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Synthesis, Characterization and Antimicrobial Activity of Certain Novel Aryl Hydrazone Pyrazoline-5-Ones Containing Thiazole Moiety

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ABSTRACT

Purpose: The aim of this article is to synthesize, characterize and evaluate the antimicrobial activity of certain novel 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N^{l}-(4-substituted thiazol-2-yl)-hydrazides. ***Methods*:** The synthesized compounds were characterized by elemental analysis and IR, NMR and mass spectral data. The antimicrobial activity of novel compounds was evaluated by broth dilution method. ***Results*:** XVe, XVf and XVg have shown better antibacterial activity than other compounds of the series. XVa, XVc, XVd and XVe have shown better antifungal activity than the other compounds of the series. ***Conclusion*:** All compounds were found to exhibit fair degree of antimicrobial activity.

Introduction

Among nitrogen containing five membered heterocycles, pyrazolines and related heterocycles demonstrate various types of biological activities. The pharmaceutical importance of these compounds lies in the fact that they can be effectively utilized as antibacterial, antifungal, antidepressant, anti inflammatory, antioxidant, antiviral, antiparasitic, antitubercular and antitumor, insecticidal agents.[1-7] On the other hand the pharmacological properties of thiazoles have been well established. They also exhibit broad spectrum of chemotherapeutic properties such as antibacterial, antifungal and antitubercular, anti-HIV, anticonvulsant, anticancer, anti-inflammatory and analgesic.[8-14] Keeping in view the easily reproducible and feasible synthetic routes for synthesis and the importance of these two moieties namely, pyrazolines and thiazoles in the field of medicine, the authors have made an attempt to synthesize some novel compounds containing both these moieties and investigated for the possible antimicrobial activity.

Materials and Methods

All chemicals were obtained from Ranbaxy Laboratories Ltd, India. Nutrient broth, nutrient agar and 5 mm diameter antibiotic assay discs were obtained from Hi-Media Laboratories Limited, India. The standard bacterial and fungal strains were procured from National Centre for Cell Science (NCCS), Pune, India. UV/Visible Spectrophotometer manufactured by Shimadzu Corporation, Japan was used for absorption measurements.

General procedure for the synthesis of [3-methyl-5-oxo-4-(4^{l}-substituted aryl hydrazono)-4,5-dihydro-pyrazol-1-yl]- acetic acid N^{l}-(4-substituted thiazol-2-yl)-hydrazide XVa – h

Preparation of phenacyl bromides II a – g

Phenyl aryl bromides II a – g employed in the preparation of aryl hydrazono pyrazoline-5-ones containing substituted thiazole moiety XV were prepared by the reaction of various acetophenones I a – g with bromine in diethyl ether in presence of anhydrous aluminum chloride at 0 ºC.

A solution of aromatic ketone I a–g (0.05 mole) in pure anhydrous diethyl ether (10 mL) was taken in a three necked flask fitted with mechanical stirrer and a thermometer. The solution was cooled to 0 ºC and anhydrous aluminium chloride (50 mg) was added. Bromine (0.05 mole) was slowly added to the above solution. Excess of ether and hydrogen bromide were removed by applying suction. The solution was filtered and washed with petroleum ether. The crystals so obtained were washed with fresh portions of the solvent and recrystallized from minimum quantity of ethanol.

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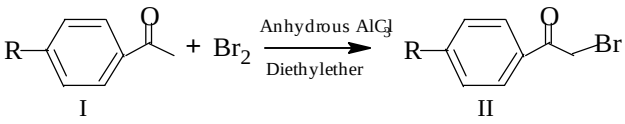
Similar procedure was applied for the synthesis of other compounds II b – g of the series (Scheme 1). The substituted aryl bromides were characterized by their characteristic melting points reported in the literature.[15-19]



Scheme 1. Synthesis procedure of compounds II series. [R = H(IIa), -CH_3 (IIb), -OCH_3 (IIc), -OH (IId), -NO_2 (IIe), -Cl (IIf), -Br (IIg)]

Synthesis of 3-(4′-substituted phenyl)-4-bromoacetyl sydnone VIII a – c

Synthesis of N-substituted glycines (aniline acetic acid)[20,21] *IV a – c:* A mixture of substituted aniline (0.5 mole), ethylchloroacetate (73.0g) and anhydrous sodium acetate (49.2 g) in 120 mL of ethyl alcohol was refluxed on an oil bath (120 ºC) for 6 hours. The reaction mixture was left overnight at room temperature and poured onto crushed ice. The precipitate formed was collected by filtration and dried. (ethyl ester of N-substituted glycine)

A mixture of ethyl ester of N-substituted glycine (0.4 mole) and sodium hydroxide (18 g) in 200 mL of water were refluxed for half an hour. The reaction mixture was cooled and acidified to a pH of 2 using hydrochloric acid. The precipitated N-substituted glycine was filtered, washed with cold water and recrystallized from ethyl alcohol.

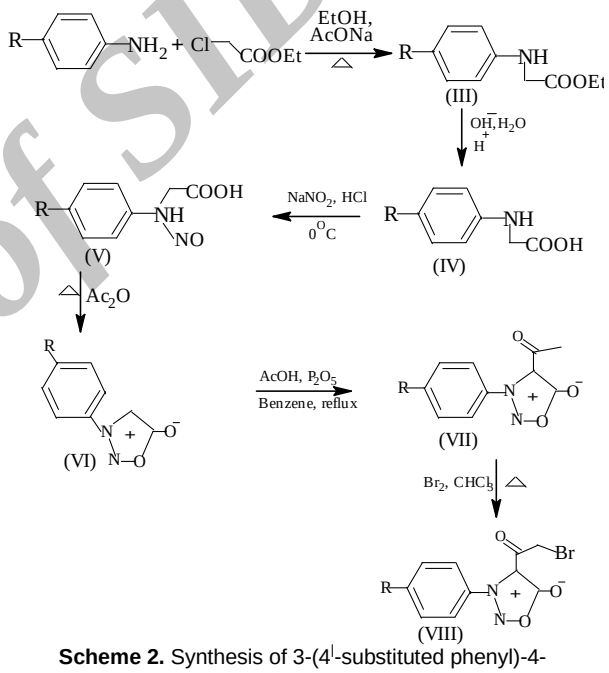
Synthesis of N-nitroso-N-substituted glycines V a – c[20]: To a suspension of N-substituted glycine IV a–c (0.1 mole) in water (120 mL) at 0 ºC, a solution of sodium nitrite (6.9 g, 0.1 mole) in water (24 mL) was added drop wise. After 2 hours, the reaction mixture was filtered and acidified with concentrated hydrochloric acid. The precipitate so formed was collected by filtration, washed with cold water, dried in air and recrystallized from aqueous alcohol.

Synthesis of 3-arylsydnone VI a – c[21]: N-nitroso-N-substituted glycine V a–c (0.1 mole) was heated with acetic anhydride (51 g) on a water bath for 3 hours. The reaction mixture was allowed to stand for 12 hours and poured into ice cold water, filtered and washed with water and then with 5% sodium bicarbonate solution. The solid obtained was washed with water, dried and recrystallized from benzene.

Synthesis of 4-acetyl-3-arylsydnone VII a – c[22]: To a suspension of phosphorous pentoxide (21.3 g, 0.15 mole) in thiophene (125 mL) taken in a three necked 500 mL round bottom flask fitted with reflux condenser equipped with a calcium chloride drying tube, 3-arylsydnone VI a – c (0.05 mole) was added. The magnetically stirred mixture was heated to reflux on a water bath. Glacial acetic acid (2.86 mL, 0.05 mole) was added drop wise through a dropping funnel. The stirred reaction mixture was heated for 5 hours. The mixture was cooled to room temperature. Benzene present was decanted and the remaining black residue was washed with 20 mL of benzene. Washings and the decanted solution were evaporated to dryness to yield a pale yellow solid. The solid was recrystallized from ethyl alcohol.

Synthesis of 4-bromoacetyl-3-arylsydnones VIII a – c[23]: To a solution of 4-acetyl-3-arylsydnone VII a–c (0.01 mole) in 30 mL of chloroform, 1.6 mL (0.01 mole) of bromine was added under irradiation of visible light (40 Watt candle). After 15 minutes, solvent was removed under vacuum. The residue was recrystallized from ethyl alcohol.

The reaction sequence is shown in Scheme 2.



Scheme 2. Synthesis of 3-(4′-substituted phenyl)-4-bromoacetyl sydnone VIII. [R = -H(a), -CH_3(b), -OCH_3(c)]

Synthesis of 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N′-(4-substituted thiazol-2-yl)-hydrazide XV a-h

Synthesis of substituted phenyl diazoniam chloride IX (A): The required primary amine was dissolved in a suitable volume of water containing 2.5 – 3.0 equivalents of hydrochloric acid (or sulphuric acid) by the application of heat if necessary. The solution obtained was cooled to 0°C to crystallize amine hydrochloride (or sulphate). An aqueous solution of sodium nitrite was added portion wise till there was free nitrous acid.

Synthesis of substituted phenyl diazonium ethyl acetoacetic ester (X): To a mixture of sodium acetate (1.0 g) in 100 mL of aqueous ethanol (50%) and a solution of ethylacetoacetate (0.1 mole) in 50 mL of

ethanol at 0 ºC, corresponding diazonium chloride was added slowly to get yellow crystals of X. The crystals were filtered, washed with water and dried.

Synthesis of 3-methyl-4-(phenyl hydrazono)-pyrozoline-5-one XI: Condensation of 4-substituted aryl hydrazono acetoacetic ester (X) and hydrazine in the presence of required amount of dimethyl formamide under microwave irradiation (microwave irradiation at 150W intermittently at 30 sec intervals for 2 minutes) led to the formation of 3-methyl-4-(4|-substituted arylhydrazono)-pyrozoline-5-one XI. After complete conversion as indicated by TLC, the reaction mixture was cooled by adding cold water. The precipitate XI was filtered and recrystallized from ethanol.

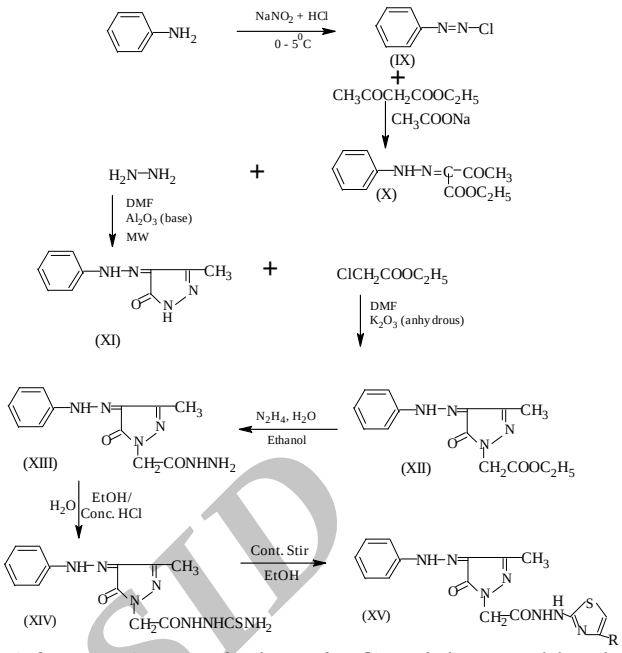
Synthesis of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid ethyl ester XII: A mixture of XI, anhydrous K_2CO_3 and DMF was stirred at room temperature for 8 hours. The reaction mixture was diluted with ice cold water. The solid separated XII was filtered and recrystalized from ethanol.

Synthesis of [3-Methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid hydrazide XIII: A solution of XII and hydrazine hydrate in ethanol were refluxed for five hours. The reaction mixture was cooled and poured onto ice cold water. The solid separated was filtered, washed with water and recrystallized from ethanol to give XIII.

Synthesis of thiosemicarbazone XIV: A mixture of [3-methyl-5-oxo -4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1yl]-acetic acid hydrazide XIII (0.01 mole), potassium thiocyanate (0.02 mole), concentrated hydrochloric acid (1 mL), ethyl alcohol (10 mL) and water (20 mL) were refluxed for 3 hours. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol-DMF mixture to give crystals of [3-methyl-5-oxo-4-(phenylhydrazono)-4,5-dihydropyrazol-1-yl]-acetothiosemicarbazone XIV.

Synthesis of [3-methyl-5-oxo-4-(phenyl hydrazono) 4,5-hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted-thiazole-2-yl)-hydrazide XV: A mixture of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro pyrazol-1-yl]-acetothiosemi-carbazone XIV (0.01 mole) in DMF (10 mL) and various bromoacetyl derivatives (0.01 mole) in ethanol (10 mL) was stirred at room temperature for about 2 hours. The solid separated was filtered, dried and recrystallized from ethanol-DMF mixture.

The above reaction of XIV with bromo acetophenone has been extended to *p*-tolyl, *p*-anisyl, *p*-hydroxy phenyl, *p*-nitrophenyl, *p*-chlorohphenyl, *p*-bromo phenyl, *N*-phenyl hydronyl, N-*p*-tolyl hydronyl, N-*p*-anisyl hydronyl substituents. The reaction sequence leading to the formation of these compounds is outlined in Scheme 3.



Scheme 3. Synthesis of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]- acetic acid *N*|-(4-substituted thiazol-2-yl)-hydrazide XV. [R = Phenyl (XVA), *p*-Tolyl (XVb), *p*-Anisyl (XVc), *p*-Hydroxy phenyl (XVd), *p*-nitro phenyl (XVe), *p*-chloro phenyl (XVf), *p*-bromo phenyl (XVg), *p*-phenyl sydnonyl (XVh), *p*-tolyl sydnonyl (XVi), *N*-*p*-anisyl sydnonyl (XVj)]

Results and Discussion

The structure of critical intermediate compounds namely XIII, XIV and XV were characterized by elemental analysis and IR, NMR and mass spectra (Table 1).

Table 1. Characterization data of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrayol-1-yl]-acetic acid hydrazide XIII.

Comp	MP (°C)	Yield (%)	Mol. formula	Found (%) (Cald)			
				C	H	N	O
XIII	152	65	$C_{12}H_{14}N_6O_2$	52.63 (52.55)	5.22 (5.14)	30.71 (30.64)	11.74 (11.67)

IR spectral details

The IR(KBr) spectra of [3-Methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid hydrazide (XIII) showed absorption bands around 3445, 3425, (2 bands) 3305, 1620, 1665, 1460 and 1455 cm^{-1} due to – NH_2, >NH, exo >C = N, cyclic carbonyl and five membered heterocyclic ring respectively.

XIII: 3445, 3425 (NH_2), 3305 (NH), 1620 (C=N), 1665 (C=O).

^{1}H NMR spectral details

The ^{1}H NMR (200MHz) spectrum of [3-Methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid hydrazide XIII was recorded in $CDCl_3$ + DMSO – d_6. The signal due to the methyl group appeared as a singlet at δ 1.0, integrating for three protons. The N-CH_2-CO protons came into resonance at δ3.85 as a singlet. The proton of NH-N = C has appeared as singlet at δ7.0. The NMR signal for CO-NH was

noticed at δ8.4 as a broad singlet. The NH_2 signal was observed at δ2.1 as a broad singlet. The aromatic protons of phenyl group have appeared at δ7.0 and δ7.14.

The characterization details of XIV are given below.

IR spectral details

The IR (KBr) spectra of XIV shows absorption bands around 3260, 1622, 1685, 1176, 2959 and 3180 cm^{-1} due to Ar-NH, C = N, C = O, C = S, C – H and NH functional groups respectively.

^{1}HNMR spectral details

The ^{1}HNMR (200MHz) spectra of XIV was recorded in $CDCl_3$+DMSO-d_6. The signals were noticed at δ2.29 (s, 3H, CH_3), δ δ3.3 (s, 2H, NH_2), δ4.80 (s, 2H, N-CH_2), δ 9.36 and δ 10.27 due to NH-NH group appeared as a two broad singlets, δ7.8 (s, 1H, Ar-NH), δ 7.4-7.6 (m, 5H, Ar-H).

Mass Spectral details

The mass spectrum of [3-methyl-5-oxo-4-(phenylhydrazono)-4,5-dihydro pyrazol-1-yl]-aceto thiosemicarbazone XIV exhibits the molecular ion peak (M^+) at m/z 347.

The fragmentation pattern noticed in mass spectrum of XIV is presented in Scheme 4. The molecular ion (M^+) was observed at m/z 347 (A, 23.7%). Disintegration (loss of NH_2 radical) of molecular ion ($M^{+\cdot}$) 'A' yielded the cation peak at m/z 331 (B, 15.7%). Elimination of CH_3CN molecule from molecular ion resulted in the fragment 'C' at m/z 306 (C, 31.5%). Expulsion of $CSNH_2$ radical from molecular ion 'A' produced the fragment 'D' at m/z 287 (D, 15.1%). Elimination of CSN_3H_4 radical afforded the cation 'E' at m/z 257 and was the base peak (100%). Disintegration (loss of $C_{11}H_{11}N_4O$ radical) of molecular ion 'A' resulted in the cation 'F' at m/z 132 (F, 51.3%). The fragmentation pattern clearly supported the structure of XIV.

The characterization (Elemental analysis and spectral data) details of XV are given below.

IR spectral details

The IR (KBr) spectrum of 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-phenyl thiazol-2-yl)-hydrazide XVa exhibited absorption band around 3230 cm^{-1} (C = Ostr), 1546 cm^{-1} (C = Nstr). Characterization data of compound XV is presented in Table 2.

IR Spectral data of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazide XV.

XVa: 3230 (NH), 2962 (CH), 1692 (C=O), 1546 (C=N)

XVc: 3240 (NH), 2868 (CH), 1687 (C=O), 1546 (C=N)

XVd: 3250 (NH), 2972 (CH), 1710 (C=O), 1552 (C=N)

XVe: 3260 (NH), 2980 (CH), 1720 (C=O), 1560 (C=N)

XVf: 3222 (NH), 2960 (CH), 1687 (C=O), 1548 (C=N)

XVh: 3276 (NH), 2930 (CH), 1690 (C=O), 1560 (C=N)

XVi: 3276 (NH), 2941 (CH), 1689 (C=O), 1559 (C=N) 1739 (sydnone C=O str).

XVj: 3269 (NH), 2910 (CH), 1681(C=O), 1541(C=N)

^{1}HNMR spectral details

The ^{1}HNMR (200MHz) spectra of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1- yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazide XV taken in $CDCl_3$ + DMSO-d_6 showed signals at δ2.23 (S, 3H.CH_3), δ4.90 (s, 2H, NCH_2CO), δ7.35 (s, H, thiazole, 4H), δ7.2 (s, H, Ar-NH), δ9.54 (s, H, NH), δ10.65 (s, H, CONH), δ7.2-7.4 (m, 10H, Ar-H).

^{1}HNMR spectral data of [3-methyl-5-oxo-1(phenyl-hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N|-(4-substituted thiazol-2-yl)-hydrazide XV.

XVa: 2.23 (s, 3H, CH_3), 4.90 (s, 2H, NCH_2CO), 7.35 (s, H, thiazole-4H), 7.2 (s, H, Ar-NH), 9.54 (s, H, NH), 10.65 (s, H, CONH), 7.2-7.4 (m, 10H, Ar-H).

XVd: 2.27 (s, 3H, CH_3), 4.90 (s, 2H, NCH_2CO), 7.46 (d, 2H, o-protons of p-hydroxy phenyl), 7.60 (d,2H, m-protons of p-hydroxy phenyl), 7.36 (s, H, thiayole-4H), 7.4 (s, H, Ar-NH), 9.56 (s, H, NH), 10.67 (s, H, CONH, 7.2-7.4 (m, 5H, Ar-H)

XVf: 2.33 (s, 3H, CH_3), 4.95 (s, 2H, NCH_2CO), 7.59 (d, 2H, o-protons of p-hydroxy phenyl), 7.77 (d, 2H, m-protons of *p*-chloro phenyl), 7.37 (s, H, thiazole-4H), 7.8 (s, H, Ar-NH), 9.69 (s, H, NH), 10.71 (s, H, CONH), 7.4-7.6 (m, 5H, Ar-H)

XVh: 2.27 (s, 3H, CH_3), 4.66 (s, 2H, NCH_2CO), 7.26 (s, H, thiazole 4H), 7.98 (s, H, Ar NH), 9.85 (s, H, NH), 10.48 (s, H, CONH), 7.6-7.77 (m, 5H, Ar-H), 7.2 (d, 2H, Ar-H), 7.4 (d, 2H, Ar-H)

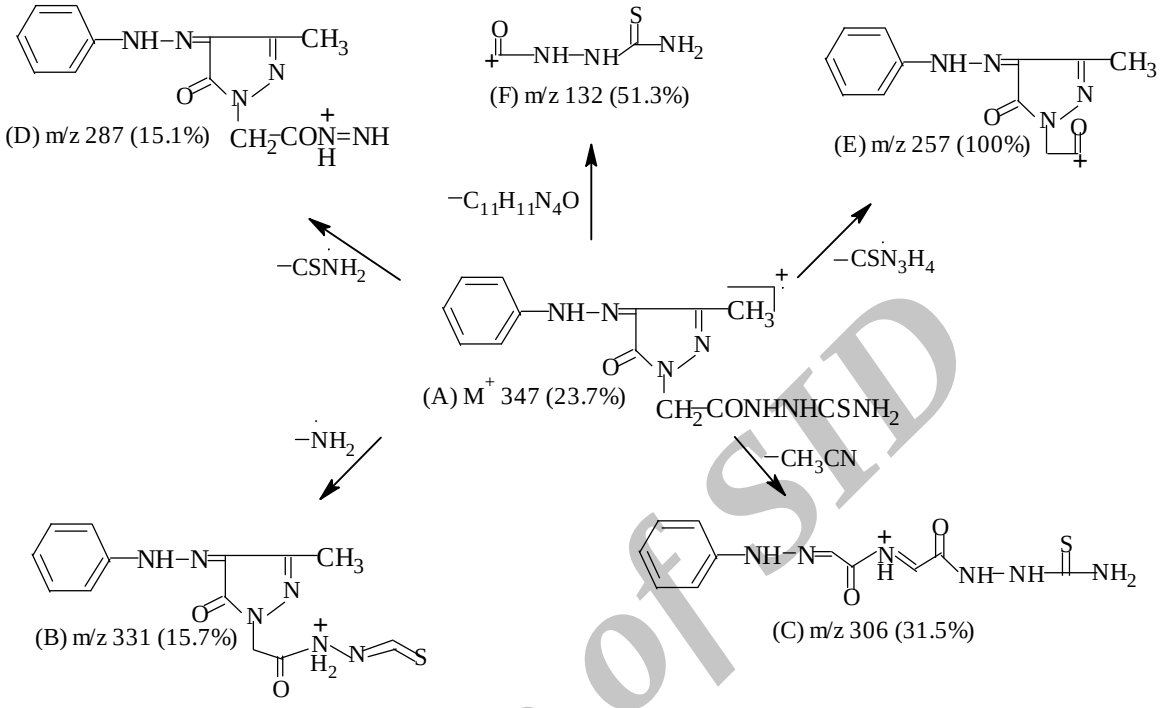
XVi: 2.26 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 4.85 (s, 2H, N-CH_2-CO), 7.13 (d, 2H, o-protons of p-methoxy phenyl), 7.36 (d, 2H, m-protons of *p*-methoxy phenyl), 7.38 (s, H, thiazole-4H), 7.8 (s, H, Ar-NH), 9.52 (s, H, NH)

XVj: 2.48 (s, 3H, CH_3), 4.85 (s, 2H, NCH_2CO), 7.53-8.11 (m, 5H, aromatic protons of coumarin), 7.37 (s, H, thiazole 4H), 7.9 (s, H, Ar-NH), 10.13 (s, H, NH), 10.72 (s, H, CONH), 7.4-7.6 (m, 5H, Ar-H).

Mass spectral details

The mass spectrum of [3-methyl-5-oxo-4-(phenyl-hydrazono)-4,5-dihydro-pyrazol-1- yl]-acetic acid N|-(4-phenyl thiazol-2-yl)-hydrazide XVa exhibited the molecular ion (M^+) peak at m/z 447 indicating the presence of odd number of nitrogens. The fragmentation pattern noticed in the mass spectrum of XVa is presented in Scheme 5. The molecular ion (M^+) was observed at m/z 447 (22.4%). Disintegration (loss of CH_3CN molecule) of molecular ion 'A' forms cation 'B' at m/z 406 (24.3%). Loss of C_6H_5 radical from

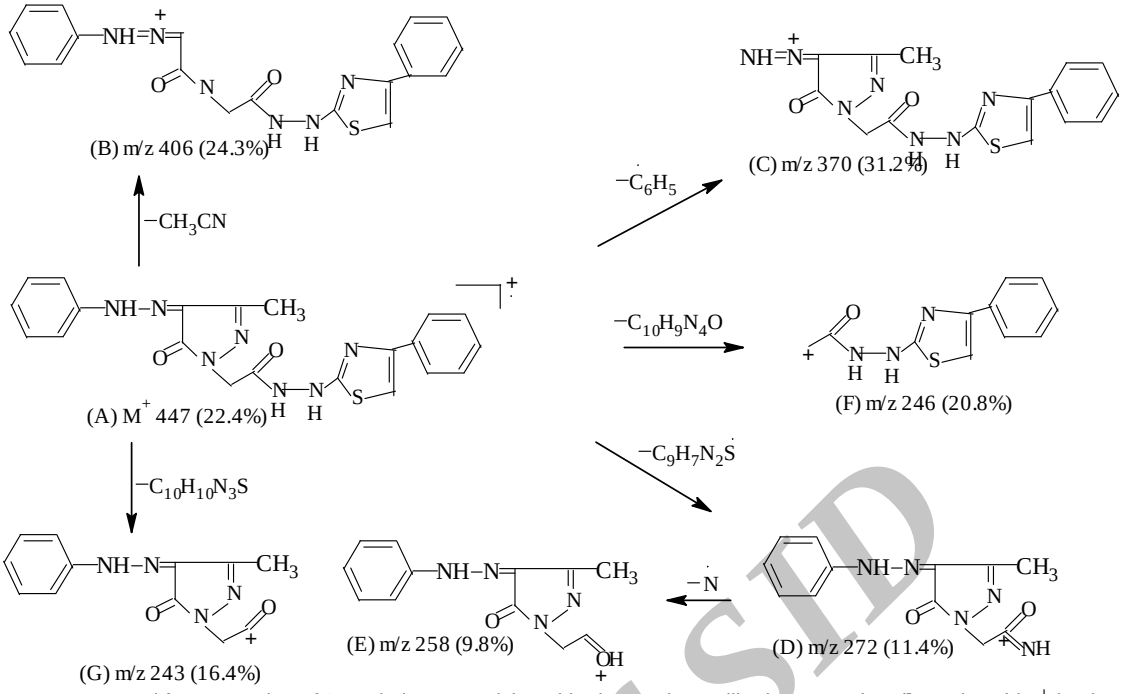
molecular ion afforded cation 'C' at m/z 370 (31.2%). Expulsion of $C_9H_7N_2S$ radical from molecular ion 'A' produced the fragment 'D' at m/z 272 (11.4%). Loss of nitrogen radical from 'D' produced cation 'E' at m/z 258 (9.8%). The molecular ion on decomposition produces cation 'F' at m/z 246 (2.8%). Loss of $C_{10}H_{10}N_3S$ radical from molecular ion 'A' resulted in the cation 'G' at m/z 243 (16.4%). The fragmentation pattern clearly supported the structure of XVa.



Scheme 4. Mass spectral fragmentation of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-aceto thiosemicarbazone XIV.

Table 2. Characterization data of [3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N^{l}-(4-substituted-thiazol-2-yl)-hydrazide. (XV)

Compd.	R	mp °C	Yield %	Mol. formula	Found (%) (calcd)						
					C	H	N	O	S	Cl	Br
XVa	phenyl	180	75	$C_{21}H_{28}N_8O_3S$	58.25 (58.18)	4.60 (4.42)	22.70 (22.62)	7.45 (7.38)	7.45 (7.40)		
XVb	*p*-tolyl	192	80	$C_{26}H_{28}N_8O_3S$	59.15 (59.05)	4.58 (4.47)	22.00 (21.91)	7.25 (7.15)	7.20 (7.17)		
XVc	*p*-anisyl	189	80	$C_{26}H_{28}N_8O_3S$	57.10 (57.01)	4.65 (4.57)	21.25 (21.15)	10.45 (10.36)	7.0 (6.92)		
XVd	*p*-hydroxy phenyl	185	75	$C_{26}H_{28}N_8O_3S$	56.24 (56.11)	4.35 (4.26)	21.90 (21.81)	10.78 (10.68)	7.25 (7.13)		
XVe	*p*-nitro phenyl	182	75	$C_{26}H_{28}N_8O_3S$	52.83 (52.71)	3.85 (3.79)	23.56 (23.42)	13.48 (13.38)	6.85 (6.70)		
XVf	*p*-chloro phenyl	183	76	$C_{26}H_{28}N_8O_3S$	54.00 (53.90)	3.98 (3.88)	21.02 (20.95)	7.01 (6.84)	7.05 (6.85)	7.62 (7.58)	
XVg	*p*-bromo phenyl	190	80	$C_{26}H_{28}N_8O_3S$	50.01 (49.23)	3.62 (3.54)	19.25 (19.14)	6.36 (6.25)	6.35 (6.26)		15.7 (15.59)
XVh	*p*-phenyl sydronyl	187	75	$C_{26}H_{28}N_8O_3S$	53.45 (53.38)	3.75 (3.67)	24.50 (24.37)	12.48 (12.37)	6.30 (6.18)		
XVi	N-*p*-tolyl sydronyl	186	75	$C_{26}H_{28}N_8O_3S$	54.35 (54.23)	4.08 (3.95)	23.85 (23.72)	12.25 (12.05)	6.20 (6.02)		
XVj	N-*p*-anisyl sydronyl	181	77	$C_{26}H_{28}N_8O_3S$	52.78 (52.65)	3.95 (3.83)	23.23 (23.03)	14.80 (14.62)	5.97 (5.85)		



Scheme 5. Mass spectral fragmentation of 3-methyl-5-oxo-4-(phenyl hydrazono)-4,5-dihydro-pyrazol-1-yl]-acetic acid N^{l}-(4-phenyl thiazol-2-yl)-hydrazide XVa.

Antibacterial activity and Antifungal activity

The antibacterial activity of synthesized compounds was studied against certain pathogenic organisms. Th gram-positive bacterial screened were *Staphylococcus aureus* NCCS 2079 and *Bacillus cereus* NCCS 2106. The gram negative bacterial screened were *Escherichia coli* NCCS 265 and *Pseudomonas aeruginosa* NCCS2200.

The antifungal activity of synthesized compounds were studied against *Aspergillus niger* nccs 1196 and *Candida albicans* NCCS 3471.

The minimum inhibitory concentration (MIC) was found by broth dilution method. MIC was noted as the concentration of the test substance, which completely inhibits the growth of the microorganism i.e. 100% transparency (Table 3).

Table 3. Antimicrobial activity details of compounds synthesized

			Zone inhibition in mm (concentration of the drug in µg/mL)					
			Bacteria				Fungi	
#	Compd.	-R	*Staphylococcus aureus* NCCS 2079	*Bacillus Cereus* NCCS 2106	*Escherichia coli* NCCS 2065	*Pseudomonas aeruginos* NCCS 2200	*Aspergillus niger* NCCS 1196	*Candida albicans* NCCS 2106
1	XVa	phenyl	1.5 (44.27)	1.75 (46.23)	1.75 (46.23)	1.5 (45.18)	5.25 (31.2)	6.25 (30.25)
2	XVb	*p*-tolyl	1.25 (45.56)	1.5 (47.34)	1.5 (47.34)	1.75 (44.26)	4.5 (32.48)	5.5 (32.48)
3	XVc	*p*-anisyl	1.5 (39.57)	1.5 (43.85)	1.75 (41.79)	1.5 (42.38)	5.5 (31.58)	6.75 (31.58)
4	XVd	*p*-hydroxy phenyl	1.75 (36.14)	1.5 (38.59)	1.5 (38.59	1.25 (40.34	5 (32.59)	6 (33.57)
5	XVe	*p*-nitro phenyl	2.75 (29.21)	3 (28.42)	3.25 (27.5)	2.75 (29.21)	5 (29.21)	6 (28.42)
6	XVf	*p*-chloro phenyl	2.5 (30.13)	2.75 (29.45)	2.75 (29.45)	2.5 (30.13)	4.25 (29.45)	4.75 (29.45)
7	XVg	*p*-bromo phenyl	2.5 (29.56)	2.25 (31.28)	2.75 (29.56)	2.5 (30.13)	3.5 (29.56	4.5 (29.56)
8	XVh	*p*- phenyl sydnonyl	1.5 (39.38)	1.75 (36.8)	1.75 (35.86)	1.75 (36.8)	4 (35.86)	4 (35.86)
9	XVi	*p*-tolyl sydnonyl	1.5 (40.68)	1.5 (37.83)	1.75 (36.62)	1.5 (37.83)	3.75 (37.83)	4.25 (37.83)
10	XVj	*N-p*-ansyl sydnonyl	1.25 (41.61)	1.5 (40.52)	1.75 (39.59)	1.5 (40.52)	4.25 (39.59)	3.75 (39.59)

Conclusion

A series of 10 novel pyrazoline-5-ones containing thiazole moiety were synthesized and characterized by elemental analysis, IR, NMR and mass spectral analysis. The antibacterial and antifungal activity of all compounds were evaluated and reported. From the study, it can be concluded that all the synthesized compounds demonstrated potential antimicrobial activity.

Conflict of Interest

There is no conflict of interest in this study.

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