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Synthesis, Characterization, and Biological Activities of New 1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-cinnamoyl) 2, 5-dichloroanilino)]-5-phenyl Pyrazoline Derivatives

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Abstract

A new series of 1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline have been synthesized in 49 to 66% yield, by the reaction of N-cinnamoyl-N-2'-cyanoethyl-2,5-dichloroaniline with 2-[(N- cinnamoyl) 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, 7d, 7e, 7j, 7n, and 7s) shown significant activity and the compound (7i, 7k, 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, 7k, 7m, and 7r) shown significant activities and compound (7a, 7d, 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 37^0C and observed, the compound (7a, 7d, 7e, 7j, and 7n) 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

Recently, several studies have been published on the synthesis and biological properties of pyrazoline and substituted Pyrazolines due to their interesting biological activities. This reflects their widely important applications in different fields, such as 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

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 discs on a Pye Unicam SP 3-300 or a Shimadzu FT-IR 8101 PC infrared spectrophotometer. The ^{1}H –NMR (200 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: 85%, M. P.: 89^{0}C, M. W.: 276. Anal. calculation for $C_{11}H_{11}N_1O_3Cl_2$: Found: C 47.7, H: 4.0, O: 17.2, N: 5.1, Cl: 25.4, Calcd. C: 47.8, H: 4.0, O: 17.4, N: 5.1, Cl: 25.7. *IR [KBr]* V_{max} Cm^{-1} : 1665-1660

[C=O diketone], 1290 [-O- Ester], 765-755 [2,5- disubstituted benzene], 1255 [C-Cl Stretching], 1595, 1525 , 1445 [C=C ring stretching], 3155 [N-H Stretching], 3040[C-H aromatic], 1330-1325 [C-H Stretching]. *PMR (DMSO):* δ 4.44 (2H, s, CO-CH_2-CO), 4.2 (2H, s, NH_2), 7.4-8.5 (3H, m, Ar-H), 9.3 (1H, s, CO-NH D_2O exchangeable), 10.5 [1H, s, Ar-NH D_2O exchangeable].

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

Cinnamoyl Chloride (10gm; 0.06 mol), dioxane (6 ml), Ethyl-2-(2,5-dichloroanilido) ethanoate (16.5 gm; 0.06 mol) and triethylamine (6.06 gm; 0.06 mol) were placed in a round bottomed flask carrying reflux condenser 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-cinnamoyl) 2, 5-dichloroanilido] ethanoate separated or solid. It was filtered under suction, dried and purified by recrystallization from aqueous methanol (1:1) in white crystals. Yield = 92 %, MP = 99°C Analytical calculation for $C_{20}H_{17}N_1O_4Cl_2$:[FW = 406], Calculated: N 3.4 , C 59.1, H 4.2 , O 15.8 , Cl 17.5 , Found : N 3.3, C 59.0 , H 4.1 , O 15.5 , Cl 17.4. *IR [KBr]* V_{max} cm^{-1}*:* 1745 [C=O diketone], 1335 [-C-O- Ester], 775[2,5- disubstituted benzene], 1085 [C-Cl Stretching], 1590, 1545 , 1475 [C=C Ring stretching], 3175 [N-H Stretching], 3055[C-H aromatic], 1340-1335 [C-H Stretching]. *PMR (DMSO):* δ 4.36 [2H, s, CO-CH_2-CO], 4.2 [2H, s, NH_2], 7.7-8.5 [3H, m, Ar-H], 9.8 [1H, s, CO-NH D_2O exchangeable], 10.4 [1H, s, Ar-NH D_2O exchangeable].

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

Ethyl-2-[(N-cinnamoyl) 2, 5-dichloroanilido]ethanoate (12.2 gm; 0.03 mol), ethanol (8 ml) and hydrazine hydrate (15 ml; 80%) were mixed together and stirred for thirty five minutes. 2-[(N-cinnamoyl) 2, 5-dichloroanilido] acetohydrazide was filtered under suction and recrystallised from ethanol in white crystals. Yield; 76%, MP = 189°C, MW 392 Analytical calculation for $C_{18}H_{15}N_3O_3Cl_2$: Calculated: N 10.7 ,C 55.1 ,H 3.8 ,O 12.2, Cl 18.1, Found: N 10.6, C 55.0, H 03.7, O 12.1, Cl 18.0. *IR [KBr]* V_{max} cm^{-1}*:* 3190 [N-H Stretching], 3070 [C-H aromatic], 1695 [C=O diketone], 1440 [C-Cl aromatic], 1580, 1560, 1455 [C=C ring stretching]. *PMR (DMSO):* δ 4.46 (2H, s, CO-CH_2-CO), 4.7 (2H, s, NH_2), 7.2-8.5 (3H, m, Ar-H), 9.2 (1H, s, CO-NH D_2O exchangeable), 10.8 (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. 258^0C/0.5mm was recovered. The N-Cyanoethyl-2, 5-dichloroaniline was

obtained as light yellow colored viscous liquid at 178-179^{0}C/mm which solidified after keeping overnight. Yield: 15.9g (97%)., M.P. 83^{0}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^{0}C/ 18-20mm pressure.

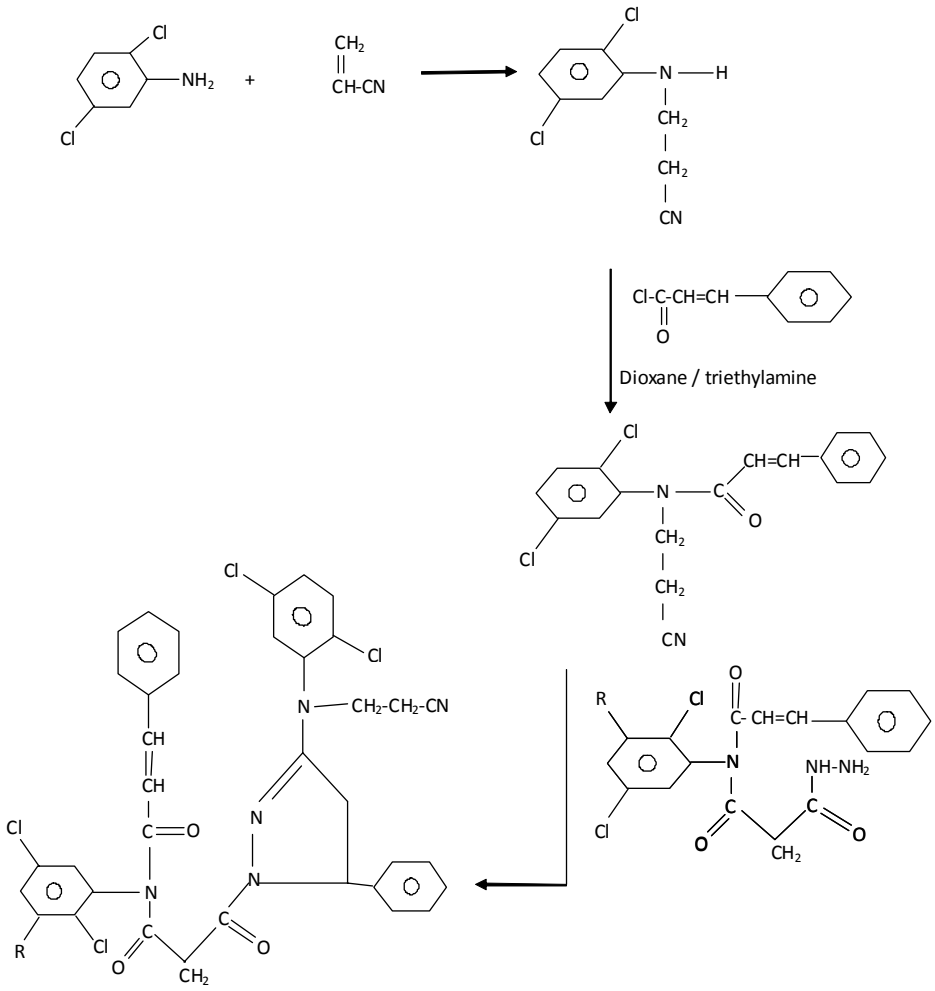
Synthesis of N-Cinnamoyl -N-2'-Cyanoethyl -2, 5-dichloroaniline [6]

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 overnight triethylamine hydrochloride separated as solid. It was filtered and contents concentrated when crystals separated out. Two crystallizations from ethanol gave shining white needles. Yield: 66 %, M.P.: 168^{0}C, Anal. Calculated for C_{18} H_{14} Cl_2 N_2 O; M.W. 345; Calcd. C:62.6; H:4.1; Cl:20.6; N: 8.1, O: 4.6; found C:62.4; H:4.0; Cl:20.5; N: 8.2, O: 4.3; *IR[KBr]* V_{max} Cm^{-1} *:* 3285-3055 (C-H stretching , aromatic), 2960 and 2895 (C-H Stretching, aliphatic (asymmetric) and C-H stretching , aliphatic (symmetric), 2225(C-N stretching), 1665(C=C stretching , benzene ring), 1655 C=O (stretching, tertiary amide), 1625, 1570, 1465, (C=C ring stretching), 1060, 765, (2, 5-disubstituted benzene).

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

A mixture of N-cinnamoyl-N-2'-cyanoethyl - 2, 5-dichloroaniline (0.345 g; 0.001 mol), 2-[(N-cinnamoyl) 2, 5-dichloroanilido] acetohydrazide (0.392g; 0.001 mol), dioxane (3 ml), and glacial acetic acid (2 drops) was refluxed for seven 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: 60%, M.P.: 263^{0}C, M.W.: 719, Anal. Calculated for C36 H27 Cl4 N5 O3 C: 60.1, H:3.8, Cl: 19.7; N: 9.7, O: 6.7; found C: 60.0, H:3.6, Cl: 19.6; N: 9.4, O: 6.5; U.V. [(λ Et OHMax nm), log ε]: 216.7 (4.95), 317.7 (4.72). IR[KBr] Vmax Cm-1 : 3310-2875 [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), 1665 [C=O and N-H (amide)] , 1590 (C=N stretching), 1580, 1495, 1420 (C=C ring stretching , aromatic), 1060, 850, (C-Cl stretching , 2, 5-disubstituted aromatic ring). 1H-NMR (250 MHz, δ ppm, DMSO-d6,): 2.35-2.50 (2H, s, CH2), 3.5-3.8 (3H, s, CH3), 4.30-4.55(1H, s, NH), 6.95-7.55 (13H, m, ArH). 3.20 (1H, dd, JAM = 18 HZ, JAX = 4.65 HZ, C4- HA of pyrazoline ring). 3.90 (1H, dd JMA = 17.80 Hz, JMX = 13.60 Hz, C4-HM of pyrazoline ring) ,

4.80 (1H, d, J = 16.22 Hz COCH geminal proton), 5.65 (1H, dd JMX 12.80 HZ , JAX = 4.66 Hz, C5-HX of pyrazoline ring). Synthetic sequence for new pyrazolines has been outlined in scheme-I.



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) confirmed the structures of the new compounds.

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

Yield: 60%, M.P.: 263^{0}C, M.W.: 719, Anal. Calculated for C36 H27 Cl4 N5 O3 C: 60.1, H:3.8, Cl: 19.7; N: 9.7, O: 6.7; found C: 60.0, H:3.6, Cl: 19.6; N: 9.4, O: 6.5; U.V. [(λ Et OHMax nm), log ε]: 216.7 (4.95), 317.7 (4.72). IR[KBr] Vmax Cm-1 : 3310-2875 [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), 1665 [C=O and N-H (amide)] , 1590 (C=N stretching), 1580, 1495, 1420 (C=C ring stretching , aromatic), 1060, 850, (C-Cl stretching , 2, 5-disubstituted aromatic ring). 1H-NMR (250 MHz, δ ppm, DMSO-d6,): 2.35-2.50 (2H, s, CH2), 3.5-3.8 (3H, s, CH3), 4.30-4.55(1H, s, NH), 6.95-7.55 (13H, m, ArH). 3.20 (1H, dd, JAM = 18 HZ, JAX = 4.65 HZ, C4- HA of pyrazoline ring). 3.90 (1H, dd JMA = 17.80 Hz, JMX = 13.60 Hz, C4-HM of pyrazoline ring) , 4.80 (1H, d, J = 16.22 Hz COCH geminal proton), 5.65 (1H, dd JMX 12.80 HZ , JAX = 4.66 Hz, C5-HX of pyrazoline ring).

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

Yield: 57%, M.P.: 271^{0}C, M.W.: 733, Anal. Calculated for $C_{37}H_{29}Cl_4N_5O_3$, C: 60.6, H:4.0, Cl: 19.4; N: 9.5, O: 6.5; found C: 60.4, H:4.0, Cl: 19.3; N: 9.3, O: 6.4; U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 214.6(4.70), 318.3 (4.80). *IR[KBr]* V_{max} Cm^{-1} : 3300-2870 [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), 1590, 1475, 1425 (C=C ring stretching , aromatic), 1065, 820, (C-Cl stretching , 2,5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.26-2.45 (2H, s, CH_2), 4.25-4.30(1H, s, NH), 6.90-7.45 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 16 H_Z, J_{AX} = 4.60H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.95 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.62(1H, d, J = 16.40 Hz COCH geminal proton), 5.90 (1H, dd J_{MX} 12.55 H_Z , J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 54%, M.P.: 268^{0}C, M.W.: 733, Anal. Calculated for $C_{37}H_{29}Cl_4N_5O_3$, C: 60.6, H:4.0, Cl: 19.4; N: 9.5, O: 6.5; found C: 60.5, H:4.0, Cl: 19.2; N: 9.4, O: 6.3; U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 214.2(4.80), 318.6 (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], 2255(C N stretching), 1665 [C=O and N-H (amide)] , 1590 (C=N stretching), 1580, 1475, 1430 (C=C ring stretching , aromatic), 1065, 820, (C-Cl stretching , 2,5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.22-2.40 (2H, s, CH_2), 4.20-4.45(1H, s, NH), 6.82-7.40 (13H, m, ArH). 3.22 (1H, dd, J_{AM} = 16 H_Z, J_{AX} = 4.60H_Z, C_4- H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.85 Hz, C_4-H_M of pyrazoline ring) , 4.65(1H, d, J = 16.40 Hz COCH geminal proton), 5.60 (1H, dd J_{MX} 12.45 H_Z , J_{AX} = 4.60 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 59%, M.P.: 270^{0}C, M.W.: 733, Anal. Calculated for $C_{37}H_{29}Cl_4N_5O_3$, C: 60.6, H:4.0, Cl: 19.4; N: 9.5, O: 6.5; found C: 60.2, H:4.1, Cl: 19.4; N: 9.4, O: 6.4; U.V. [($\lambda^{Et\,OH}_{M\,ax}$ nm), log ε]: 213.8(4.95), 318.2 (4.80). *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], 2245(C N stretching), 1645 [C=O and N-H (amide)] , 1575 (C=N stretching), 1565, 1460, 1420 (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,): 2.18-2.30 (2H, s, CH_2), 4.25-4.50(1H, s, NH), 6.80-7.55 (13H, m, ArH). 3.25 (1H, dd, J_{AM} = 16 H_Z, J_{AX} = 4.75H_Z, C_4- H_A of pyrazoline ring). 3.95 (1H, dd J_{MA} = 17.80 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.65(1H, d, J = 16.50 Hz COCH geminal proton), 5.80 (1H, dd J_{MX} 12.55 H_Z , J_{AX} = 4.55 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 49%, M.P.: 262^{0}C, M.W.: 753.5, Anal. Calculated for C_{36} H_{27} Cl_5 N_5 O_3 , C: 57.3, H:3.6, Cl: 23.6; N: 9.3, O: 6.4; found C: 57.2, H:3.5, Cl: 23.4; N: 9.2, O: 6.2; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 212.6 (5.30), 316.2 (5.20). *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], 2290(C N stretching), 1675 [C=O and N-H (amide)] , 1585 (C=N stretching), 1530, 1485, 1430 (C=C ring stretching , aromatic), 1080, 875, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 3.25-3.35 (2H, s, CH_2), 4.19-4.40(1H, s, NH), 6.80-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 4.12 (1H, dd J_{MA} = 18.25 Hz, J_{MX} = 13.90 Hz, C_4-H_M of pyrazoline ring) , 4.75 (1H, d, J = 16.20 Hz COCH geminal proton), 5.45 (1H, dd J_{MX} 13.20 H_Z , J_{AX} = 5.25 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 52%, M.P.: 267^{0}C, M.W.: 753.5, Anal. Calculated for C_{36} H_{27} Cl_5 N_5 O_3 , C: 57.3, H:3.6, Cl: 23.6; N: 9.3, O: 6.4; found C: 57.3, H:3.4, Cl: 23.5; N: 9.1, O: 6.3; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 213.6 (5.20), 315.8 (5.30). *IR[KBr]* V_{max} Cm^{-1} : 3300-2855 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2275(C N stretching), 1655 [C=O and N-H (amide)] , 1570 (C=N stretching), 1570, 1480, 1465 (C=C ring stretching , aromatic), 1075, 890, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 3.30-3.45 (2H, s, CH_2), 4.35-4.50(1H, s, NH), 7.20-7.40 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.85 H_Z, C_4- H_A of pyrazoline ring). 4.40 (1H, dd J_{MA} = 18.15 Hz, J_{MX} = 13.70 Hz, C_4-H_M of pyrazoline ring) , 4.85 (1H, d, J = 16.30 Hz COCH geminal proton), 5.50 (1H, dd J_{MX} 13.40 H_Z , J_{AX} = 5.35 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 50%, M.P.: 270^{0}C, M.W.: 753.5, Anal. Calculated for C_{36} H_{27} Cl_5 N_5 O_3 , C: 57.3, H:3.6, Cl: 23.6; N: 9.3, O: 6.4; found C: 57.0, H:3.2, Cl: 23.5; N: 9.3, O: 6.1; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 213.0 (5.10), 315.9 (5.28). *IR[KBr]* V_{max} Cm^{-1} : 3300-

2870[broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2265(C N stretching), 1660 [C=O and N-H (amide)] , 1560 (C=N stretching), 1565, 1475, 1435 (C=C ring stretching , aromatic), 1055, 875, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 3.20-3.35 (2H, s, CH_2), 4.10-4.30(1H, s, NH), 6.90-7.20 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.70 H_Z, C_4- H_A of pyrazoline ring). 4.30 (1H, dd J_{MA} = 18.25 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.25 Hz COCH geminal proton), 5.40 (1H, dd J_{MX} 13.25 H_Z , J_{AX} = 5.20 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 58%, M.P.: 254^{0}C, M.W.: 749, Anal. Calculated for $C_{37}\ H_{29}\ Cl_4\ N_5\ O_4$ C: 59.3, H:3.9, Cl: 19.0; N: 9.3, O: 8.5; found C: 59.2, H:3.7, Cl: 19.0; N: 9.2, O: 8.3; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.8(5.25), 318.0(4.75). *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], 2260(C N stretching), 1640 [C=O and N-H (amide)] , 1570 (C=N stretching), 1565, 1455, 1420 (C=C ring stretching , aromatic), 1045, 835, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.35-2.60 (2H, s, CH_2), 4.20-4.65(1H, s, NH), 6.85-7.25 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 17 H_Z, J_{AX} = 4.45 H_Z, C_4- H_A of pyrazoline ring). 3.80 (1H, dd J_{MA} = 17.90 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.65 (1H, d, J = 16.20 Hz COCH geminal proton), 5.55 (1H, dd J_{MX} 11.90 H_Z , J_{AX} = 4.95Hz, C_5-H_X of pyrazoline ring).

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

Yield: 61%, M.P.: 262^{0}C, M.W.: 749, Anal. Calculated for $C_{37}\ H_{29}\ Cl_4\ N_5\ O_4$ C: 59.3, H:3.9, Cl: 19.0; N: 9.3, O: 8.5; found C: 59.1, H:3.8, Cl: 19.0; N: 9.1, O: 8.4; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.3 (5.12), 318.2(4.85). *IR[KBr]* V_{max} Cm^{-1} : 3300-2870 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2245(C N stretching), 1645 [C=O and N-H (amide)] , 1580 (C=N stretching), 1555, 1450, 1430 (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,): 2.25-2.45 (2H, s, CH_2), 4.10-4.55(1H, s, NH), 6.90-7.40 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.55 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.95 Hz, J_{MX} = 13.75 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.15 Hz COCH geminal proton), 5.40 (1H, dd J_{MX} 12.10 H_Z , J_{AX} = 4.90 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 65%, M.P.: 267^{0}C, M.W.: 749, Anal. Calculated for $C_{37}\ H_{29}\ Cl_4\ N_5\ O_4$ C: 59.3, H:3.9, Cl: 19.0; N: 9.3, O: 8.5; found C: 59.3, H:3.8, Cl: 19.1; N: 9.1, O: 8.1; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 214.0 (5.05), 318.2(4.70). *IR[KBr]* V_{max} Cm^{-1} : 3300-2865[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), 1655 [C=O and N-H (amide)] , 1575 (C=N stretching), 1550, 1455, 1430 (C=C ring stretching , aromatic), 1040, 845, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-$d_{6,}$): 2.30-2.60 (2H, s, CH_2), 4.10-4.45(1H, s, NH), 6.75-7.10 (13H, m, ArH). 3.20 (1H, dd, J_{AM} = 18 $H_{Z,}$ J_{AX} = 4.40 H_Z, C_4- H_A of pyrazoline ring). 3.75 (1H, dd J_{MA} = 18.10 Hz, J_{MX} = 13.80 Hz, C_4-H_M of pyrazoline ring) , 4.75 (1H, d, J = 16.30 Hz COCH geminal proton), 5.45 (1H, dd J_{MX} 12.15 H_Z , J_{AX} = 4.80 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 57%, M.P.: 240^{0}C, M.W.: 737, Anal. Calculated for C_{36} H_{26} Cl_4 F_1N_5 O_3 C: 58.6, H:3.5, Cl: 19.3; N: 9.5, O: 6.5; F: 2.6 found C: 58.4, H:3.4, Cl: 19.5; N: 9.4, O: 6.5; F: 2.5 U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 217.1 (4.95), 318.1 (4.70). *IR[KBr]* V_{max} Cm^{-1} : 3300-2825[broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2285(C N stretching), 1690 [C=O and N-H (amide)] , 1540 (C=N stretching), 1545, 1425, 1410 (C=C ring stretching , aromatic), 1080, 825, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-$d_{6,}$): 2.30-2.55 (2H, s, CH_2), 4.10-4.65(1H, s, NH), 6.60-7.10 (13H, m, ArH). 3.25 (1H, dd, J_{AM} = 18 $H_{Z,}$ J_{AX} = 4.25 H_Z, C_4- H_A of pyrazoline ring). 3.75 (1H, dd J_{MA} = 17.90Hz, J_{MX} = 13.40 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.20 Hz COCH geminal proton), 5.20 (1H, dd J_{MX} 12.50 H_Z , J_{AX} = 4.45 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 52%, M.P.: 254^{0}C, M.W.: 799, Anal. Calculated for C_{36} H_{26} Br_1 Cl_4 N_5 O_3 C: 54.1, H:3.3, Cl: 17.8; N: 8.8, O: 6.0; Br: 10; found C: 54.0, H:3.2, Cl: 17.7; N: 8.7, O: 6.1; Br: 10.1; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 213.1 (4.80), 318.2 (4.60). *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], 2245(C N stretching), 1635 [C=O and N-H (amide)] , 1565 (C=N stretching), 1614, 1535, 1485 (C=C ring stretching , aromatic), 1070, 835, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-$d_{6,}$): 2.30-2.60 (2H, s, CH_2), 4.30-4.55(1H, s, NH), 6.90-7.25 (13H, m, ArH). 3.27 (1H, dd, J_{AM} = 18 $H_{Z,}$ J_{AX} = 4.76 H_Z, C_4- H_A of pyrazoline ring). 4.25 (1H, dd J_{MA} = 17.85 Hz, J_{MX} = 13.45 Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.60 Hz COCH geminal proton), 5.80 (1H, dd J_{MX} 13.25 H_Z , J_{AX} = 4.65 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 60%, M.P.: 259^{0}C, M.W.: 764, Anal. Calculated for C_{38} $H_{31}Cl_4$ N_5 O_4 C: 59.7, H:4.1, Cl: 18.6; N: 9.2, O: 8.4; found C: 59.6, H:4.0, Cl: 18.5; N: 9.3, O: 8.3; U.V.

[($\lambda_{Max}^{Et\ OH}$ nm), log ε]: 212.8 (4.50), 318.5 (4.95). *IR[KBr] V_{max} Cm^{-1}* : 3300-2900 [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), 1630 [C=O and N-H (amide)] , 1560 (C=N stretching), 1560, 1450, 1420 (C=C ring stretching , aromatic), 1060, 865, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.25-2.40 (2H, s, CH_2), 4.10-4.35(1H, s, NH), 6.75-7.15 (13H, m, ArH). 3.10 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.40 H_Z, C_4- H_A of pyrazoline ring). 3.80 (1H, dd J_{MA} = 17.70 Hz, J_{MX} = 13.45 Hz, C_4-H_M of pyrazoline ring) , 4.55 (1H, d, J = 16.25 Hz COCH geminal proton), 5.35(1H, dd J_{MX} 12.85 H_Z , J_{AX} = 4.55 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 57%, M.P.: 248^{0}C, M.W.: 764, Anal. Calculated for C_{38} $H_{31}Cl_4$ N_5 O_4 C: 59.7, H:4.1, Cl: 18.6; N: 9.2, O: 8.4; found C: 59.5, H:4.1, Cl: 18.4; N: 9.1, O: 8.2; U.V. [($\lambda_{Max}^{Et\ OH}$ nm), log ε]: 213.1 (4.75), 318.3 (5.15). *IR[KBr] V_{max} Cm^{-1}* : 3300-2900 [broad band due to (I) N-H stretching, secondary amide (Intra molecular hydrogen bond), (II) C-H stretching , aromatic , (iii) C-H stretching , aliphatic], 2215(C N stretching), 1645 [C=O and N-H (amide)] , 1545 (C=N stretching), 1560, 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,): 2.10-2.30 (2H, s, CH_2), 4.05-4.30(1H, s, NH), 6.75-7.05 (13H, m, ArH). 3.25 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.25 H_Z, C_4- H_A of pyrazoline ring). 3.55 (1H, dd J_{MA} = 17.65 Hz, J_{MX} = 13.55 Hz, C_4-H_M of pyrazoline ring) , 4.55 (1H, d, J = 16.10 Hz COCH geminal proton), 5.25(1H, dd J_{MX} 12.70 H_Z , J_{AX} = 4.40 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 61%, M.P.: 256^{0}C, M.W.: 764, Anal. Calculated for C_{38} $H_{31}Cl_4$ N_5 O_4 C: 59.7, H:4.1, Cl: 18.6; N: 9.2, O: 8.4; found C: 59.6, H:4.0, Cl: 18.3; N: 9.1, O: 8.3; U.V. [($\lambda_{Max}^{Et\ OH}$ nm), log ε]: 213.4 (4.96), 318.2 (4.88). *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], 2230(C N stretching), 1650 [C=O and N-H (amide)] , 1555 (C=N stretching), 1570, 1460, 1440 (C=C ring stretching , aromatic), 1055, 845, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.20-2.45 (2H, s, CH_2), 4.25-4.55(1H, s, NH), 6.85-7.25 (13H, m, ArH). 3.35 (1H, dd, J_{AM} = 19 H_Z, J_{AX} = 4.75 H_Z, C_4- H_A of pyrazoline ring). 3.90 (1H, dd J_{MA} = 17.60 Hz, J_{MX} = 13.70Hz, C_4-H_M of pyrazoline ring) , 4.70 (1H, d, J = 16.20 Hz COCH geminal proton), 5.50(1H, dd J_{MX} 12.75 H_Z , J_{AX} = 4.90 Hz, C_5-H_X of pyrazoline ring).

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

Yield: 55%, M.P.: 255^{0}C, M.W.: 799, Anal. Calculated for C_{36} H_{26} Br_1 Cl_4 N_5 O_3 C: 54.1, H:3.3, Cl: 17.8; N: 8.8, O: 6.0; Br: 10; found C: 54.1, H:3.1, Cl: 17.5; N: 8.5, O:

6.0; Br: 10.2; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 212.7 (4.90), 317.9 (4.80). *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], 2275(C N stretching), 1680 [C=O and N-H (amide)] , 1610 (C=N stretching), 1570, 1520, 1475 (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,): 2.35-2.65 (2H, s, CH_2), 4.35-4.55(1H, s, NH), 6.70-7.25 (13H, m, ArH). 3.24 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.60 H_Z, C_4- H_A of pyrazoline ring). 4.50 (1H, dd J_{MA} = 17.30 Hz, J_{MX} = 13.20 Hz, C_4-H_M of pyrazoline ring) , 4.60 (1H, d, J = 16.40 Hz COCH geminal proton), 5.60 (1H, dd J_{MX} 13.15 H_Z , J_{AX} = 4.60Hz, C_5-H_X of pyrazoline ring).

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

Yield: 53%, M.P.: 261^{0}C, M.W.: 799, Anal. Calculated for $C_{36}\ H_{26}\ Br_1\ Cl_4\ N_5\ O_3$ C: 54.1, H:3.3, Cl: 17.8; N: 8.8, O: 6.0; Br: 10; found C: 54.0, H:3.2, Cl: 17.6; N: 8.6, O: 6.1; Br: 10.1; U.V. [($\lambda^{Et\ OH}_{Max}$ nm), log ε]: 212.7 (4.90), 318.2 (4.85). *IR[KBr]* V_{max} Cm^{-1} : 3300-2865 [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), 1610 [C=O and N-H (amide)] , 1585 (C=N stretching), 1555, 1525, 1445 (C=C ring stretching , aromatic), 1025, 825, (C-Cl stretching , 2, 5-disubstituted aromatic ring). ^{1}H-NMR (250 MHz, δ ppm, DMSO-d_6,): 2.26-2.48 (2H, s, CH_2), 4.23-4.32(1H, s, NH), 6.82-7.35 (13H, m, ArH). 3.26 (1H, dd, J_{AM} = 18 H_Z, J_{AX} = 4.42H_Z, C_4- H_A of pyrazoline ring). 4.52 (1H, dd J_{MA} = 16.90 Hz, J_{MX} = 13.45 Hz, C_4-H_M of pyrazoline ring) , 4.52 (1H, d, J = 16.33 Hz COCH geminal proton), 5.75 (1H, dd J_{MX} 13.0 H_Z , J_{AX} = 4.65Hz, C_5-H_X of pyrazoline ring).

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

CS. No.	R	Color	*M.P. (˚C)*	*Yield (%)*	*M.W.*	*Molecular Formula*
7a.	H	Yellow	263	60	719	$C_{36}H_{27}Cl_4\ N_5O_3$
7b.	CH_3(o)	Cream	271	57	733	$C_{37}H_{29}Cl_4\ N_5O_3$
7c.	CH_3(m)	Light Yellow	268	54	733	$C_{37}H_{29}Cl_4\ N_5O_3$
7d.	CH_3(p)	Light Yellow	270	59	733	$C_{37}H_{29}Cl_4\ N_5O_3$
7e.	Cl(o)	white	262	49	753.5	$C_{36}H_{27}Cl_5\ N_5O_3$
7f.	Cl(m)	Light Yellow	267	52	753.5	$C_{36}H_{27}Cl_5\ N_5O_3$
7g.	Cl(p)	Cream	270	50	753.5	$C_{36}H_{27}Cl_5\ N_5O_3$
7h.	O-CH_3(o)	Yellow	254	58	749	$C_{37}H_{29}Cl_4\ N_5O_4$
7i.	O-CH_3(m)	White	262	61	749	$C_{37}H_{29}Cl_4\ N_5O_4$
7j.	O-CH_3(p)	Cream	267	65	749	$C_{37}H_{29}Cl_4\ N_5O_4$
7k.	F(p)	Yellow	240	57	737	$C_{36}H_{26}Cl_4N_5O_3F_1$

7l.	Br(o)	Dark brown	254	52	799	$C_{36}H_{26}Cl_4N_5O_3Br_1$
7m.	O-C_2H_5 (o)	L. Brown	259	60	764	$C_{38}H_{31}Cl_4N_5O_4$
7n.	O-C_2H_5(m)	Brown	248	57	764	$C_{38}H_{31}Cl_4N_5O_4$
7o.	O-C_2H_5 (p)	Brown	256	61	764	$C_{38}H_{31}Cl_4N_5O_4$
7p.	CO_2H (o)	Brown	247	66	763	$C_{37}H_{27}Cl_4N_5O_5$
7q.	CO_2H (m)	Brown	241	61	763	$C_{37}H_{27}Cl_4N_5O_5$
7r.	CO_2H (p)	L. brown	262	57	763	$C_{37}H_{27}Cl_4N_5O_5$
7s.	Br(m)	Brown	259	53	799	$C_{36}H_{26}Cl_4N_5O_3Br_1$
7t.	Br(p)	Brown	254	58	799	$C_{36}H_{26}Cl_4N_5O_3Br_1$

All compounds gave satisfactory elemental analysis.

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 μg/mL concentration. Ampicillin and Tetracycline used as a reference compound. The compound *(7a, 7d, 7e, 7j, 7n, and 7s* shown significant activity and the compound *(7i, 7k, 7t,) 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 *(7c, 7k, 7m, and 7r)* shown significant activities and compound *(7a, 7d, 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.

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 *(7a, 7d, 7e, 7j, and 7n)* 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
7a.	1-[(2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N-cinnamoyl) -2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0

7b.	1- [(o-methyl) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7c.	1- [(m-methyl) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7d.	1- [(p-methyl) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7e.	1- [(o-chloro) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7f.	1- [(m-chloro) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7g.	1- [(p-chloro) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7h.	1- [(o-methoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7i.	1- [(m-methoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7j.	1- [(p-methoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7k.	1- [(p-floro) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline .	+	+
7l.	1- [(o-bromo) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7m.	1- [(o-ethoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7n.	1- [(m-ethoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	0
7o.	1- [(p-ethoxy) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7s.	1- [(m-bromo) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 2, 5-dichloroanilino)]-5- phenyl pyrazoline	+	+
7t.	1- [(p-bromo) -2, 5-dichloroanilinomalonyl)-3-(N-2'-cyanoethyl)-2-(N- cinnamoyl) 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-cinnamoyl) -2, 5-dichloroanilino)]-5- phenyl pyrazoline have been synthesized by the reaction of* N-cinnamoyl-N-2'-cyanoethyl-2,5-dichloroaniline with 2-[(N-*cinnamoyl*) 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, 7d, 7e, 7j, 7n, and 7s)* shown significant activity and the compound *(7i, 7k, 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, 7k, 7m, and 7r)* shown significant activities and compound *(7a, 7d, 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 37^0C and observed, the compound *(7a, 7d, 7e, 7j, and 7n)* 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 *(7a, 7d, 7e, 7j, 7n, and 7s)* shown significant activity and the compound *(7i, 7k, 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, 7k, 7m, and 7r)* shown significant activities and compound *(7a, 7d, 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 37^0C and observed, the compound *(7a, 7d, 7e, 7j, and 7n)* inhibited the growth of *Mycobacterium tuberculosis* at 100mg/mL concentration other compounds were found to be inactive.

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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] Munawar 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.* , 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).