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SYNTHESIS, CHARACTERIZATION AND MICROBIOLOGICAL ACTIVITY OF 4-THIAZOLIDINONE COMPOUNDS 1-(2,4-DINITROPHENYL)-4-(SUBSTITUTEDPHENYL)-6-[2-(4-CHLOROPHENYL)-4-OXO-1,3-THIAZOLIDIN-3-YL]-3-METHYL-1,4-DIHYDROPYRANO[2,3-C] PYRAZOLE-5-CARBONITRILE

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ABSTRACT

A new series of 4-thiazolidinone compound was synthesized by 1-(2,4-dinitrophenyl)-4-(4-hydroxyphenyl)-6-{[(3-nitrophenyl)methylene]amino}-3-methyl-1,4-dihydropyrano[2,3-c] pyrazole-5-carbonitrile, thioglycolic acid and anhydrous zinc chloride in absolute ethanol were refluxed and then product obtained was obtained. The synthesized compounds were characterized by means of their IR, 1H-NMR spectral data and elemental analysis. All the synthesized products were evaluated for their antimicrobial activities by Cupborer method.

KEYWORDS: *thioglycolic acid, zinc chloride, Ethanol.*

INTRODUCTION

Thiazolidinones are derivatives of thiazolidine and are an important group of heterocyclic compounds. There are three types of thiazolidinones in which carbonyl group is attached at any one of the 2, 4 and 5 position. Among these three types of thiozolidinones the most important thiozolidinones is contains carbonyl group at 4th position. It is known as 4-oxo-thiazolidine or 4-thiazolidinone. Synthesis of 4-thiazolidinones has been reported either by cyclisation of acyclic compounds or by inter conversion among appropriately substituted thiozolidinone derivatives. Different methods for the preparation of 4-thiozolidinones are narrated in the literature.[1-3] Thioglycolic acid has been extensively used for the synthesis of

4-thiozolidinones. Thioglycolic acid reacts with schiff base in different solvent it produce a wide variety of 4-thiazolidinones.[4-5] Kavitha *et al*. have prepared bioactive venlafaxine analogs such as 2,3-disubstituted 1,3-thiazolidin-4-ones as antimicrobial agents.[6] Vicini and his co-workers have synthesized novel 2-thiazolylimino-5- arylidene- 4-thiazolidinones and screened their antimicrobial activity.[7] Rana and his co-workers have synthesized 2-[(2'-chloro-7'-methoxyquinoline-3'-yl)]-3-[3''-hydroxy-6''-(substitutedphenyldiazenyl) phenyl]-5-methyl-1,3-thiazolidin-4-one and screened for antimicrobial activity.[8] Srivastava and Sen have synthesized [(2''-substituted aryl)-4"-oxo-1",3"-thiazolidine-3"-imino-acetyl]-2-aminobenzothiazole and studied their antimicrobial activity.[9]

Thiazolidinones have been synthesized an evaluated for their convulsant activity[10], 2-Imino-3-(4-arylthiazol-2-yl)-thiazolidin-4-ones and Their 5-Arylidene Derivatives have a anti fungicidal Activity[11], 3-(4'- bromo - 2' - carboxy phenyl) - 2 - (2"-flouro phenyl) -5-methyl-4- thiazolidinone have a anti-inflammatory[12], 2-(substituted phenyl)-3-[(N:N di methyl amino) propyl] 1,3-thiazolidine-4-one have anti histaminic activity[13],4-thiazolidinones of benzal-4-bromoanilines derivatives have fungitoxicity activitys[14],4-thiazolidinones have anti tubercular agent.[15]

MATERIAL METHOD

6-amino-4-(substitutedphenyl)-1-(2,4-dinitrophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile(B 1 to 10)

A mixture of 2-(2,4-dinitrophenyl)-5-methyl-2,4-dihydro-pyrazol-3-one, malononitryle, substitutedbenzaldehyde and piperidine in ethanol medium were refluxed for 5 hours. After completion of the reaction, the mixture was cooled and the resulting solid was crystallized from ethyl acetate.

1-(2,4-dinitrophenyl)-4-(substitutedphenyl)-6-{[(4-chloroyphenyl)methylene]amino}-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile [C 1 to 10]

6-amino-4-(4-chlorophenyl)-1-(2,4-dinitrophenyl)-3-methyl-1,4-dihydropyrano [2,3-c] pyrazole -5-carbonitrile(0.01M) react with 4-chlorobenzaldehyde (0.01M) and absolute alcohol(30ml)were placed and 1 to 2 drops of hydrochloric acid was added and the mixture was then heated on water bath for 6 hours and then cooled and the precipitates were filtered off and re-crystallized from ethanol.

1-(2,4-dinitrophenyl)-4-(substitutedphenyl)-6-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-3-methyl-1,4-dihydropyrano-[2,3-c]pyrazole-5-carbonitrile (D 1 to 10)

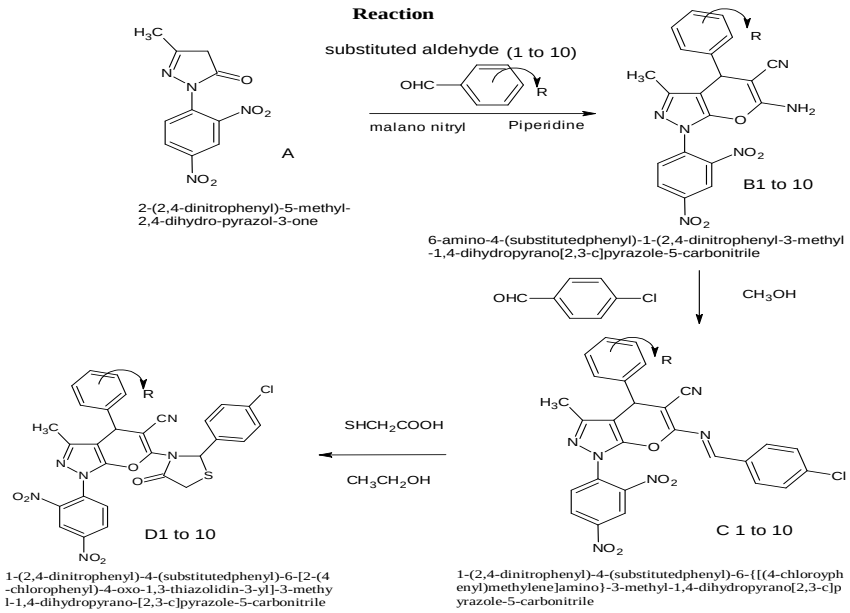
A solution of compound 1-(2,4-dinitrophenyl)-4-(4-hydroxyphenyl)-6-{[(3-nitrophenyl) methylene]amino}-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile, thioglycolic acid and anhydrous zinc chloride in absolute ethanol were refluxed for 8 hours, concentrated, cooled and poured into crushed ice and then filtered. The product obtained was purified by recrystallization from acetone. Melting points were taken in open capillary tube and were uncorrected. IR spectra were recorded on I.R. Spectrophotmeter of Bruker scientific Model No. Alpha E and instrument used for NMR Spectroscopy was recorded in DMSO on Bruker Advance II 400 MHz spectrometer using TMS as an internal standard. Purity of the compounds were checked by tlc on silica- G plates.

I.R.: D-1: 3080cm^{-1}(**=C-H**), 2920 cm^{-1}(**-C-H (Stretch)**, 2200 cm^{-1}(**-CN**), 1725 cm^{-1} (**>C=O (Stretch)**, 1590 cm^{-1}(**>C=N- (Stretch)**, 1530 cm^{-1}(**>C=C< aromatic**), 1480 cm^{-1} (**-N=O**), 1470 cm^{-1}(**-CH_2- (bend)**, 1385 cm^{-1}(**-CH_3 (bend)**, 1340 cm^{-1}(**C-N**), 1260 cm^{-1} (**N-N**), 1165 cm^{-1}(**C-O-C),** 770 cm^{-1}(**C-Cl),** 720 cm^{-1} (**C-S-C).**

NMR: D-9 (DMSO): 1H NMR (DMSO); **D-9**: 2.5975, singlate (3H)(-CH3), 3.3384, singlate (2H) (-CH3), 3.8928 singlet signal (3H) (-OCH3), 4.6989, singlate(1H) (>CH-), 5.9632, singlate(1H)(>CH-Thiazolidine), 6.5719-8.5267, multiplate(11H) (Ar-H).

TABLE – 1: Physical constant of 1-(2,4-dinitrophenyl)-4-(substitutedphenyl)-6-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-3-methyl-1,4-dihydropyrano-[2,3-c]pyrazole-5-carbonitrile

sub	substuted aldehyde	Molecular formula	Mol.Wt (g/m)	yield %	MP oC	C%		H%		N%	
D1	4-Cl	$C_{29}H_{18}Cl_2N_6O_6S$	649.46	65	131	53.58	53.63	2.76	2.79	12.90	12.94
D2	2-Cl	$C_{29}H_{18}Cl_2N_6O_6S$	649.46	68	120	53.60	53.63	2.75	2.79	12.89	12.94
D3	3-OCH3, 4-OCH3	$C_{31}H_{23}ClN_6O_8S$	675.06	72	102	55.10	55.15	3.40	3.43	12.40	12.45
D4	H	$C_{29}H_{19}ClN_6O_6S$	615.01	70	117	55.58	56.63	3.07	3.11	13.60	13.66
D5	2-OH	$C_{29}H_{19}ClN_6O_7S$	631.01	68	84	55.14	55.20	3.00	3.03	13.27	13.32
D6	3-OCH3 4-OH	$C_{30}H_{21}ClN_6O_8S$	661.04	65	97	54.46	54.51	3.16	3.20	12.67	12.71
D7	4-OH	$C_{29}H_{19}ClN_6O_7S$	631.01	70	85	55.15	55.20	3.00	3.03	13.28	13.32
D8	4-N(CH3)2	$C_{31}H_{24}ClN_7O_6S$	658.08	72	118	56.51	56.58	3.65	3.68	14.85	14.90
D9	4-OCH3	$C_{30}H_{21}ClN_6O_7S$	645.04	68	105	55.80	55.86	3.25	3.28	13.00	13.03
D10	3-NO2	$C_{29}H_{18}ClN_7O_8S$	660.01	71	138	52.72	52.77	2.71	2.75	14.80	14.86



Microbiological activity

Synthesized compounds suggests their moderate antibacterial and antifungal activity as compared to the standard drugs Penicillin, Chloramphenlcol, Streptomycin, Tetracyclin and Amphotericin using cupboar method. Antibiotic solution is prepared in sterile distilled water. Penicillin: 12 units, Chloramphenicol: 30 µg/ml, Streptomycin: 30 µg/ml, Tetracycline: 30 µg/ml.

Culture activation

The culture was activated in nutrient broth and potato dextrose broth for bacteria and yeast respectively. One colony of each organism was inoculated and incubated at 37^0C (bacteria) and 28^0C (yeast) temperature for 24 hours. 200 µl of activated culture was inoculated in 25 ml of molted Nutrient agar and Yeast peptone agar for bacteria and yeast respectively. After proper mixing of culture it was poured in sterile 100mm Petri dish.

Synthesized compounds suggests their moderate antibacterial and antifungal activity as compared to the standard drugs Penicillin, Chloramphenlcol, Streptomycin, Tetracyclin.

TABLE – 2: Antimicrobial activity of 1-(2,4-dinitrophenyl)-4-(substitutedphenyl)-6-[2-(4-chlorophenyl)-4-oxo-1,3thiazolidin-3-yl]-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile

Sample code	Microorganisms							Yeast
	E.coli NCIM 2066	S.aureus MTCC 737	B.spizinzenii MTCC 441	P.aeruginosa MTCC 1688	S.paratyphi A MTCC 735	B.pumillus MTCC 1607	K.pneumoniae MTCC 432	C.albicans MTCC 227
D 1	21	20	18	13	18	20	18	18
D 2	19	21	16	12	20	21	21	21
D 3	17	18	22	14	21	18	17	17
D 4	16	16	16	11	16	16	15	18
D 5	17	20	NI	15	18	18	18	19
D 6	20	17	16	17	19	20	20	17
D 7	NI	16	21	16	20	21	NI	17
D 8	16	14	21	14	16	19	16	20
D 9	16	16	17	16	15	24	22	19
D 10	20	17	19	17	18	17	17	18

E.coli NCIM 2066

The present investigation suggest that D-1,D-6 and D-10 were showed good microbiological activity against E.coli NCIM 2066.

S.aureus MTCC 737

Over all analysis of the results suggest D-8 was showed good microbiological activity against s.aureus then the standard drug.

S.paratyphi A MTCC 735

A compound such as D-2,D-3,D-7 were showed high anti-bacterial activity then the standard tested drugs used for bio-assay for S.paratyphi A.

B.pumilus MTCC 1607

The synthesized compound D-9 were showed very good anti-bacterial activity then the standard tested drugs tetracycline for B.pumilus. Hence these compounds should be further tested under various conditions for their pharmaceutical applications.

K.pneumoniae MTCC 432

A compound such as D-2,D-6 and D-9 were showed high anti-bacterial activity for K.pneumoniae than the standard tested drugs used for bio-assay Chloramphenicol.

CONCLUSION

The Main focus of this research work was to synthesize, characterize and evaluate anti fungal activities of the newly synthesized compounds were confirmed and characterized with the

help of analytical and spectral data's such as IR and 1H-NMR. Biological screening result of activities 1-(2,4-dinitrophenyl)-4-(substitutedphenyl)-6-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-3-methyl-1,4-dihydropyrano-[2,3-c]pyrazole-5-carbonitrile derivatives as above.

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