4, N: 4.3%. 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: 711 [M]. Most of

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

CS. No.	R	Color	M.P. (*C)	Yield (%)	M.W.	Molecular Formula
7a.	H	Yellow	262	62	631	$C_{29}H_{23}Cl_4N_5O_3$
7b.	CH_3(o)	Cream	269	43	646	$C_{30}H_{25}Cl_4N_5O_3$
7c.	CH_3(m)	Light Yellow	260	52	646	$C_{30}H_{25}Cl_4N_5O_3$
7d.	CH_3(p)	Light Yellow	247	57	666.5	$C_{30}H_{25}Cl_4N_5O_3$
7e.	Cl(o)	white	264	48	666.5	$C_{29}H_{22}Cl_5N_5O_3$
7f.	Cl(m)	Light Yellow	268	59	666.5	$C_{29}H_{22}Cl_5N_5O_3$
7g.	Cl(p)	Cream	263	63	666.5	$C_{29}H_{22}Cl_5N_5O_3$
7h.	O-CH_3(o)	Yellow	251	66	662	$C_{30}H_{25}Cl_4N_5O_4$
7i.	O-CH_3(m)	White	255	70	662	$C_{30}H_{25}Cl_4N_5O_4$
7j.	O-CH_3(p)	Cream	263	72	662	$C_{30}H_{25}Cl_4N_5O_4$
7k	F(p)	Yellow	248	51	650	$C_{29}H_{22}Cl_4N_5O_3F_1$
7l.	Br(o)	Dark brown	257	59	711	$C_{29}H_{22}Cl_4N_5O_3Br$
7m.	O-C_2H_5(o)	L. Brown	266	63	676	$C_{31}H_{27}Cl_4N_5O_4$
7n.	O-C_2H_5(m)	Brown	252	64	676	$C_{31}H_{27}Cl_4N_5O_4$
7o.	O-C_2H_5(p)	Brown	249	60	676	$C_{31}H_{27}Cl_4N_5O_4$
7p.	CO_2H(o)	Brown	257	68	676	$C_{30}H_{23}Cl_4N_5O_5$
7q.	CO_2H(m)	Brown	253	63	676	$C_{30}H_{23}Cl_4N_5O_5$
7r.	CO_2H(p)	L. brown	256	51	676	$C_{30}H_{23}Cl_4N_5O_5$
7s.	Br(m)	Brown	250	57	711	$C_{29}H_{22}Cl_4N_5O_3Br$
7t.	Br(p)	Brown	258	48	711	$C_{29}H_{22}Cl_4N_5O_3Br$

All compounds gave satisfactory elemental analysis.

the pyrazolines are high melting point and light yellow or cream colored solids. The data of new products are furnished in Table 1.

BIOLOGICAL EVALUATION

Anti-bacterial activity

Newly synthesized compounds *(7a-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 ìg/mL concentration. Ampicillin and Tetracycline used as a reference compound. The compound (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j*, 7*m*, and 7*r*) shown significant activity and the compound (7*i*, 7*k*, 7*l*, 7*p*, 7*t*) *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 (7*c*, 7*j*, 7*m*, and 7*r*) shown significant activities and compound (7*a*, 7*b*, 7*f* and 7*g*) 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°C and observed, weekly for the growth of organism for eight weeks. The compound (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j* and 7*m*) inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration other compounds were found to be inactive. Results are assembled in Table 2.

Table 2 : Tuberculostatic Activity of new pyrazolines.

S.No.	Compounds	Growth at conc. [mg/mL] 10	100
7a.	1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7b.	1- [(o-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7c.	*1- [(m-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline*	+	0
7d.	1- [(p-methyl) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7e.	1- [(o-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7f.	*1- [(m-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline*	+	0
7g.	1- [(p-chloro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7h.	1- [(o-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7i.	1- [(m-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7j.	1- [(p-methoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7k.	1- [(p-floro) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline .	+	+
7l.	1- [(o-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7m.	1- [(o-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0

(*Contd...*)

S.No.	Compounds	Growth at conc. [mg/mL] 10	100
7n.	1- [(m-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7o.	1- [(p-ethoxy) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7s.	1- [(m-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7t.	1- [(p-bromo) 2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-acetyl) 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)-2-(N-acetyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline have been synthesized by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2,5-dichloroaniline with Ethyl-2-[(N-acetyl) 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 (7a-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 (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j*, 7*m* and 7*r*) shown significant activity and the compound (7*i*, 7*k*, 7*l*, 7*p*, 7*t*) *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 (7*c*, 7*j*, 7*m*, and 7*r*) shown significant activities and compound (7*a*, 7*b*, 7*f*, and 7*g*) 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°C and observed, the compound (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j* and 7*m*) inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration other compounds were found to be inactive.

CONCLUSION

Newly synthesized compounds (7a-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 (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j*, 7*m*, and 7*r*) shown significant activity and the compound (7*i*, 7*k*, 7*l*, 7*p*, 7*t*) 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 (7*c*, 7*j*, 7*m*, and 7*r*) shown significant activities and compound (7*a*, 7*b*, 7*f*, and 7*g*) 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°C and observed, the compound (7*a*, 7*b*, 7*c*, 7*f*, 7*g*, 7*j* and 7*m*) inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration other compounds were found to be inactive.

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