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Synthesis and evaluation of some substituted pyrazole derivatives of biological interest

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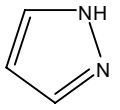
Pyrazole and their derivatives are found to have profound biological activity. In the present work some novel substituted pyrazole derivatives were synthesized. Pyrazole are synthesized by treating ethyl bis [methylthio] -2-cyanoacrylate with hydrazide derivatives. The derivatives of pyrazole were prepared by Schiff base reaction.All the synthesized compounds were characterized by IR, ^{1}H-NMR and Elemental Analysis. All the newly synthesized derivatives were evaluated for antimicrobial activity on different micro-organisms (*E.coli, S. aureus, A.niger, C. albicans)*at the concentration of 200µcg/mL by using cup-plate agar diffusion method. The activity was measured in terms of zone of inhibition and compared with standard drug ciprofloxacin for antibacterial and griseofulvin for antifungal activity. These compounds were also evaluated for antitubercular activity (*M. tuberculli*) at 25, 50 and 100 µcg/mL concentrations. All the compounds were screened for *in-vitro* anti-inflammatory activity at different concentration like200 µg/ml, and 300 µg/ml, by inhibition of protein denaturation method. Ibuprofen was used as standard drug. Potent compounds were screened for *in vivo* anti-inflammatory activity in albino rats at 200 µg/ml concentration to confirm the results.

Keywords:Pyrazoles; Antibacterial; Antitubercular and Anti-inflammatory.

1. INTRODUCTION

Pyrazoles

Pyrazoles refers to the class of heterocyclic compounds characterized by 5 – memberedaromatic ring structure composed of three carbon atoms and two nitrogen atoms inadjacent positions, of two nitrogen atoms one basic nitrogen and neutral nitrogen, thearomatic nature arises from the four electrons and the unshared pair of electrons on the –NH nitrogen.



pyrazole

Pyrazole derivatives have a long history of application in agrochemicals as herbicides andinsecticides and in pharmaceutical industry as antipyretic and anti-inflammatory.Antipyrine is the one of the earliest synthetic drugs and is named after its antipyreticproperties. Butazolidine, another pyrazolone is a powerful anti- inflammatorydrug usedin rheumatic conditions. Many pyrazole derivatives are associated with anti-fungal, anti-diabetic and anti-inflammatory properties. The success of pyrazole COX-2 inhibitor hasfurther highlighted the importance of this heterocycles in medicinal chemistry.

Pyrazole derivatives have been reported to show a broad spectrum of biological activity including antimicrobial [29-44], anti-inflammatory [45-54], antituberculosis [55, 56], antiviral [57, 58], hypoglycemic [59, 60], anti-tumor [20-25], antihypertensive [26-28]. Due to its wide range of biological activity, pyrazoleshave received a considerable interest in the field of drug discovery and therefore pyrazolering constitutes a relevant synthetic target in pharmaceutical industry. In fact, such a heterocyclic moiety represents the core structure of a number of drugs.

RESULTS AND DISSCUSSON

The twelve Pyrazole derivatives have been synthesized during the course of research work.

The synthesized compounds were subjected to various antibacterial, antifungal and antitubercular and anti-inflammatory screening by the standard methods.

- ***Antibacterial activity:*** All the compounds were screened for antibacterial activity at 200 µg/ml concentration. However the compounds **A_2**,

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A_3, **B_2**, **C_2** and **C_3** have shown maximum antibacterial activity, while the remaining compounds have also shown moderate antibacterial activity, when compared with standard drug **Ciprofloxacin** against *Staphylococcus aureus* (Gram positive) and *Escherichia coli* (Gram negative) .

- ***Antifungal activity*:** All the compounds were screened for antifungal activity. However Compound **A_2, B_2,B_3**, **C_2**and**C_3**have showed maximum activity, while the remaining compounds have also shown moderate Antifungal activity, when compared with standard **Griseofulvin** against *Aspergillusniger*&*Candida albicans*.
- ***Antitubercular activity*:** All the compounds were screened for antitubercular activity by Middle brook 7H9 agar medium as described by Elmer WK et al. against H_{37}Rv Strain. However Compounds **A_4**, **B_1**, **B_2**, **B_3** and **B_4** have shown promising antitubercular activity against *Mycobacterium tuberculosis* of H_{37}Rv Strain. **Streptomycin** was use as std. drug.
- ***Anti-inflammatory activity*:** All the compounds were screened for *in-vitro* anti-inflammatory activity at different concentration like200 µg/ml, and 300 µg/ml, by inhibition of protein denaturation method. Compounds **A_2**, **A_3**, **B_2, B_3**, **C_3** and **C_4** have shown promising anti-inflammatory activity. **Ibuprofen** was used as standard drug. The Compounds **A_1**, **A_2, B_3**, **B_4**, **C_2** and **C_3** were screened for the *in vivo* anti-inflammatory activity at 200 µg/ml concentration. Compound**A_2, B_3**, **B_4**, **C_2** and **C_3** shows good anti-inflammatory activity.

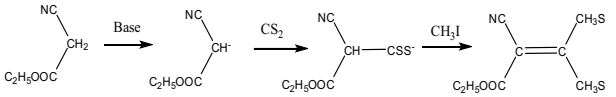
Regarding the above result, it is suggested that compounds substituted with electron-releasing groups (-OCH_3, -OH) increase the antimicrobial activity and anti-inflammatory activity.

The proposed work has given out many active antibacterial, antifungal, antitubercular and anti-inflammatory agents. Some of the compounds have showed moderate activities. These compounds with suitable modification can be explored better for their therapeutic activities in the future.

The experimental work comprises of scheme (procedures) [55,56,57,58,59]

1. Synthesis of ethyl bis(methylthio)- 2 cynoacrylate.
2. General procedure for synthesis of ethyl 5-amino-3-(methylthio)-1-substituted-1Hpyrazole-4-carboxylate
3. General procedure for synthesis of 1-substituted-5-amino-4-[(hydrazinooxy)carbonyl]-1H-pyrazole.
4. General Procedure for synthesis of 2-{[5-amino-1-substituted-3-(methylthio)-1H-pyrazole-4-yl]carbonyl}-5-methyl-2,4-dihydro-3H-pyrazole-3-one.(V)
5. General procedure for synthesis of derivative of pyrazole.

Step 1: Synthesis of ethyl bis(methylthio)- 2 cynoacrylate(I): Pulverized potassium hydroxide (0.2mol) was suspended in dioxane (100mL) and a solution of ethylcynoacetate (0.1mol) and carbon disulphide(0.1mol) in dioxane(50mL) was added with stirring and cooling to maintain temperature of 15-20^{o}c. After stirring for 20 min, the solution was diluted with 250 ml ether. The yellow precipitate was filtered, washed with dioxane-ether and dried in vacuo over NaOH and P_2O_5. A solution of dithiolates (2mM) and methyl iodide (4mM) in abs. ethanol was kept at 0^{o}C for 2 days. The ethanol was removed by evaporation in vacuo and water added to the residue. The insoluble solid was filtered and dried on recrystalised ether to yield colorless crystal.



Step 2: General procedure for synthesis of ethyl 5-amino-3-(methylthio)-1-substituted-1H-pyrazole-4-carboxylate (III): A hydrazide derivative (100 mM) and ketene dithioacetal derivative (150 mM) in methanol (70 mL) was heated under reflux till completion of reaction. The reaction was monitored by thin layer chromatography using mixture of chloroform and methanol (8:2) as eluent. The reaction mass was cooled to 0-5° C to crystallize the product. On filtration and washing with chilled methanol it afforded pyrazole derivatives

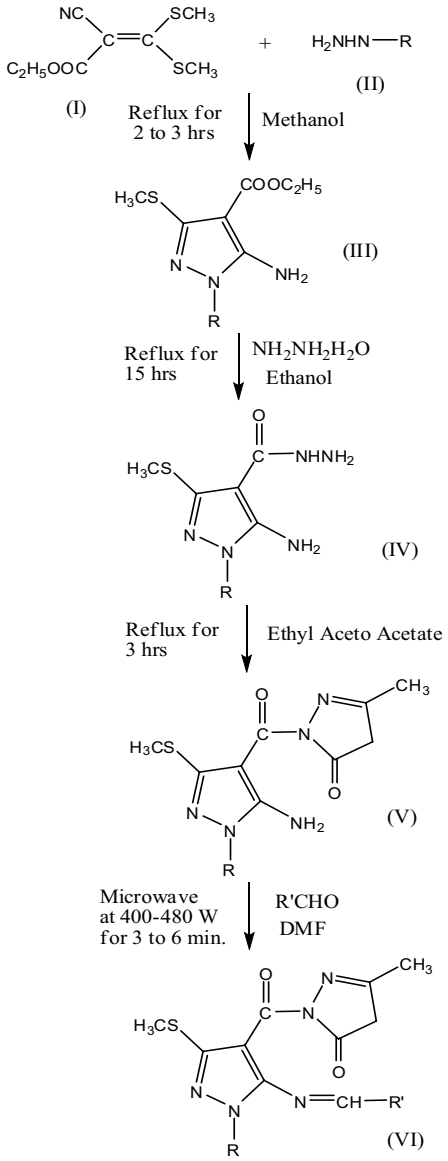
Step 3:General procedure for synthesis of 1-substituted-5-amino-4- [(hydrazinooxy)carbonyl]-1H-pyrazole(IV): A mixture of 0.01 mole of com.(III) and 0.2 mole (10mL) of Hydrazine hydrate were taken in 250 mL round bottom flask attached to a refluxed condenser and refluxed with50 ml of 95% ethanol for 15 hrs. The resultant mixture was concentrated in 250 ml beaker. It was cooled at room temperature and kept in refrigerator for 2 hrs. The solid mass thus separated out was filtered, dried and purified by recrystallization from ethanol.

Step 4:General Procedure for synthesis of 2-{[5-amino-1-substituted-3(methylthio)-1H-pyrazole-4-yl]carbonyl}-5-methyl-2,4-dihydro-3H-pyrazole-3-one.(V): A mixture of the hydrazide (IV) (10 mM) and ethyl acetoacetate (10 mM) in

absolute ethanol was heated at reflux for 3 h. The reaction mixture was cooled and the formed precipitate was filtered off, dried and recrystallized from acetic acid.

Step 5: General procedure for Microwave Assisted synthesis of derivative of pyrazole(VI): A mixture of 2 mM of aldehyde and 2 mM of different aryl or alkyl amines (V) was taken and triturated in a mortar pestle. Then above mixture was transferred to a vessel which was then kept in microwave for synthesis. 4 to 5 mL of DMF was also added to mixture before putting it in microwave. Microwave was run at 400-480 W for 3 to 6 min for depending on reaction mixtures. Reaction completion was monitored continuously after each run by TLC. Then product was washed with ethanol, solvent was evaporated, dried and recrystalized with ethanol.

Scheme:



SPECTRAL DATA

Infra Red / ^{1}H-NMR spectral study of the synthesized compounds. (A_1-C_4)

A_1

IR Bands (cm^{-1}): 2997, 1712, 1630, 1602, 1112, 668

Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-S-C

δ Values in ppm: 8.76-9.34, 7.52-7.83, 1.94-2.53

No. Of Protons: 3H of Pyrazine, 6 H of Aryl, 2 H of Methyl.

A_2

IR Bands (cm^{-1}): 2992, 1710, 1645, 1610, 1142, 1086, 686.

Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-O, C-S-C.

δ Values in ppm: 8.76-9.34, 7.62-7.84, 2.53.

No. Of Protons: 3H of Pyrazine, 4 H of Aryl, 1 H of Methyl.

A_3

IR Bands (cm^{-1}): 3398, 2988, 1698, 1634, 1592, 1286, 1046, 694

Types of Vibrations: 10.9, 8.7-8.6, 8.0, 7.65-7.03, 2.8, 2.5, 1.8

δ Values in ppm: 8.76-9.34, 7.62-7.84, 2.8.

No. Of Protons: 3H of Pyrazine, 4 H of Aryl, 3 H of Methyl.

A_4

IR Bands (cm^{-1}): 2998, 1702, 1653, 1612, 1574, 1086, 674

Types of Vibrations: C-H, C=O, C=N, C=C, C=C, C-N, C-S-C

δ Values in ppm: 8.76-9.34, 7.33-7.60, 1.94-2.53.

No. Of Protons: 3H of Pyrazine, 5 H of Benzene, 2 H of Methyl.

B_1

IR Bands (cm^{-1}):1699, 1634, 1597, 1080, 683

Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-S-C

δ Values in ppm: 7.92-, 7.33-7.60, 1.94-2.53.

No. Of Protons: 4 H of 4-Pyridine , 6 H of Aryl, 2 H of Methyl.

B_3

IR Bands (cm^{-1}): 3400, 2994, 1689, 1622, 1586, 1124, 1078, 697

Types of Vibrations: O-H, C-H, C=O, C=N, C=C, C-N, C-O, C-S-C

δ Values in ppm: 7.92-8.89, 7.08-8.59, 1.94-2.53.

No. Of Protons: 4 H of 4-Pyridine , 5 H of Aryl, 2 H of 2 Methyl.

B_4
IR Bands (cm^{-1}): 2997, 1762, 1699, 1621, 1015, 681
Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-S-C.
δ Values in ppm: 7.92-8.84, 7.33-8.60, 1.94-2.53.
No. Of Protons: 4 H of 4-Pyridine , 5 H of 1-Benzene, 2 H of 2 Methyl.

C_1
IR Bands (cm^{-1}): 3016, 1709, 1642, 1602, 1087, 690
Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-S-C
δ Values in ppm: 7.92-8.84, 7.33-8.60, 1.94-2.53.
No. Of Protons: 5 H of Benzene , 5 H of Aryl, 2 H of Methyl.

C_2
IR Bands (cm^{-1}): 3021, 1702, 1641, 1578, 1210, 1043, 673
Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-O, C-S-C
δ Values in ppm: 1.6-4.22, 6.8-8.59, 7.45-8.04
No. Of Protons: 5 H of 1-Benzene , 5 H of Aryl,2 H of Methyl

C_3
IR Bands (cm^{-1}): 3024, 1731, 651, 1597, 1253, 1104, 686
Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-O, C-S-C
δ Values in ppm: 7.02-8.59, 7.45-8.04, 1.94-2.53
No. Of Protons: 5 H of 1-Benzene , 4 H of Aryl, 2 H of Methyl

C_4
IR Bands (cm^{-1}): 3026, 1714, 1640, 1600, 1131, 692
Types of Vibrations: C-H, C=O, C=N, C=C, C-N, C-S-C
δ Values in ppm: 7.33-8.04, 5.5-6.6, 1.94-2.53
No. Of Protons: 10 H of 1-Benzene ,2 H of methylene, 2 H of Methyl

INSTRUMENTAL DETAILS

Infrared Spectra

The peaks in IR Spectrum gave an idea about the probable structure of the compound. IR region ranges between 4000-650 cm^{-1}. The derivatives including intermediates were recorded on Jasco FT/IR 4100, which showed different vibration levels of molecules by using potassium bromide (KBr) pellet technique.

^{1}H-NMR Spectra

NMR Spectroscopy enables us to record differences in magnetic properties of the various magnetic nuclei present and to deduce in the large measure about the position of these nuclei within the molecule. We can deduce how many different kinds of environment are there in the molecules and also which atoms are present in neighboring groups. The proton NMR spectra, enables us to know different chemical and magnetic environments corresponding to protons in molecules.

^{1}H-NMR of the title compounds were recorded on sophisticated multinuclear FT NMR Spectrometer model Avance-II (Bruker), DMSO-d6 as internal standards. The instrument is equipped with a Gyromagnet of field strength 9.4T. Its ^{1}H frequency is 400 MHz.The chemical shift data were expressed as δ-values related to TMS.

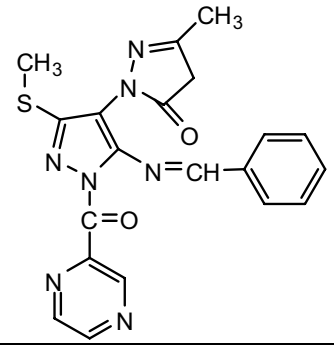
C H N Analysis

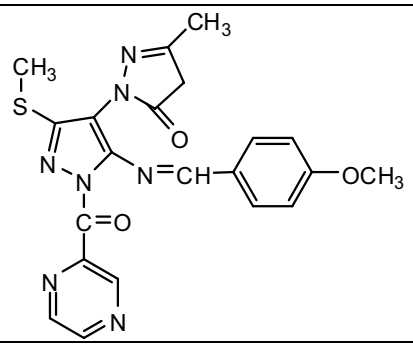
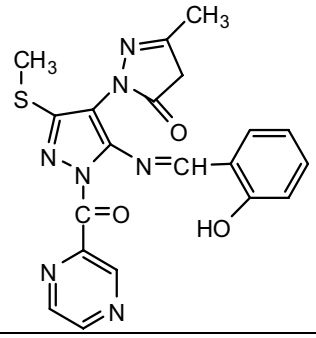
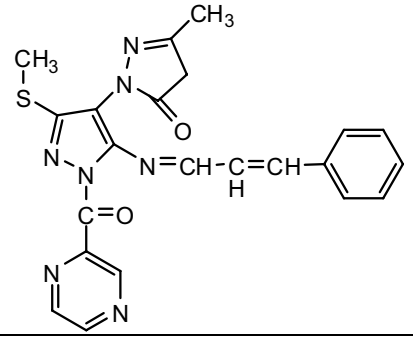
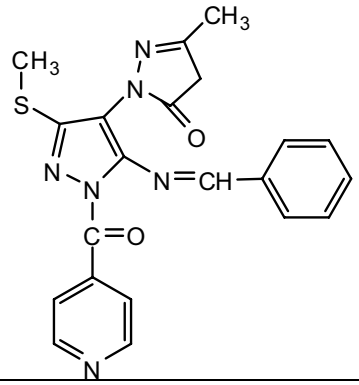
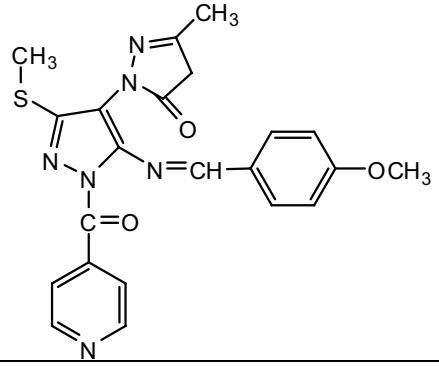
The permiscible limit for C H N analysis were performed on Thermo finnigan. Model: FLASH EA 1112 series.

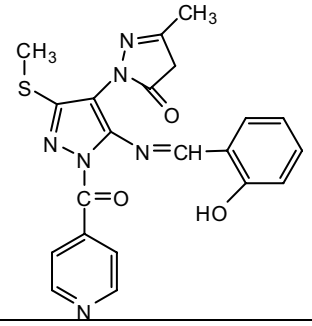
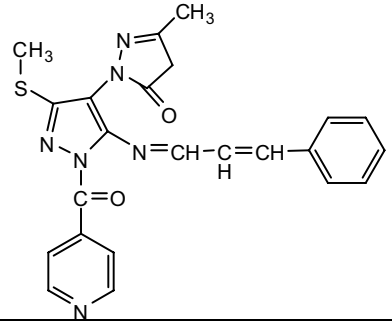
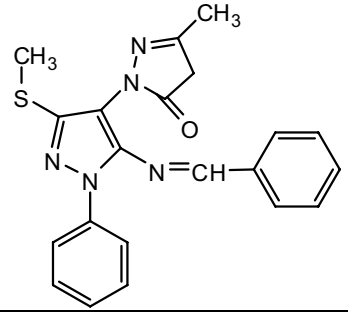
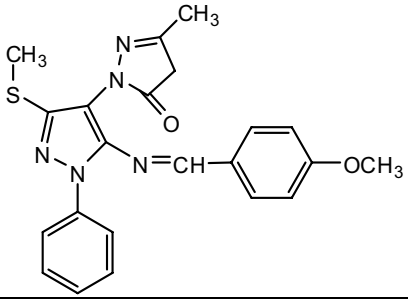
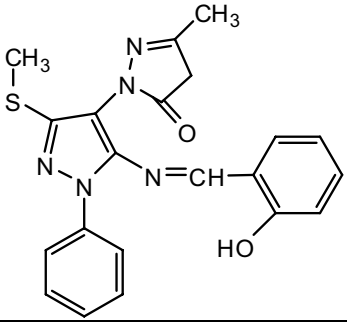
Microwave Synthesis

Microwave synthesis were performed on instrument of LG company, Model no.:MH-6349 EB.

Table of derivatives. List of synthesized compounds with their IUPAC names.

A_1	1-(5-(benzylideneamino)-3-(methylthio)-1-(pyrazine-2-carbonyl)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	

A_2	1-(5-(4- methoxybenzylideneamino)-3-(methylthio)-1-(pyrazine-2-carbonyl)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
A_3	1-(5-(2- hydroxybenzylideneamino)-3-(methylthio)-1-(pyrazine-2-carbonyl)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
A_4	3-methyl-1-(3-(methylthio)-5-(3-phenylallylideneamino)-1-(pyrazine-2-carbonyl)-1*H*–pyrazole-4-yl)-1*H*–pyrazole-5(4*H*)-one	
B_1	1-(5-(benzylideneamino)-1-isonicotinoyl-3-(methylthio)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
B_2	1-(1-isonicotinoyl-5-(4-methoxybenzylideneamino)-3- 3-(methylthio)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	

B_3	1-(5-(2-hydroxybenzylideneamino)-1-isonicotinoyl-3-(methylthio)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
B_4	1-(1-isonicotinoyl-3-(methylthio)-5-(3-phenylallylideneamino)-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
C_1	1-(5-(benzylideneamino)-3-(methylthio)-1-phenyl-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
C_2	1-(5-(4- methoxybenzylideneamino)-3-(methylthio)-1-phenyl-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	
C_3	1-(5-(2- hydroxybenzylideneamino)-3-(methylthio)-1-phenyl-1*H*–pyrazole-4-yl)-3-methyl-1*H*–pyrazole-5(4*H*)-one	

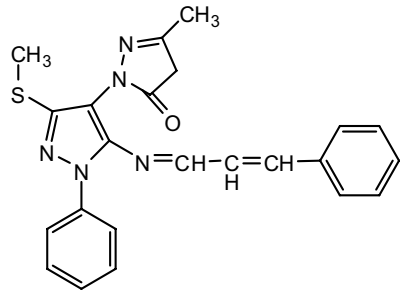
C_4	3-methyl-1-(3-(methylthio)-5-(3-phenylallylideneamino)-1-phenyl-1*H*–pyrazole-4-yl)-1*H*–pyrazole-5(4*H*)-one	

Table. Analytical data of synthesized compounds

Comp.	Mol. Formula	Mol. Wt.	M.P ^{0}C	Rf Value	Yield %	Elemental analyses Calcd. (Found)		
						C	H	N
A_1	$C_{20}H_{17}N_7O_2S$	419.46	140-142	0.74	71	57.27 (57.22)	4.09 (4.20)	23.37 (23.34)
A_2	$C_{21}H_{19}N_7O_3S$	449.49.	143-145	0.70	67	56.11 (56.15)	4.26 (4.30)	21.81 (21.84)
A_3	$C_{20}H_{17}N_7O_3S$	435.46	152-154	0.67	63	55.16 (55.11)	3.93 (3.90)	22.52 (22.49)
A_4	$C_{22}H_{19}N_7O_2S$	445.50	194-196	0.72	79	59.31 (59.42)	4.30 (4.02)	22.01 (22.10)
B_1	$C_{21}H_1N_6O_2S$	418.47	178-180	0.76	58	60.27 (60.31)	4.34 (4.30)	20.08 (20.06)
B_2	$C_{22}H_{20}N_6O_3S$	448.50	145-147	0.75	56	58.92 (58.89)	4.49 (4.54)	18.74 (18.78)
B_3	$C_{21}H_{18}N_6O_3S$	434.47	146-148	0.71	65	58.05 (58.03)	4.18 (4.24)	19.34 (19.33)
B_4	$C_{23}H_{20}N_6O_2S$	444.51	186-188	0.68	70	62.15 (62.10)	4.54 (4.55)	18.91 (18.90)
C_1	$C_{21}H_{19}N_5OS$	389.47	126-128	0.76	63	64.47 (64.45)	4.92 (4.89)	17.98 (17.94)
C_2	$C_{22}H_{21}N_5O_2S$	419.50	139-141	0.68	64	62.99 (62.78)	5.05 (5.31)	16.69 (16.58)
C_3	$C_{21}H_{19}N_5O_2S$	405.47	146-148	0.65	68	62.21 (62.22)	4.72 (4.73)	17.21 (17.18)
C_4	$C_{23}H_{21}N_5OS$	415.51	165-167	0.72	72	66.48 (66.44)	5.09 (5.05)	16.85 (16.86)

TLC Solvents: Methanol:Benzene (1:9)

PHARMACOLOGICAL AND MICROBIOLOGICAL SCREENING

Anti-bacterial and Anti-fungal activity of synthesized compounds:

Compd.	Zone of inhibition at 200µcg/mL (in mm.)			
	E. coli ATCC 25922	*S. aureus* ATCC 25923	*A. niger* NCIM 596	*C. albicans* NCIM 3102
A_1	16	14	12	16
A_2	18	23	21	23
A_3	21	24	21	18
A_4	15	16	14	18
B_1	12	14	16	14
B_2	18	22	24	25
B_3	16	19	23	24
B_4	18	17	14	22
C_1	13	14	12	20
C_2	18	21	22	24
C_3	22	24	20	26
C_4	18	12	17	13
Ciprofloxacin	28	26	-	-
Griseofulvin	-	-	28	25

Compounds **A_2**, **A_3** ,**B_2**, **C_2** and **C_3** have shown promising antibacterial activity against **Std. Ciprofloxacin.** Compounds **A_2, B_2, B_3**, **C_2**, and **C_3** have exhibited excellent antifungal activities against **Std. Griseofulvin.**

Anti-tubercular activity of the synthesized compounds:

Compound code	*25 µcg /Ml*	*50 µcg /mL*	100 µcg /mL
A_1	R	R	**S**
A_2	R	R	R
A_3	R	R	**S**
A_4	R	**S**	**S**
B_1	R	**S**	**S**
B_2	R	**S**	**S**
B_3	R	**S**	**S**
B_4	R	**S**	**S**
C_1	R	R	R
C_2	R	R	R
C_3	R	R	R
C_4	R	R	R
Streptomycin	**S**	**S**	**S**

R- Resistance; **S**- Sensitive

Compounds **A_4**, **B_1**, **B_2**, **B_3** and **B_4** have shown promising antitubercular activity at both the concentration 50 and 100 µcg /mL. H_{37} Rv strain was used as standard tubercular organism. Streptomycin was used as standard drug. However, Streptomycin has shown antitubercular activity at 25 µcg /mL.

In-vitro Anti-inflammatory activityof the synthesized compounds:

Compound	Absorbance Value (Mean + SE)		Inhibition of Denaturation (in %)	
	200 µg/mL	300 µg/mL	200 µg/mL	300 µg/mL
Control	0.095	0.095	-	-
Ibuprofen	0.180	0.195	89.4%	105.2%
A_1	0.142	0.152	49.47%	60.00%
A_2	0.162	0.173	70.52%	82.10%
A_3	0.156	0.169	64.21%	77.89%
A_4	0.130	0.143	36.84%	50.52%
B_1	0.134	0.141	41.05%	48.42%
B_2	0.146	0.157	53.68%	65.26%
B_3	0.155	0.167	63.15%	75.78%
B_4	0.135	0.146	42.10%	53.68%
C_1	0.130	0.139	36.84%	46.31%
C_2	0.141	0.152	48.42%	60.00%
C_3	0.160	0.174	68.42%	83.15%
C_4	0.142	0.158	49.47%	66.31%

The percentage inhibition of denaturation was calculated by using following formula:

% of Inhibition = 100 X [Vt / Vc – 1]

Where, Vt = Mean absorbance of test sample. Vc = Mean absorbance of control.

In-vivo Anti-inflammatory activity of the synthesized compounds

Compound	Increase paw volume			% Decrease paw volume after 3 hour
	1 hour	2 hour	3 hour	
Control	0.37(±0.02)	0.39(±0.008)	0.45(±0.03)	
Diclofenac sodium	0.10(±0.03) ***	0.10(±0.05) ***	0.12(±0.011) ***	73.33
A_1	0.12(±0.007) ***	0.23(±0.03) **	0.26(±0.02) **	42.22
A_2	0.08(±0.02) ***	0.09(±0.05) ***	0.13(±0.009) ***	71.22
B_3	0.08(±0.009) ***	0.12(±0.05) ***	0.17(±0.011) ***	62.23
B_4	0.10(±0.06) ***	0.13(±0.009) ***	0.16(±0.02) ***	64.45
C2	0.07(±0.04) ***	0.09(±0.05) ***	0.14(±0.009) ***	68.89
C3	0.11(±0.03) ***	0.14(±0.07) ***	0.16(±0.012)***	64.45

The results are expressed as mean ± SEM (n =6). Significance was calculated byusing one-way ANOVA with Dunnet's t- test. The difference in results was considered significant when $p<0.05$. *$p<0.05$ vs control at 200 mg/kg b.w; **$p<0.01$ vscontrol at 200 mg/kg b.w; ***$p< 0.001$ vs control at 200 mg/kg b.w.

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СИНТЕЗА И ОХАРАКТЕРИЗИРАНЕ НА НЯКОИ ЗАМЕСТЕНИ ПРОИЗВОДНИ НА ПИРАЗОЛА С БИОЛОГИЧНО ПРИЛОЖЕНИЕ

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(Резюме)

Пиразолът и неговите производни имат голяма биологична активност. В настоящата работа са синтезирани нови заместен производни на пиразола. Те са синтезирани чрез третирането на етил бис-[метилтио] -2-цианоакрилатс производни на хидразида. Производните на пиразола са получени чрез реакция с Шифови бази. Всички получени съединения са охарактеризирани с IR, ^{1}H-NMR и елементен анализ. Всички новосинтезирани съединения са изпитани за антимикробна активност върху различни микроорганизми (*E.coli, S. aureus, A.niger, C. albicans)* при концентрации 200µg/mL чрез дифузия в агар в стъкла на Петри. Активността е определяна чрез зоните на инхибиране и сравнена с действието на стандартното лекарство ципрофлоксацин за антимикробна и с гризеофулвин за антигъбична активност. Изпитаните съединения са тествани и за антитуберкулозна активност спрямо *M. tuberculli* при концентрации от 25, 50 и 100 µg/mL, а за *in-vitro* противо-възпалителна активност – при концентрации 200 µg/ml и 300 µg/ml по метода на денатурирането на протеини. Като стандартно лекарство е използван ибупрофен. Съединенията са изпитани за *in vivo* противо-възпалителна активност спрямо бели мишки при 200 µg/ml за потвърждение на резултатите.