Available online at www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2017; 9(12): 702-709

ISSN- 0975 1556

Research Article

Synthesis and Characterization of 1,2,4-Triazole- Pyridine Hybrids as Potential Antimicrobial Agents

Ahirwar J[1*], Ahirwar D[1], Lanjhiyana S[1], Jha A K[2]

[1]*School of Pharmacy, Chouksey Engineering College, Bilaspur Chhattisgarh, India.*
[2]*Shri Shankaracharya Institute of Pharmaceutical Science, Bhilai, Chhattisgarh, India.*

Received: 21st Nov, 17; Revised 1st Dec, 17, Accepted: 15th Dec, 17; Available Online:25th Dec, 17

ABSTRACT

A novel 1,2,4-Triazole-Pyridine hybrid derivatives was synthesized by the reaction of nicotinohydrazide with carbon disulfide to yield *potassium-3-pyridyl-dithiocarbazate* (**I**). This was further cyclized with ammonia solution to yield 5-mercapto-substituted 1,2,4-Triazole-Pyridine hybrid (**II**). This was finally reacted with different substituted benzyl derivatives to produce 1,2,4-Triazole-Pyridine hybrid derivatives (**III**). Purity of the derivatives was confirmed by thin layer chromatography and melting point. Structure of these derivatives was set up by determining infrared spectroscopy, nuclear magnetic resonance spectroscopy and mass spectroscopy. Further, the synthesized derivatives were evaluated for their *in vitro* antibacterial activity against the two gram-negative bacteria (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 424)) and two gram positive bacteria (*Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442), and antifungal activity against the *Aspergillus niger* (MTCC 282), *Aspergillus clavatus* (MTCC 1323), *Candida albicans* (MTCC 227) by cup-plate method. Out of all synthesized derivatives, two derivatives *i.e. 3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* and *3-(5-(3,5-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent antibacterial activity while *3-(5-(2,4-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent anti fungal activity.

Keywords: 1,2,4-triazole, nicotinohydrazide , substituted benzyl derivatives , pyridine hybrid, antimicrobial activity.

INTRODUCTION

The emerging infectious diseases and the increasing number of multi-drug resistant microbial pathogens are the main challenge behind the treatment of infectious diseases. In spite of wide range of anti-microbial drugs with different mechanisms of action used to treat with microbial infections either alone or in combination and also the existence many compounds used in different phases of clinic trials, microbial infections have been becoming a worldwide problem. An increase in mortality might be due to emergence of antimicrobial resistance. The toxic side effects and the increasing chances of microbial resistance are the problem with clinically used drugs that are often dose limiting[1-5]. Moreover, the long term use of several drugs to treat microbial infections may cause serious health problems, especially in patients with impaired liver or kidney functions.

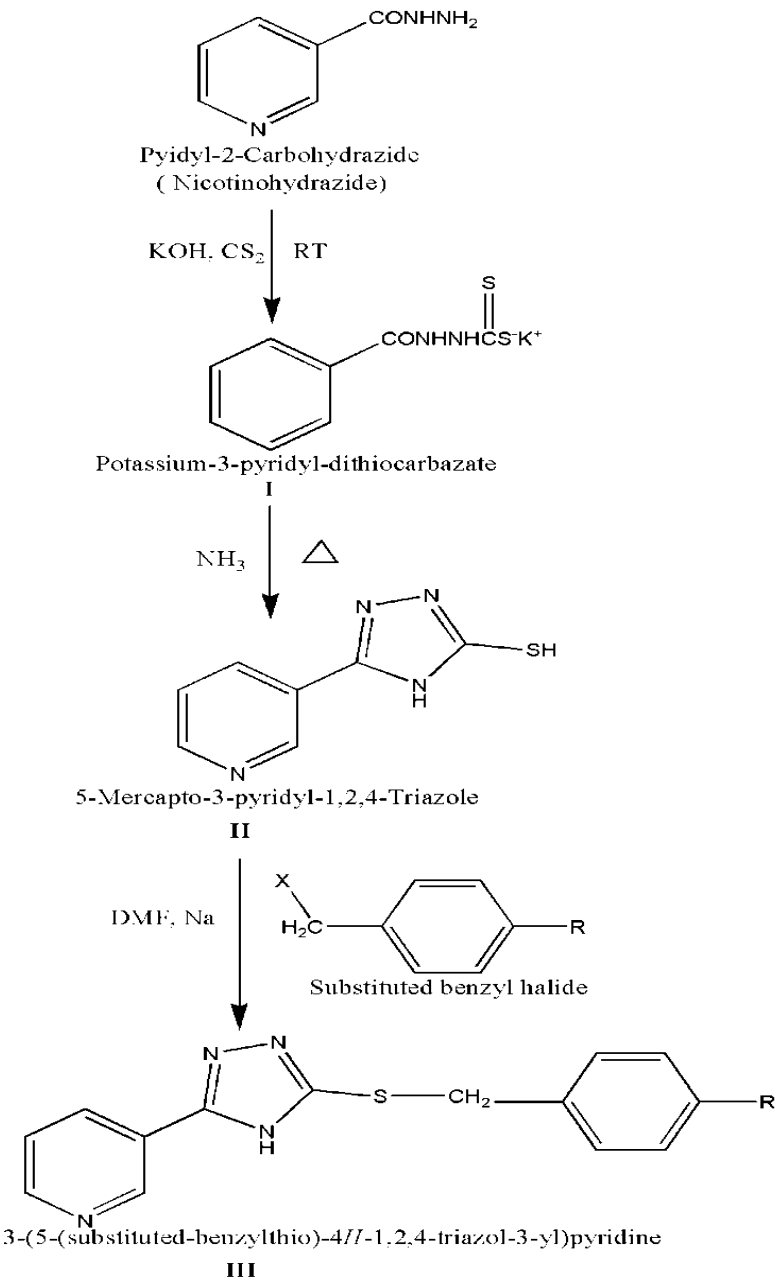
To search and synthesize of combinational chemotherapeutic drugs with different mechanisms of action and with low side effects constitute an important part of the methods that aims to overcome the antimicrobial resistance. Beside the development of completely new agents possessing chemical characteristics that clearly differ from those of existing ones, there is another approach containing to

combine two or more pharmacophores into a single molecule. Therefore, a single molecule containing more than one pharmacophores, each with different mode of action, could be beneficial for the treatment of microbial infectious. These merged pharmacophores may be addressing the active site of different targets and offer the possibility to overcome drug resistance. In addition, this approach can also reduce unwanted side effects[6-11].

Amongst the broad range of heterocyclic that are being explored for expansion of new components in the field of medicinal chemistry, 1,2,4-Triazole-Pyridine hybrids and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. The triazole is an attractive bridge group, which could connect two pharmacophores to produce novel bifunctional molecules, while it is almost impossible to be hydrolyzed, oxidized or reduced.

Based on these literature data and the features described previously[12-24], we have created a small library of 1,2,4-Triazole-Pyridine hybrid derivatives as per Figure I. A series of 1,2,4-Triazole-Pyridine hybrid derivatives linked with substituted benzyl group was synthesized by the reaction of nicotinohydrazide with carbon disulfide to yield *potassium-3-pyridyl-dithiocarbazate* (I). This was further treated with ammonia solution to yield 5-mercapto-substituted 1,2,4-Triazole-Pyridine hybrid (II). This was finally reacted with different benzyl derivatives to produce series of 1,2,4-Triazole-Pyridine hybrid derivatives (III).

**Author for Correspondence: jyoti01ahirwar@gmail.com*



3a:R=-4OCH_3	3c:R=-2OCH_3	3e:R=-3NO_2	3g:R=-3,5$(NO_2)_2$
3b:R=-3OCH_3	3d:R=-4NO_2	3f:R=-2NO_2	3h:R= 2,4$(NO_2)_2$

Figure 1: Representation of the series of reactions for the synthesis of novel **1**,2,4-Triazole- Pyridine hybrids.

These 1,2,4-Triazole-Pyridine hybrid derivatives, were characterized by thin layer chromatography and melting point. Structure of these derivatives was set up by determining infrared spectroscopy, nuclear magnetic resonance spectroscopy and mass spectroscopy. All the synthesized compounds were screened for their biological activities. Their antimicrobial and antifungal activities were tested and compared with the ones of some commercial antibiotics.

Table 1: Characterization data of synthesized 1,2,4-triazole derivatives.

Derivatives	R_1	Molecular formula	Molecular weight	Melting point (°C)	Appearance	Retention factor	Solubility	% yield (w/w)	λ max (nm)	Chemical Name
3a.	4-OCH_3	$C_{15}H_{14}N_4OS$	298	215	Yellow solid	0.65	DMF	78.46	326	3-(5-(4-methoxybenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3b.	3-OCH_3	$C_{15}H_{14}N_4OS$	298	258	Yellow solid	0.63	Ethanol	67.74	325	3-(5-(3-methoxybenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3c.	2-OCH_3	$C_{15}H_{14}N_4OS$	298	300	Yellow solid	0.64	Ethanol	72.89	326	3-(5-(2-methoxybenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3d.	4-NO_2	$C_{14}H_{11}N_5O_2S$	313	320	Yellow solid	0.84	Ethanol	85.47	365	3-(5-(4-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3e.	3-NO_2	$C_{14}H_{11}N_5O_2S$	313	328	White Solid	0.82	DMF	85.47	365	3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3f.	2-NO_2	$C_{14}H_{11}N_5O_2S$	313	324	White Solid	0.84	DMF	73.25	365	3-(5-(2-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3g.	3,5-$(NO_2)_2$	$C_{14}H_{10}N_6O_4S$	358	349	Brown Solid	0.91	Ethanol	69.36	366	3-(5-(3,5-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine
3h.	2,4-$(NO_2)_2$	$C_{14}H_{10}N_6O_4S$	358	366	Brown Solid	0.91	DMF	89.26	367	3-(5-(2,4-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine

Experimental

Open capillary method was adopted to determine the melting points and the purity of compounds was checked by TLC. Fourier transform infrared (FTIR) spectra (KBR, cm^{-1}) were recorded on Perkins Elmer Infrared-283 FTIR, 1HNMR ($CDCl_3$) were on a Bruker 300MHz spectrometer using TMS as an internal reference and the MS were recorded on Aapi 3000 LC-MS.

The synthesized compounds **3a–3h** were examined for their *in vitro* antibacterial activity against the two gram-negative bacteria (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 424)) and two gram positive bacteria (*Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442)), by cup-plate method [25-27]. Zone of inhibition of all derivatives was determined and compared with standard Streptomycin and Clotrimazole, which were used as reference drug. Moreover, *Aspergillus niger* (MTCC 282), *Aspergillus clavatus* (MTCC 1323), *Candida albicans* (MTCC 227) were chosen based on their clinical and pharmacological importance. In order to investigate the antifungal activity of the compounds, a modified microdilution technique was used[28,29].

Synthesis of potassium-3-pyridyl-dithiocarbazate (I)

A solution of 8.4g (0.15M) of potassium hydroxide, 200ml of absolute ethanol and 13.7g (0.10M) of pyidyl-2-carbohydrazide was treated to the addition of 11.4g (0.15M) of carbon disulfide. The mixture was diluted with 150ml of absolute ethanol and agitated for 12-16 hr. It was then diluted with 200ml of dry ether and dried at 65^0C. The salts, prepared as described above were obtained is nearly quantitatively yield and were employed without further purification.

Synthesis of 5-mercapto-3-pyridyl-1,2,4-Triazole (II)

A suspension of **I** (24g, 0.096M), 95% Ammonia 20ml(0.864M) and water 40ml was refluxed with stirring for 3 to 4 hrs. The color of this reaction mixture changed to yellow, hydrogen sulfide was evolved and a homogeneous solution resulted. A white solid was precipitated by dilution with cold water (100ml) and acidify with conc. HCL, filtered and washed with cold water and recrystallized.

Synthesis of 3-benzylthio-5-pyridin-3-yl,1,2,4-Triazole (III)

A mixture of **II** (0.006M), (0.69g,6M) in dry N,N-dimethyl formamide(3ml) was added to a solution of sodium(0.14g, 6M) in dry methanol (2ml). After 10 min of stirring at room temperature, benzyl halide (6M) was added. The resultant suspension was stirred with $CaCl_2$ guar tube at room temperature 1-23 hrs. The completion of reaction was confirmed by TLC and then resultant solution was poured in crushed ice.

In-vitro Antibacterial Screening of Synthesized Compounds

The synthesized compounds were tested for their *in vitro* antibacterial activity against the two gram-negative bacteria (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 424)) and two gram positive bacteria (*Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442)), by cup-

Table 2. Combustion analysis of synthesized derivatives.

Derivatives	Combustion Analysis	
	Theoretical Value	Observed Values
a.	C (60.38%) H (4.73%) N (18.78%) O (5.36%) S (10.75%)	C (59.30%) H (4.70%) N (18.65%) O (5.32%) S (10.70%)
b.	C (60.38%) H (4.73%) N (18.78%) O (5.36%) S (10.75%)	C (59.30%) H (4.70%) N (18.65%) O (5.32%) S (10.70%)
c.	C (60.38%) H (4.73%) N (18.78%) O (5.36%) S (10.75%)	C (59.30%) H (4.70%) N (18.65%) O (5.32%) S (10.70%)
d.	C (53.66%) H (3.54%) N (22.35%) O (10.21%) S (10.23%)	C (52.60%) H (3.51%) N (22.15%) O (10.17%) S (10.20%)
e.	C (53.66%) H (3.54%) N (22.35%) O (10.21%) S (10.23%)	C (52.60%) H (3.51%) N (22.15%) O (10.17%) S (10.20%)
f.	C (53.66%) H (3.54%) N (22.35%) O (10.21%) S (10.23%)	C (52.60%) H (3.51%) N (22.15%) O (10.17%) S (10.20%)
g.	C (46.93%) H (2.81%) N (23.45%) O (17.86%) S (8.95%)	C (46.13%) H (2.80%) N (23.35%) O (17.79%) S (8.90%)
h.	C (46.93%) H (2.81%) N (23.45%) O (17.86%) S (8.95%)	C (46.13%) H (2.80%) N (23.35%) O (17.79%) S (8.90%)

plate method. Clotrimazole and Streptomycin were used as standard drug for antibacterial studies. Nutrient Agar (Beef extract 10 gm, Peptone 10 gm, Sodium Chloride 5 gm, Agar 20 gm, urfied water 1000ml) was employed as culture media for antibacterial studies. The ingredients were dissolved in water, and adjust the PH to 7.2 to 7.4 by using dilute alkali/dilute acid and autoclave at 120 ºC for 20 min.30-35 ml of nutrient agar was transferred to the Petri dish. 1000µg/disc and 500µg/disc concentration of the test compounds are prepared & Dimethyl Foramide (DMF) was used as vehicle and Chlotrimazole & Streptomycin was used as standard. Nutrient agar plates were prepared aseptically to get a thickness of 5-6 mm. The plates were allowed to solidify and inverted to prevent condensate falling on the agar surface. The plates were dried at 37 ºC just before inoculation. The standard inoculums is inoculated in the plates prepared earlier aseptically by dipping a sterile swab in the inoculums, removing the excess of inoculums by pressing and rotating the swab firmly against the sides of the culture tube above the level of the liquid and finally streaking the swab all over the surface of 60 after each application. Finally press the swab round the edge of the agar surface. The sterilized discs for the test drugs were placed in the Petri dishes aseptically. Incubate the Petri dish at 37 ºC ± 0.2 ºC for about 18-24 hrs, after placing them in the refrigerator for one hour to facilitate uniform diffusion. The average zone diameter of the plates were measured and recorded. All compounds synthesized were tested for antibacterial activity against gram-negative bacteria and gram positive bacteria.

Antifungal activity

Aspergillus niger (MTCC 282), *Aspergillus clavatus* (MTCC 1323), *Candida albicans* (MTCC 227) were chosen based on their clinical and pharmacological importance. In order to investigate the antifungal activity of the compounds, a modified microdilution technique was used. The funga spores were washed from the surface of agar plates with sterile 0.85% saline containing 0.1% Tween 80 (v/v) and spore suspension was adjusted with sterile saline to a concentration of 1.0×10^5. Compound solutions were added to the broth Malt medium with inoculum. DMSO was used as a negative control, and commercial fungicides, griseofulvin and ketoconazole were used as positive controls. Five percent DMSO was used as a negative control. The sensitivities of the microorganism species to the synthesized derivatives were determined by measuring the sizes of inhibitory zones (including the diameter of disk) on the agar surface around the disks, and values <8 mm were considered as not active against microorganisms.

RESULTS AND DISCUSSION

In current investigation we are synthesized derivatives of 1,2,4-Triazole-Pyridine hybrids and screened for potential antimicrobial and antifungal action. Also, for the first time we have used nicotinohydrazide as a starting material for the synthesis of above mentioned derivatives. The newly synthesized 1,2,4-Triazole-Pyridine hybrid derivatives were subjected to confirmation of physical and analytical parameters by using techniques like TLC, IR, NMR and MS. Finally, these compounds were screened for *in vitro* antibacterial activity against the two gram-negative bacteria (*Escherichia coli* (MTCC 443), *Pseudomonas aeruginosa* (MTCC 424)) and two gram positive bacteria (*Staphylococcus aureus* (MTCC 96), *Streptococcus pyogenes* (MTCC 442), and antifungal activity against the *Aspergillus niger* (MTCC 282), *Aspergillus clavatus* (MTCC 1323), *Candida albicans* (MTCC 227) by cup-plate method.

Strategy for the synthesis of different 1,2,4-Triazole-Pyridine hybrid derivatives is outlined in **Figure 1**. Total 08 different 1,2,4-Triazole-Pyridine hybrid derivatives were prepared by treating 5-mercapto-substituted 1,2,4-Triazole-Pyridine hybrid with different substituted benzyl derivatives**.** Chemical structure, melting point and other physical data were mentioned in Table 1. Formation of different 1,2,4-Triazole-Pyridine hybrid derivatives was recognized by using different spectral techniques like IR, ^{1}H NMR and MS.

Table 3. Spectral data of synthesized 1,2,4-triazole derivatives.

Derivatives	IR (KBr cm^{-1})	1H NMR δ (ppm) (DMSO-d_6)	MS
3a	2998.46(Ar-C-H str), 1598.35.47(Ar-C=C str), 1155.47 (Ar–C–C str), 1510.36(C=Nstr), 1285.47(-C-N- str), 641.81(-C-S str), 1165.79(OCH_3 str)	6.66-7.95 (m 4H, Ar-H), 4.18 (s 2H, -CH_2), 7.48-8.82 (m 4H, pyridine ring), 3.67 (s 3H, -CH_3)	297^+
3b	2942.56(Ar-C-H str), 1643.56(Ar-C=C str), 1121.67(Ar–C–C str), 1511.12(C=Nstr), 1213.87(-C-N- str), 631.78(-C-S str), 1105.13(OCH_3 str)	6.76-7.81 (m 4H, Ar-H), 4.15 (s 2H, -CH_2), 7.44-8.86 (m 4H, pyridine ring), 3.76 (s 3H, -CH_3)	297^+
3c	2840.45(Ar-C-H str), 1611.76(Ar-C=C str), 1106.45(Ar–C–C str), 1511.10(C=Nstr), 1286.45(-C-N- str), 698.34(-C-S str), 1112.12(OCH_3 str)	6.65-7.28 (m 4H, Ar-H), 4.17 (s 2H, -CH_2), 7.50-8.84 (m 4H, pyridine ring), 3.57 (s 3H, -CH_3)	297^+
3d	3168.46(Ar-C-H str), 1628.35.47(Ar-C=C str), 1145.47 (Ar–C–C str), 1510.36(C=Nstr), 1285.47(-C-N- str), 619.81(-C-S str), 1365.79(-NO_2 str)	7.26-8.01 (m 4H, Ar-H), 4.19 (s 2H, -CH_2), 7.60-8.85 (m 4H, pyridine ring)	312^+
3e	2912.56(Ar-C-H str), 1613.56(Ar-C=C str), 1121.67(Ar–C–C str), 1522.12(C=Nstr), 1243.87(-C-N- str), 641.78(-C-S str), 1335.13(-NO_2 str)	7.36-8.11 (m 4H, Ar-H), 4.16 (s 2H, -CH_2), 7.62-8.64 (m 4H, pyridine ring)	312^+
3f	2890.45(Ar-C-H str), 1621.76(Ar-C=C str), 1108.45(Ar–C–C str), 1551.10(C=Nstr), 1246.45(-C-N- str), 688.34(-C-S str), 1312.12(-NO_2 str)	6.76-7.31 (m 4H, Ar-H), 4.15 (s 2H, -CH_2), 7.60-8.62 (m 4H, pyridine ring)	312^+
3g	3134.78(Ar-C-H str), 1622.89(Ar-C=C str), 1156.89(Ar–C–C str), 1501.21(C=Nstr), 1254.76(-C-N- str), 698.98(-C-S str), 1342.45(-NO_2 str)	8.38-8.93 (m 3H, Ar-H), 4.19 (s 2H, -CH_2), 7.60-8.60 (m 4H, pyridine ring)	357^+
3h	3078.45(Ar-C-H str), 1632.67(Ar-C=C str), 1109.78(Ar–C–C str), 1520.90(C=Nstr), 1215.43(-C-N- str), 685.56(-C-S str), 1332.56(-NO_2 str)	7.58-9.00 (m 3H, Ar-H), 4.18 (s 2H, -CH_2), 7.65-8.68 (m 4H, pyridine ring)	357^+

IR spectrum of one 1,2,4-Triazole-Pyridine hybrid derivative, (3e) i.e. *3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showed strong C=N stretching (str) band at 1522.12 cm^{-1} and C-N absorption band at 1243.87 cm^{-1} which indicate ring closure of 1, 2, 4-triazole ring. An absorption band at 2912.56 cm^{-1} is due to aromatic (Ar) C-H str, band at 1613.56 cm^{-1} is due to C=C str, band at 1335.13 cm^{-1} is due to -NO_2 str str and band at 1121.67cm^{-1} is due to C-C str. Strong absorption at around 3078.85 cm^{-1} and around 1620.47 cm^{-1} was present in all final derivatives, which was confirmation for aromatic C-H and C=C bonds respectively. The presence of specific functional groups in final synthesized derivatives was confirmed by ^{1}H NMR data. The ^{1}H NMR spectrum of 1,2,4-Triazole-Pyridine hybrid derivative, (3e) i.e. *3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* shown in the region 7.36-8.11 is due to four aromatic proton, 7.62-8.64 is due to four pyridine proton, and 4.16 is due to two methylene proton. The mass spectra of 1,2,4-Triazole-Pyridine hybrid derivative, (3e) i.e. *3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showed molecular ion peak at *m/z* 312 which is in conformity with the molecular formula $C_{14}H_{11}N_5O_2S$. In the same way, spectral data of remaining derivatives are given in Table 3.

Table 4 Anti –Bacterial Activity of synthesized 1,2,4-triazole derivatives using plate hole diffusion method:

Compounds	Zone of inhibition (mm)							
	Gram-ve bacteria				Gram +ve bacteria			
	E.Coli		*P. aeruginosa*		*S.aureus*		*S.pyrogenes*	
	500 µg/ml	1000 µg/ml	*500* µg/ml	1000 µg/ml	*500* µg/ml	1000 µg/ml	*500* µg/ml	1000 µg/ml
3a.	12	16	11	16	10	15	09	16
3b.	11	15	10	16	10	15	10	17
3c.	12	15	12	17	08	13	08	14
3d.	08	12	08	14	11	15	10	16
3e.	12	18	08	13	12	17	10	17
3f.	10	16	10	16	11	16	09	16
3g.	12	17	13	18	12	16	10	16
3h.	12	16	10	16	12	16	10	16
Streptomycin	15	24	14	23	--	--	--	--
Clotrimazole	--	--	--	--	15	24	16	25
DMF(control)	--	--			--		--	

#Diameter of zone of inhibition expressed in mm

Table 5 Anti –Fungal Activity of synthesized 1,2,4-triazole derivatives using plate hole diffusion method:

Compounds	Zone of inhibition (mm)					
	A. niger		*A. clavatus*		*C.albicans*	
	500 µg/ml	1000µg/ml	*500* µg/ml	1000µg/ml	*500* µg/ml	1000µg/ml
	10	16	10	18	12	19
	09	15	10	19	12	18
	11	19	13	20	13	19
	09	16	08	14	09	15
	09	18	10	16	19	17
	10	16	12	17	10	16
	12	19	13	18	13	20
	13	20	13	21	14	22
Ketonazole	18	24	17	23	15	28
Griseofulvin	20	28	22	29	20	28
DMSO (solvent)	-	-	-	-	-	-

#Diameter of zone of inhibition expressed in mm

The synthesized derivatives are evaluated for antibactrtial and antifungal potantial. The tested derivatives exhibited 12-18 mm zone of inhibition in 1000µg/ml concentration against Gram-ve bacteria and Gram+ve bacteria, whereas standard drug Streptomycin and Clotrimazole showed 24-25 mm zone of inhibition (Table 4). Similarly, derivatives also elicited 14-22 mm zone of inhibition 1000µg/ml concentration against fungas, whereas standard drug Ketonazole and Griseofulvin produced showed 23-28 mm zone of inhibition (Table 5).

Out of all synthesized derivatives, two derivatives *i.e. 3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* and *3-(5-(3,5-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent antibacterial activity while *3-(5-(2,4-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent anti fungal activity.

It was found that the 3-position and 5-postion of triazole nucleus are extremely important sites for molecular modification, which can play a dominant role in determining the pharmacological activities of triazole derivatives. Therefore we have attempted to develop the derivatives of triazole nucleus at 3-position and 5-postion with a view to evaluate further the potency of the molecules. In the present study, as discussed above we have synthesized the 1,2,4-Triazole-Pyridine hybrid derivatives. The resulting compounds produced around 75% efficacy as compared to standard against gram-ve, gram+ve bacteria and fungi. Results revealed that novel 1,2,4-Triazole-Pyridine hybrid showed significantly antibacterial and anti fungal activities as compared to other 1,2,4-Triazole-Pyridine hybrids (Table 4 & 5).

CONCLUSION

A new series of different 1,2,4-Triazole-Pyridine hybrid derivatives were prepared by treating 5-mercapto-substituted 1,2,4-Triazole-Pyridine hybrid with different substituted benzyl derivatives, by a simple, suitable and well-organized synthetic route. Physical and analytical parameters of the newly synthesized 1,2,4-Triazole-Pyridine hybrid derivatives were confirmed by TLC, IR, NMR and MS. Subsequently, in antimicrobial screening, the compounds showed antibacterial and anti fungal activities. In antimicrobial screening, *3-(5-(3-nitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* and *3-(5-(3,5-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent antibacterial while *3-(5-(2,4-dinitrobenzylthio)-4H-1,2,4-triazol-3-yl)pyridine* showing more potent anti fungal activity as compare to other derivatives. Thus, we feel that the data of present study may pave a way for the development of novel antibacterial and antifungal agents with good efficacy and lesser adverse effects.

ACKNOWLEDGEMENT

The authors thank to the Management of School of Pharmacy, Chouksey Engineering College, Bilaspur, for providing necessary infrastructural facilities, and RGPV, Bhopal for providing immense help in the spectral analysis.

CONFLICT OF INTEREST

None

REFERENCES

1. Rawal RK, Phabhakar YS, Kati SB, De Clercq E. 2-(Aryl)-3-furan-2-ylmethyl-thiazolidin-4-ones as selective HIV-RT Inhibitors. Bioorganic & Medicinal Chemistry 2005; 13 (24): 6771-6776.
2. Bonde CG, Gaikwad NJ. Synthesis and preliminary evaluation of some pyrazine containing thiazolines and thiazolidinones as antimicrobial agents Bioorganic & Medicinal Chemistry 2004; 12 (9): 2151-2161.
3. Rawal RK, Tripathi R, Kati SB, Pannecouque C, De Clercq E. Design, synthesis, and evaluation of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones as anti-HIV agents. Bioorganic & Medicinal Chemistry 2007; 15 (4): 1725-1731.

4. Dixit PP, Patil VJ, Nair PS, Jain S, Sinha N, Arora SK. Synthesis of 1-[3-(4-benzotriazol-1/2-yl-3-fluoro-phenyl)-2-oxo-oxazolidin-5-ylmethyl]-3-substituted-thiourea derivatives as antituberculosis agents. European Journal of Medicinal Chemistry 2006; 41(3): 423-428.
5. Kaplancikli ZA, Turan-Zitouni G, Özdemir A, Revial G. New triazole and triazolothiadiazine derivatives as possible antimicrobial agents. European Journal of Medicinal Chemistry 2008; 43(1): 155-159.
6. Solomon VR, Hua C, Lee H, Design and synthesis of anti-breast cancer agents from 4-piperazinylquinoline: A hybrid pharmacophore approach. Bioorganic & Medicinal Chemistry 2010; 18 (4): 1563-1572.
7. Hu C, Solomon VR, Ulibarri G, Lee H. The efficacy and selectivity of tumor cell killing by Akt inhibitors are substantially increased by chloroquine. Bioorganic & Medicinal Chemistry 2008; 16 (17): 7888-7893.
8. Hu C, Solomon VR, Cano P, Lee H, A 4-aminoquinoline derivative that markedly sensitizes tumor cell killing by Akt inhibitors with a minimum cytotoxicity to non-cancer cells. European Journal of Medicinal Chemistry 2010; 45 (2): 705-709.
9. Kouznetsov VV, Gomez-Barrio A. Recent developments in the design and synthesis of hybrid molecules basedon aminoquinoline ring and their antiplasmodial evaluation. European Journal of Medicinal Chemistry 2009;. 44 (8): 3091-3113.
10. Adamec J, Beckert R, Weiss D, Klimesova V, Waisser K, Mollmann U, Kaustova J, Buchta V. Hybrid molecules of estrone: new compounds with potential antibacterial, antifungal, and antiproliferative activities. Bioorganic & Medicinal Chemistry 2007; 15(8): 2898-2906.
11. Meunier B. Hybrid molecules with a dual mode of action: dream or reality? Accounts of Chemical Research 2008; 41 (1): 69-72.
12. Tozkoparan B, Kupeli E, Yesilada E, Ertan M. Preparation of 5-aryl-3-alkylthio-l,2,4-triazoles and corresponding sulfones with antiinflammatory-analgesic activity. Bioorganic & Medicinal Chemistry Letters 2007; 15(14): 1808-1814.
13. Turan-Zitouni G, Kaplancikli ZA, Erol K, Killic FS. Synthesis and analgesic activity of some triazoles and triazolothiadiazines. Farmaco 1999; 54(4): 218-223.
14. Czarnocka-Janowicz A, Foks H, Nasal A, Petrusewicz J, Damasiewicz B, Radwanska A, Kaliszan R. Synthesis and analgesic activity of some triazoles and triazolothiadiazines. Pharmazie 1991; 46(2): 109-112.
15. Mhasalkar MY, Shah MH, Nikam ST, Ananthanarayana KG, Deliwala CV. 4-alkyl-5-aryl-4H-1,2,4-triazole-3-thiols as hypoglycemic agents. Journal of Medicinal Chemistry 1970; 13(4):672-674.
16. E. Przegalinski E, A. Lewandowska A. The effect of etoperidone, a new potential antidepressant drug, on the central serotonin system. Journal of Neural Transmission 1979;46(4): 303-312.
17. Langley MS, Clissold SP. Brotizolam. A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy as an hypnotic. Drugs 1988; 35(2):104-122.
18. Kelley JL, Koble CS, Davis RG, McLean EW, Soroko FE, Cooper BR. 1-(Fluorobenzyl)-4-amino-1H-1,2,3-triazolo[4,5-c]pyridines: synthesis and anticonvulsant activity. Journal of Medicinal Chemistry 1995; 38(4): 4131-4134.
19. Kumar D, Kumar NM, Chang KH, Shah K. Synthesis and anticancer activity of 5-(3-indolyl)-1,3,4-thiadiazoles. European Journal of Medicinal Chemistry 2010; 45(10): 4664-4678.
20. 20 El-Nassan HB. Synthesis and antitumor activity of novel pyrido[2,3-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5-one derivatives. European Journal of Medicinal Chemistry 2011; 46(6): 2031-2036.
21. El Sayed Aly MR, Saad HA, Mohamed MAM. Click reaction based synthesis, antimicrobial, and cytotoxic activities of new 1,2,3-triazoles. Bioorganic & Medicinal Chemistry Letters 2015; 25(14): 2824-2830.
22. Petrova KT, Potewar TM, Correia-da-Silva P, Barros MT, Calhelha RC, Ciric A, Sokovic M, Ferreira ICFR. Antimicrobial and cytotoxic activities of 1,2,3-triazole-sucrose derivatives. Carbohydrate Research 2015;417: 66-71.
23. Zhao PL, Ma WF, Duan AN, Zou M, Yan YC, You WW, Wu SG. One-pot synthesis of novel isoindoline-1,3-dione derivatives bearing 1,2,4-triazole moiety and their preliminary biological evaluation. European Journal of Medicinal Chemistry 2012; 12(54): 813-822.
24. Kotaiah Y, Nagaraju K, Harikrishna N, Venkata C, Yamini L, Vijjulatha M. Synthesis, docking and evaluation of antioxidant and antimicrobial activities of novel 1,2,4-triazolo[3,4-b][1,3,4]thiadiazol-6-yl)selenopheno[2,3-d]pyrimidines. European Journal of Medicinal Chemistry 2014;75:195-202.
25. Dewangan D, Pandey A, Sivakumar T, Rajavel R, Dubey R. Synthesis of some Novel 2, 5- Disubstituted 1, 3, 4-Oxadiazole and its Analgesic, AntiInflammatory, Anti-Bacterial and Anti-Tubercular Activity. International Journal of ChemTech Research 2010; 2(3):1397-1406.
26. Dewangan D, Tripathi DK, Verma T, Nagori K, Shah V, Rajawel R. Synthesis, Characterization and Anti-Inflammatory, Analgesic, and Antimicrobial activities of substituted 4-(4- oxo-2-phenylquinazolin-3(4H)-yl) N-aryl-methylene benzenesulfonamide derivatives. International Journal of ChemTech Research 2011; 3(1): 948-956.
27. Badwaik H, Vekatraman S, Thakur D, Vinod M, Raamamurthy J, Dshmukh K. Antibacterial Evaluation of Novel 2-Aryl-Quinoline-3-Carbaldehyde Derivatives. Asian Journal of Research In Chemistry 2011; 4 (6): 893-895.
28. Rajput S, Sisodia D, Badwaik H, Thakur D, Nagori K. Synthesis, Characterization and Antimicrobial Activity of A 5(4-(4-

Substituted)Aminobenzylidine)Thiazolidine-2,4-Dione Derivatives. Asian Journal of Research In Chemistry 2011; 4 (1): 40-43.

29. Badwaik H, Sonkar S, Singh M, Rajput S, Sisodiya D, Pandey A. Synthesis and Antibacterial Evaluation of Some Novel Phenyl Thiazolyl Quinazoline-4-(3H)-one Derivatives. Asian Journal of Research In Chemistry 2009; 2(4): 544-54