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Synthesis, characterization, and biological activities of some new pyrazoline derivatives, derived from ethyl-2-(2, 3-dichloroanilido) acetohydrazide

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ABSTRACT

A series of new *1-[(2, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl-N-2, 3-dichloroanilino)-5-phenyl pyrazoline have been synthesized in 48 to 77% yield, by the reaction of* N-cinnamoyl-N-2'-cyanoethyl-2, 3-dichloroaniline with Ethyl-2-(2,3-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^{0}C 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.

Key words: 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, 3-dichloroanilido] Ethanoate [1]

A mixture of 2, 3-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, 3-dichlorodianilide separated out. It was filtered under suction. The filtrate was poured on to crushed ice (Ca160g) and stirred when ethyl-2-(2, 3-dichloroanilido) ethanoate precipitated as green mass. On recrystallization from aqueous ethanol (50%), ester was obtained as white crystals. Yield,81%, M.P. 88^{0}C, M.W.276.Anal. calculation for $C_{11}H_{11}N_1O_3Cl_2$: 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], 760-755 [2, 3- di substituted 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): ä 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, 3- dichloroanilido) acetohydrazide [2]

Ethyl-2-(2, 3-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, 3-dichloroanilido) acetohydrazide was filtered under suction and recrystallised from ethanol in white crystals. Yield, 80%, m.p. = 168°C, M.W. 262: Analytical calculation for $C_9H_9N_3O_2Cl_2$: Calculated , N 09.04 ,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], 1432 [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, 3-dichloroaniline [3]

A 250 ml three necked flask equipped with a stirrer, reflux condenser and thermometer was charged with 2, 3-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, 3-dichloro aniline B.P. 252^{0}C/ 0.5mm was recovered. The N-Cyanoethyl-2, 3-dichloroaniline was obtained as light yellow colored viscous liquid at 175-176^{0}C/mm which solidified after keeping overnight. Yield: 15.7g (97%)., m.p. 82^{0}C

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^{0}C/ 18-20mm pressure.

Synthesis of N-Cinnamoyl –N-2'-Cyanoethyl -2, 3-dichloroaniline [5]

Solution of cinnamoyl chloride (3.5 g, 0.02 mol), dioxane (2ml), N-2'-cyanoethyl -2, 3-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: 55 %, M.P.: 156^{0}C, 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} :* 3280-3050 (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, 3-disubstituted benzene).

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

A mixture of N-cinnamoyl-N-2'-cyanoethyl -2, 3-dichloroaniline (0.345 g, 0.001 mol), Ethyl-2-(2, 3-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: 66%, m.p. 252^{0}C, 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. [(ë $^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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 1.

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, 3-dichloro anilinomalonyl)] -3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6a]

Yield: 66%, m.p. 252^{0}C, 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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, ä 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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 b]

Yield: 48%, m.p. 275^{0}C, 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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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 , 2,3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, ä 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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 c]

Yield: 56%, m.p.: 266^{0}C, M.W.: 604, Anal. Calculated for C_{28} H_{23} Cl_4 N_5 O_2 Cl: 13.2, N: 6.5, found Cl: 13.0, N: 6.3%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 d]

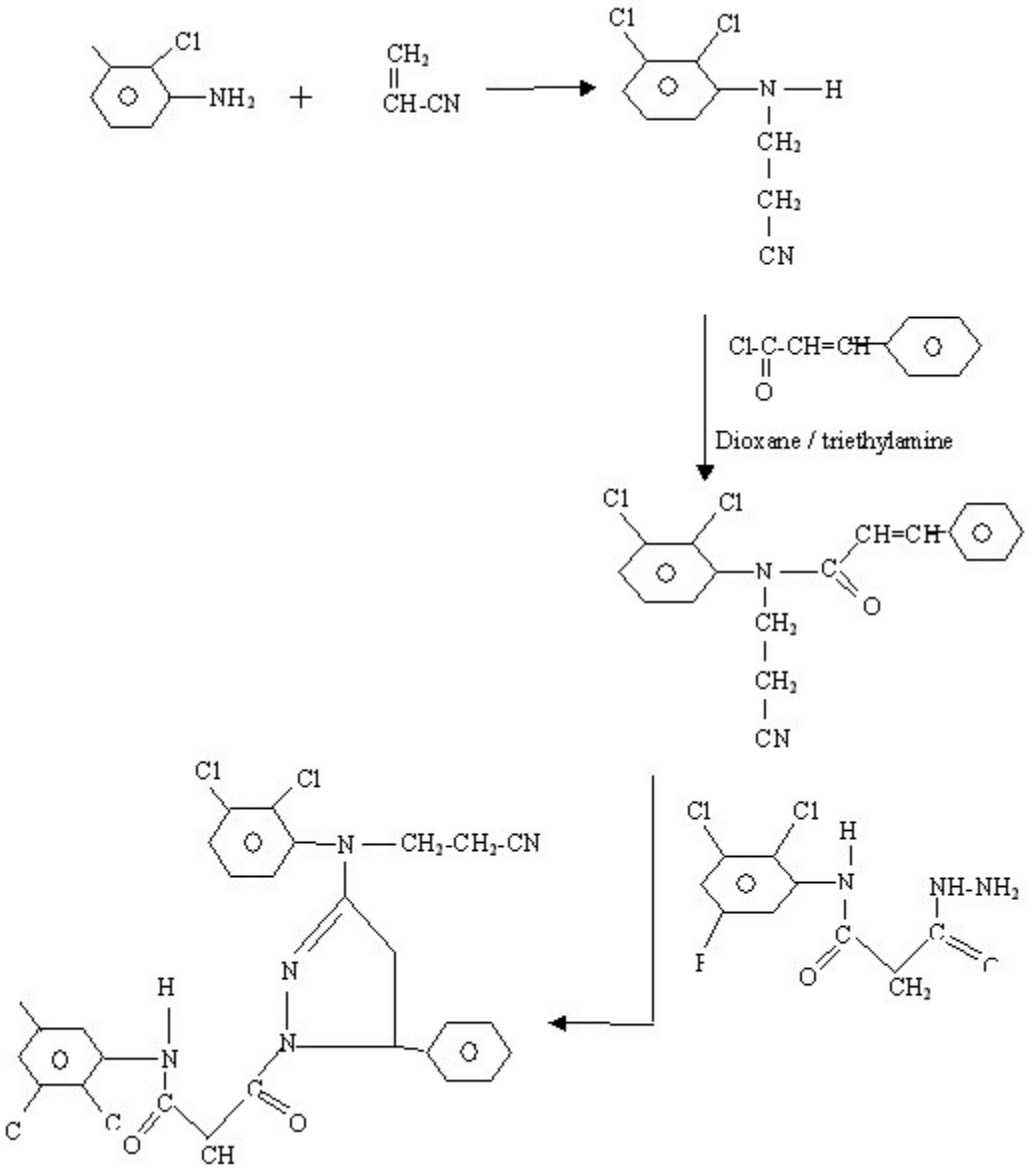
Yield: 66%, m.p. 242^{0}C, M.W.: 604, Anal. Calculated for C_{28} H_{23} Cl_4 N_5 O_2 Cl: 15.5, N: 7.6, found Cl: 15.1, N: 7.6%. U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log å]: 227.3 (4.96), 319.6 (4.70). *IR[KBr] V_{max} Cm^{-1}* **:** 3300-3040 [broad band due to (I) N-H stretching, secondary amide (Intra 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 e]

Yield: 55%, m.p. 271^{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. [($\lambda^{Et\ OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, ä 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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 f]

Yield: 61%, m.p. 263^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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



Scheme 1: (The reaction scheme for the complete synthesis of compounds)

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

Yield: 64%, m.p.: 267^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, ä 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: 623 [M], 624 [M+1].

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

Yield: 68%, m.p. 241^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5-phenyl pyrazoline [6 i]

Yield: 74%, m.p.: 257^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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: 620[M].

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

Yield: 77%, m.p. 266^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 k]

Yield: 54%, m.p. 234^{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. [(λ $^{Et\ OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 l]

Yield: 64%, m.p. 258^{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. [(λ $^{Et\ OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 m]

Yield: 69%, m.p. 264^{0}C, M.W.: 634, Anal. Calculated for $C_{29}H_{25}Cl_4$ N_5 O_3, Cl: 15.5, N: 7.6, found Cl: 15.2, N: 7.5%. U.V. [(ë $^{Et\ OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, ä 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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5-phenyl pyrazoline [6 n]

Yield: 65%, m.p. 249^{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. [($\lambda^{Et\ OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 o]

Yield: 61%, m.p. 245^{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. [($\lambda^{Et\ OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-

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

CS. No.	R	Color	m.p.(°C)	Yield (%)	M.W.	Molecular Formula
6a.	H	Yellow	252	66	589	$C_{27}H_{21}Cl_4N_5O_2$
6b.	CH_3(o)	Cream	275	48	604	$C_{28}H_{23}Cl_4N_5O_2$
6c.	CH_3(m)	Light Yellow	266	56	604	$C_{28}H_{23}Cl_4N_5O_2$
6d.	CH_3(p)	Light Yellow	242	66	604	$C_{28}H_{23}Cl_4N_5O_2$
6e.	Cl(o)	white	271	55	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6f.	Cl(m)	Light Yellow	263	61	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6g.	Cl(p)	Cream	267	64	623.5	$C_{27}H_{20}Cl_5N_5O_2$
6h.	O-CH_3(o)	Yellow	241	68	620	$C_{28}H_{23}Cl_4N_5O_3$
6i.	O-CH_3(m)	White	257	74	620	$C_{28}H_{23}Cl_4N_5O_3$
6j.	O-CH_3(p)	Cream	266	77	620	$C_{28}H_{23}Cl_4N_5O_3$
6k.	F(p)	Yellow	234	54	608	$C_{27}H_{20}Cl_4F_1N_5O_2$
6l.	Br(o)	Dark brown	258	64	669	$C_{27}H_{20}Cl_4N_5O_2Br$
6m.	O-C_2H_5 (o)	L. Brown	264	69	634	$C_{29}H_{25}Cl_4N_5O_3$
6n.	O-C_2H_5 (m)	Brown	249	65	634	$C_{29}H_{25}Cl_4N_5O_3$
6o.	O-C_2H_5 (p)	Brown	245	61	634	$C_{29}H_{25}Cl_4N_5O_3$
6p.	CO_2H (o)	Brown	253	70	634	$C_{28}H_{21}Cl_4N_5O_4$
6q.	CO_2H (m)	Brown	248	65	634	$C_{28}H_{21}Cl_4N_5O_4$
6r.	CO_2H (p)	L. brown	267	59	634	$C_{28}H_{21}Cl_4N_5O_4$
6s.	Br(m)	Brown	243	63	669	$C_{27}H_{20}Cl_4N_5O_2Br$
6t.	Br(p)	Brown	256	54	669	$C_{27}H_{20}Cl_4N_5O_2Br$

All compounds gave satisfactory elemental analysis.

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

Yield: 63%, 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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-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, 3-dichloroanilinomalonyl)]-3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazoline [6 t]

Yield: 54%, m.p. 256^{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. [($\lambda^{Et\,OH}_{Max}$ nm), log å]: 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, 3-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, d 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.

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 ìg/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,) h*ave* 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 *M. tuberculosis* at 100mg/mL concentration other compounds were found to be inactive. Results are assembled in Table 2.

RESULTS AND DISCUSSION

Newly synthesized *1-[(2, 3-dichloroanilinomalonyl)] -3-(N-2'-cyanoethyl -N-2, 3-dichloroanilino)-5- phenyl pyrazolines have been*

Table 2: Tuberculostatic Activity of new pyrazolines

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

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

synthesized by the reaction of N-cinnamoyl-N-2'-cyanoethyl -2, 3-dichloro aniline with *Ethyl-2-(2, 3-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°C 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.

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