Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2023, Vol. 39, No.(1):
Pg. 129-135

Rational Design, Synthesis, Characterization, and Anti-bacterial activity of Urea Derivatives Bearing 1,2,4-triazoles as Molecular Hybrid Scaffolds

SUNIL KUMAR CHOUDHARY[1], PRIYA GOTHWAL[1], NIDHI SOGANI[2], AJAY SAINI[3] and SUMAN SWAMI[4]*

[1]Department of Biotechnology and Allied Sciences, Faculty of Education and Methodology, Jayoti Vidyapeeth Women's University, Jaipur, India.
[2]Department of Chemistry, Parishkar College of Global excellence, Jaipur, India.
[3]Central Analytical Facilities, Manipal University Jaipur, Rajasthan, India.
[4]Department of Chemistry, Chandigarh University, NH-95, Ludhiana-Chandigarh State Hwy, Punjab 140413, India.
*Corresponding author E-mail: sumanswami1994@gmail.com

http://dx.doi.org/10.13005/ojc/390115

(Received: December 30, 2022; Accepted: February 04, 2023)

ABSTRACT

A new set of molecular hybrids, urea derivatives carrying 1,2,4-triazole as molecular hybrid scaffolds, were developed, synthesised, characterised, and assessed for potential anti-bacterial action. Triazole scaffolds are key moieties in many pharmacological compounds, and their inclusion with urea moiety makes them more valuable for biological purposes. As a result, urea derivatives containing 1*H*-1,2,4-triazole and 3-(methylthio)-1*H*-1,2,4-triazole moieties were produced by reacting carbamates of 4-amino-1,2,4-triazoles and 3-(methylthio)-4-amino-1,2,4-triazole with amines in DMF using trimethyl amine for 15 h at ca. 60°C. ^{1}H NMR, ^{13}C NMR, FTIR, and HRMS techniques were used to characterise all of the produced compounds. The anti-bacterial activity of all produced derivatives was examined against *Enterococcus faecalis, Pseudomonas, E. Coli, Klebsiella pneumonia, Candida albicans, Bacillus anthracis, Proteus mirabilis*, and *Staphylococcus aureus*.

Keywords: 4H-1,2,4-triazol-4-amine, Urea, 3-(methylthio)-4H-1,2,4-triazol-4-amine, Molecular hybrid scaffold, Anti-bacterial activity.

INTRODUCTION

Despite the rising demand for medicinally potent molecules for drug development, molecular hybridization techniques have rapidly arisen and strengthened over the years. A molecular hybridization is a technique in which two separate active pharmacophores are combined with or without the assistance of a linker to form a new hybrid scaffold.[1,2] The novel hybrid scaffold is expected to have higher effectiveness and selectivity profiles than the parent medications, and it may help reduce the possibility of multiple drug resistance.[3] As a result of the ever-increasing need for medicinal molecules,

This is an Open Access article licensed under a Creative Commons license: Attribution 4.0 International (CC- BY).
Published by Oriental Scientific Publishing Company © 2018

heterocyclic compounds have long been an intriguing subject. Because of their moderate dipole character, stiffness, and durability *In vivo*, hydrogen bonding capabilities, the triazoles (1H-1,2,3-triazole, 1H-1,2,4-triazole) are good surrogates in bioactive compounds with a wide range of pharmacological activities.[4-6] These motifs have potential uses in HIV, anticancer, anti-protozoal, antibacterial, anti-proliferative, ß-lactamase inhibitory, anti-inflammatory, agrochemical, and material research. Some of the most potent antifungal compounds are those containing a triazole nucleus, such as itraconazole, fluconazole, and the new generation of triazoles posaconazole, voriconazole, and ravuconazole.[7-11] Among the triazoles, 1,2,4-triazole has been shown to have excellent pharmacological properties. For example, 1H-1,2,4-triazole carrying compounds are being explored as 5-lipoxygenase inhibitors, antiepileptics, anticancer drugs, and Pt(II) complexes containing 1H-1,2,4-triazoles exhibit activity like cis-platin.12-14 Aside from pharmaceutical uses, various 1,2,4-triazole-based agro-fungicides with 1H-1,2,4-triazole as a core component are also available, such as Triadimefon, Triadimenol, Diniconazole, Flusilazole, and Difenoconazole.[15-17] (Figure 1).

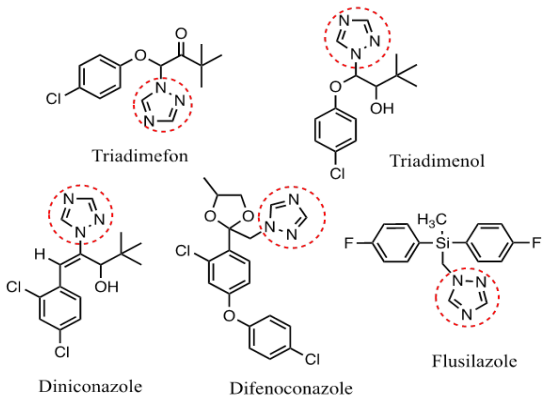


Fig. 1. Structure of bioactive compounds containing triazole moiety

Urea derivatives ($R_2N(CO)NR_2$), on the other hand, are used as solvents, medications, and fertilisers.[18,19] Some urea derivatives are antituberculosis, antibacterial, and anticonvulsant agents.[20-24] Given the biological relevance of these two pharmacophoric units, 1,2,4 triazole and urea, it was intriguing to create a new class of heterocyclics by molecular hybridization, in which the powerful 1,2,4-triazole moiety relates to urea derivatives. Since Bladin described the first synthetic mehtod of 1H-1,2,4-triazole in 1885,[25] many protocols to improve yield have been investigated, including the reaction of formyl-hydrazine with formamide (K.T.Potts, 1961),[26] condensation of hydrazine sulphate with formamide (M. Sekiya and S. Ishikawa, 1958),[14,27] and the reaction of N, N-Diformylhydrazine with excess ammonia (C. Ainsworth and R. G. Jones, 1955).[28] Most of the synthetic techniques based on this procedure have low yield formation. As a result, considerable attempts have been made in recent years to enhance the yield of 1,2,4-triazoles. Thus, in concern, production of 1,2,4-triazoles with high yield, followed by hybridization of the 1,2,4-triazoles with urea moiety to develop important pharmacophores. We began by preparing carbamates of 4-amino-1,2,4-triazoles using a multistep technique, and then we performed reactions of created carbamates of 4-amino-1,2,4-triazoles **(1a-g)** with amines. We also tested the hybrid scaffolds for antibacterial activity against *Enterococcus feacalis, Pseudomonas, E. coli, Klebsiella pneumonia, Candida albicans, Bacillus anthracis, Proteus mirabilis*, and *Staphylococcus aureus*.

EXPERIMENTAL

Without additional purification, commercially available reagents were utilized. Column chromatography was used to manufacture and purify carbamates. Freshly dried and distilled solvents TLC was used to monitor all the reactions on pre-coated silica gel plates. Before usage, silica gel (60-80 Mesh) and anhydrous sodium sulphate were activated in a muffle furnace. The melting points were calculated using a Tempo device and results have not been modified. Bruker-DPX-300 (300 MHz) spectrometer was used to record NMR spectra. In nuclear magnetic resonance, the operational frequency of ^{1}H NMR is 300MHz, whereas ^{13}C NMR at 100 MHz frequency (using TMS as the internal reference). The FLASH Ea 1112 series CHN analyzer was utilized to carry out the elemental analysis procedures for C, H, and N. The Water's Xevo G2-S Q Tof mass spectrometer was used to acquire the mass spectra.

Generalized synthesis procedure and characterization of urea derivatives (3a-3i and 5a-c)

Carbamate derivatives (1.0 equiv) were dissolved in DMF (20 vol. eq.) in a round bottom flask

of 100 mL. This solution was treated with triethyl amine (2.5 eq.) and amine (1.5 eq.) before being stirred 60°C for 15 hours. TLC (thin layer chromatography) was used to track the development of the reaction (solvent: n-hexane: EtOAc:30:70 v/v%). Upon reaction finalization, 45 mL of distilled water was used to "quench" the reaction kinetics. Following three separate 50 mL ethyl acetate extractions, the product extracted with 100 mL of brine. Thus far the received organic layer was blended and dried, over anhydrous Na_2SO_4. An off-white solid was obtained after under low pressure solvent evaporation and the residue was flushed through silica gel (200-300 mesh) column for purification using ethyl acetate/n-hexane as the eluent.

3a derivative: Off-white solid, Yield: 32.0 %; m.p. 170-174°C; ^{1}H NMR: 10.11 (s, 1H), 9.76 (s, 1H), 8.03 (d, *J*=7.6 Hz, 1H), 7.86 (dd, *J*=6.8, 2.9 Hz, 4H), 7.63–7.45 (m, 7H), 7.31 (q, *J*=8.7 Hz, 4H) ppm; m/z calcd: 389.20. Found: 390.8, 392.6 (3:1) (M^{+1}).

3b derivative: Off-white solid, Yield: 44.6 %; m.p. 162-164°C; ^{1}H NMR: 9.93 (s, 1H), 7.88–7.79 (m, 4H), 7.56 (q, *J*=3.0 Hz, 6H), 7.29 (d, *J*=2.6 Hz, 1H), 2.40 (s, 1H), 0.61 (s, 2H), 0.31 (s, 2H) ppm; m/z calcd: 319.14. Found: 320.4 (M^{+1}).

3c derivative: Off-white solid, Yield: 33.6 %; m.p. 172-174°C; ^{1}H NMR: 10.15 (s, 1H), 9.81 (s, 1H), 8.03 (s, 1H), 7.87 (s, 2H), 7.80–7.46 (m, 5H), 7.46–7.18 (m, 5H), 6.31 (d, *J*=15.9 Hz, 1H) ppm; m/z calcd: 407.09. Found: 407.9, 409.2 (3:1) (M^{+1}).

3d derivative: Off-white solid, m.p. 156-160°C; Yield: 51.8 %; ^{1}H NMR: 9.99 (s, 1H), 7.83 (dd, *J*=6.9, 3.1 Hz, 2H), 7.75–7.52 (m, 6H), 7.48–7.35 (m, 2H), 2.39 (d, *J*=9.3 Hz, 1H), 0.61 (s, 2H), 0.31 (s, 2H) ppm; m/z calcd: 337.13. Found: 338.6 (M^{+1}).

3e derivative: Off-white solid, m.p. 168-170°C; Yield: 33.7 %; ^{1}H NMR: 10.07 (s, 1H), 9.76 (s, 1H), 7.86 (dd, *J*=7.0, 2.8 Hz, 2H), 7.62–7.49 (m, 5H), 7.31–7.03 (m, 6H), 2.32 (s, 6H) ppm; m/z calcd: 417.14. Found: 418.0, 420.2 (3:1) (M^{+1}).

3f derivative: Off-white solid, m.p. 181-183°C; Yield: 52.3 %; ^{1}H NMR: 9.92 (s, 1H), 7.88–7.78 (m, 2H), 7.59–7.51 (m, 3H), 7.44 (s, 2H), 7.28 (s, 1H), 7.18 (s, 1H), 2.41 (s, 1H), 2.35 (s, 6H), 0.63 (s, 2H), 0.32 (s, 2H) ppm; m/z calcd: 347.17. Found: 348.1(M^{+1}).

3g derivative: Off-white solid, m.p. 167-169°C; Yield: 47.2 %; ^{1}H NMR: 10.14 (br, 1H), 9.84 (br, 1H), 7.82–7.14 (m, 11H), 2.47 (s, 3H), 2.31 (s, 3H) ppm; m/z calcd: 435.13. Found: 436.1, 437.3 (3:1) (M^{+1}).

3h derivative: Off-white solid, m.p. 174-178°C; Yield: 53.6 %; ^{1}H NMR: 9.99 (s, 1H), 7.82-7.14 (m, 7H), 2.50 (s, 6H), 1.24 (s, 1H), 0.45 (dd, *J*=177.7, 77.9 Hz, 4H) ppm; m/z calcd: 365.17. Found: 366.3 (M^{+1}).

3i derivative: Off-white solid, m.p. 169-171°C; Yield: 56.1 %; ^{1}H NMR: 9.87 (s, 1H), 7.71-7.39 (m, 4H), 7.24-7.06 (m, 2H), 6.75 (m, 1H), 2.36 (s, 6H), 1.24 (m, 1H), 0.56 (m, 2H), 0.27 (m, 2H) ppm; m/z calcd: 381.14. Found: 382.4, 384.1 (3:1), (M^{+1}).

5a derivative: Off-white solid, m.p. 190-194°C; Yield: 59.5%; ^{1}H NMR: 9.99 (s, 1H), 9.81 (s, 1H), 7.79 (s, 2H), 7.66–7.24 (m, 7H), 2.65 (s, 3H). ppm; m/z calcd: 359.83. Found: 360.0, 362.6 (3:1) (M^{+1}).

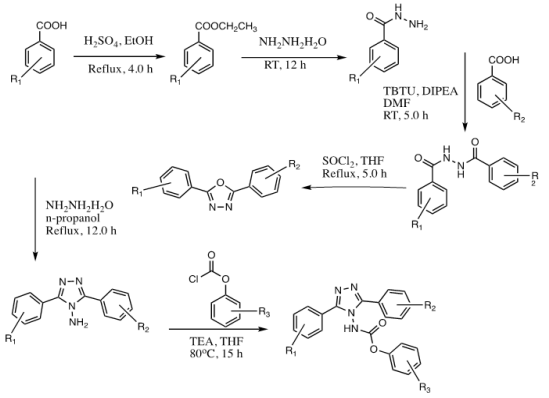
5b derivative: Off-white solid, m.p. 184-187°C; Yield: 50.4 %; ^{1}H NMR: 9.97 (s, 1H), 9.50 (s, 1H), 7.43 (d, *J*=62.3 Hz, 8H), 2.66 (s, 3H) ppm; m/z calcd: 394.28. Found: 395.6, 397.4 (3:1) (M^{+1}).

5c derivative: Off-white solid, m.p. 176-180°C; Yield: 49.0 %; ^{1}H NMR: 9.97 (s, 1H), 9.61 (s, 1H), 7.75–7.43 (m, 2H), 7.32 (s, 1H), 7.14 (s, 1H), 6.09 (s, 1H), 2.42 (s, 3H), 1.24 (m, 1H), 0.58 (m, 2H), 0.29 (m, 2H) ppm; m/z calcd: 323.80. Found: 324.8, 326.3 (3:1) (M^{+1}).

RESULTS AND DISCUSSION

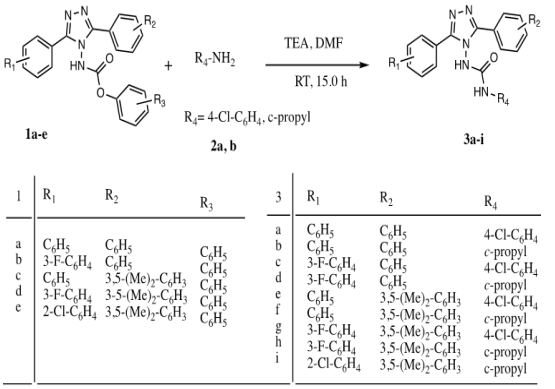
As a result, Scheme 1 shows the final synthesis pathway for the 4H-1,2,4-triazol-4-amine **(1a-g)**. In the first phase, ethyl benzoate was synthesized by reacting a benzoic acid solution in ethanol with sulphuric acid. The produced ethyl benzoate was then treated with hydrazine hydrate in the second step, resulting in the

synthesis of benzohydrazide. Following that, in the third stage, N-benzoyl benzohydrazides were synthesized by reacting benzohydrazides with benzoic acid. Following the synthesis, N-benzoyl benzohydrazides were treated with thionyl chloride to produce 2,5-diphenyl-1,3,4-oxadiazole. Following the reaction of 2,5-diphenyl-1,3,4-oxadiazoles with hydrazine hydrate, 3,5-diphenyl-4*H*-1,2,4-triazole-4-amines are formed. In the last phase, phenyl (3,5-diphenyl-4*H*-1,2,4-triazole-4-yl) carbamates are made by reacting 3,5-diphenyl-4*H*-1,2,4-triazole-4-amines with phenyl formate under reflux conditions in the presence of THF and triethylamine.



Scheme 1. Synthetic pathway for the 4-amino-4H-1,2,4-triazoles (1a-g)

The interaction of the generated 4*H*-1,2,4-triazol-4-amine **(1a-g)** with amines **(2a, b)** in DMF using trimethyl amine at about 60°C for 15 h yielded urea derivatives **(3a-i)** in moderate yield (30 to 60%). (Scheme 2, Table 1). All the products are off-white solids that have been identified using spectral and elemental analysis.

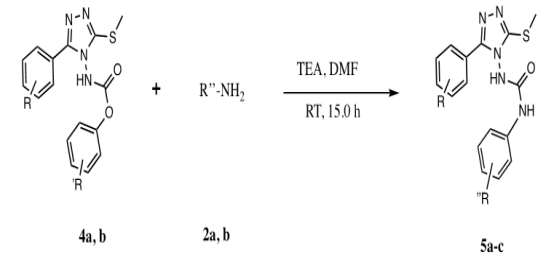


1	R_1	R_2	R_3
a	C_6H_5	C_6H_5	C_6H_5
b	3-F-C_6H_4	C_6H_5	C_6H_5
c	C_6H_5	3,5-$(Me)_2$-C_6H_3	C_6H_5
d	3-F-C_6H_4	3-5-$(Me)_2$-C_6H_3	C_6H_5
e	2-Cl-C_6H_4	3,5-$(Me)_2$-C_6H_3	C_6H_5

3	R_1	R_2	R_4
a	C_6H_5	C_6H_5	4-Cl-C_6H_4
b	C_6H_5	C_6H_5	*c*-propyl
c	3-F-C_6H_4	C_6H_5	4-Cl-C_6H_4
d	3-F-C_6H_4	C_6H_5	*c*-propyl
e	C_6H_5	3,5-$(Me)_2$-C_6H_3	4-Cl-C_6H_4
f	C_6H_5	3,5-$(Me)_2$-C_6H_3	*c*-propyl
g	3-F-C_6H_4	3,5-$(Me)_2$-C_6H_3	4-Cl-C_6H_4
h	3-F-C_6H_4	3,5-$(Me)_2$-C_6H_3	*c*-propyl
i	2-Cl-C_6H_4	3,5-$(Me)_2$-C_6H_3	*c*-propyl

Scheme 2. Synthesis of urea derivatives from 4-amino-1,2,4-triazoles based Carbamates

Based on the previous results, the interaction of methylthio substituted 4*H*-1,2,4-triazol-4-amine-based carbamate compounds **(4a-c)** with **2a, b** was also explored under identical reaction conditions (Scheme 2, Table 2). All the products are off-white solids that have been characterized using spectral and elemental analysis.



4	R	R'
a	C_6H_5	C_6H_5
b	2-Cl-C_6H_4	C_6H_5

2	R''
a	4-Cl-C_6H_4
b	*c*-propyl

5	R	R''
a	C_6H_5	4-Cl-C_6H_4
b	2-Cl-C_6H_5	4-Cl-C_6H_4
c	2-Cl-C_6H_5	*c*-propyl

Scheme 3. Synthesis of urea derivatives from 3-(methylthio)-4-amino-1,2,4-triazole based Carbamates

Table 1: Synthesis of urea derivatives from 4-amino-1,2,4-triazoles based Carbamates (Scheme 1).

Entry	Compound	R	R^1	R^3	Yield(%)
1	3a	C_6H_5	C_6H_5	4-Cl-C_6H_4	32.0%
2	3b	C_6H_5	C_6H_5	c-propyl	44.6%
3	3c	3-F-C_6H_5	C_6H_5	4-Cl-C_6H_4	33.6%
4	3d	3-F-C_6H_5	C_6H_5	c-propyl	51.8%
5	3e	C_6H_5	3,5-(Me)2-C_6H_3	4-Cl-C_6H_4	33.7%
6	3f	C_6H_5	3,5-(Me)2-C_6H_3	c-propyl	52.3%
7	3g	3-F-C_6H_4	3,5-(Me)2-C_6H_3	4-Cl-C_6H_4	47.2%
8	3h	3-F-C_6H_4	3,5-(Me)2-C_6H_3	c-propyl	53.6%
9	3i	2-Cl-C_6H_4	3,5-(Me)2-C_6H_3	c-propyl	56.1%

Optimization

However, as the penultimate stage in the synthesis of urea preparation via carbamates, we received a highly messy product with low yield, which we then optimized as tabulated in Table 3. A reaction between 3,5-diphenyl substituted 4H-1,2,3-triazole-

4-amine and phenyl formate in the organic solvents (i.e., THF, Acetonitrile, DMF, and 1,4-dioxane) and bases (i.e., K_2CO_3, Cs_2CO_3, DIPEA, pyrimidine and triethylamine) yielded phenyl substitited carbamate. Using carbamate in a refluxing mixture of THF and triethylamine with phenyl formate, we obtained excellent results at a range of temperatures.

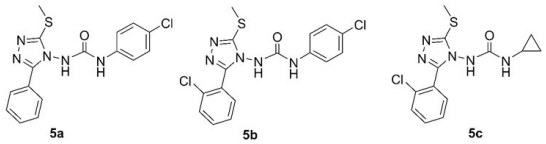


Table 2: Synthesis of urea derivatives from 3-(methylthio)-4-amino-1,2,4-triazole based Carbamates. (Scheme 2)

Entry	Compound	R	R^2	Yield%
1	5a	C_6H_5	4-Cl-C_6H_4	59.5%
2	5b	2-Cl-C_6H_4	4-Cl-C_6H_4	50.4%
3	5c	2-Cl-C_6H_4	c-propyl	49.0%

Table 3: Optimization of reaction media for the synthesis of target compounds

Entry	Solvents	Time (h)	Yields (%)
1	THF	26 h	59%%
2	Acetonitrile	25 h	46%
3	1,4-dioxane	28 h	42%
4	DMF	15 h	50%

Note: Each solvent system explored with K_2CO_3, Cs_2CO_3, DIPEA, pyrimidine and triethylamine base, the best result obtained with the combination of THF solvent-triethylamine base

Biological activity

Anti-bacterial activity

The anti-bacterial activities of the synthesised urea derivatives were evaluated against the following bacterial species: *Enterococcus faecalis* (EF) **(ATCC 29212)**, *Klebsiella pneumoniae* (KP) **(ATCC 700603)**, *Candida albicans* (CA) **(MTCC 3017)**, *Escherichia coli* (EC) **(ATCC 25922)**, *Pseudomonas aeruginosa* (PA) **(ATCC 15442)**, *Bacillus anthracis* (BA) **(ATCC 14578)**. According to the findings, the urea derivatives **(3a-i and 5b)** exhibited substantial anti-bacterial action *In vivo* (Fig. 2). Table 4 displays the results of anti-bacterial efficiencies testing *In vitro*.

Anti-bacterial activity

Synthesized carbamate derivatives were tested for antibacterial activity using the disc-diffusion technique against *Enterococcus faecalis* (EF) **(ATCC 29212)**, *Pseudomonas aeruginosa* (PA) **(ATCC 15442)**, *Escherichia coli* (EC) **(ATCC 25922)**, *Candida albicans* (CA) **(MTCC 3017)**, *Klebsiella pneumoniae* KP) **(ATCC 700603)**, *Bacillus anthracis* (BA) **(ATCC 14578)**. By inoculating the bacterial cultures into nutritional agar, they were cultured for 24 h at 30 0.1°C. Urea derivatives were kept dry at room temperature and solubilized in dimethyl sulfoxide (20 mg in per mL DMSO). Mueller The petri dishes were filled with Hinton Agar Media (15 cm^3) and heated to 45°C to harden the medium. Specifically, 50 µL of normal saline solution were poured onto 9 cm Petri dishes and incubated to grow the aforementioned culture medium (105-106 bacteria per mL). Carbamate (50 µL) injections were made into discs and firmly pushed onto the solid agar medium. For 24 h, the Petri plates were kept at 37°C. At the conclusion of the time, the inhibition zones created on the medium were measured in millimetres using a zone reader. Similarly, the standard disc zone (tetracycline) was computed.

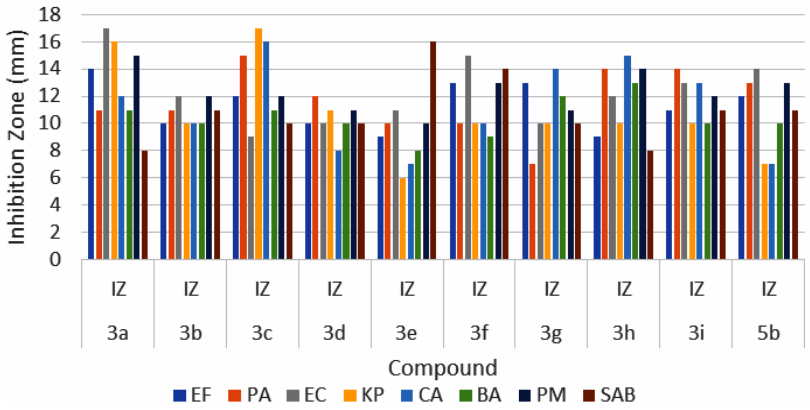


Fig. 2. Zone of inhibition (mm) against 3(a-i) and 5b derivatives

Table 4: Anti-bacterial activities of carbamate extracts

Compound name		EF	PA	EC	KP	CA	BA	PM	SAB
Standard	IZ	21,30,31 Mean=61.3	34,34,45 Mean=83	23,35,30 Mean=70	33,16,34 Mean=60.3	31,15,31 Mean=56.3	38,34,40 Mean=85.3	21,26,40 Mean=60.3	32,36,40 Mean=81.3
3a	IZ	14mm	11mm	17mm	16mm	12mm	11mm	15mm	8mm
	AI	0.2	0.1	0.2	0.2	0.2	0.1	0.2	0.09
3b	IZ	10mm	11mm	12mm	10mm	10mm	10mm	12mm	11mm
	AI	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
3c	IZ	12mm	15mm	9mm	17mm	16mm	11mm	12mm	10mm
	AI	0.1	0.1	0.1	0.2	0.2	0.1	0.1	0.1
3d	IZ	10mm	12mm	10mm	11mm	8mm	10mm	11mm	10mm
	AI	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
3e	IZ	9mm	10mm	11mm	6mm	7mm	8mm	10mm	16mm
	AI	0.1	0.1	0.1	0.09	0.1	0.09	0.1	0.1
3f	IZ	13mm	10mm	15mm	10mm	10mm	9mm	13mm	14mm
	AI	0.2	0.1	0.2	0.1	0.1	0.1	0.2	0.1
3g	IZ	13mm	7mm	10mm	10mm	14mm	12mm	11mm	10mm
	AI	0.2	0.08	0.1	0.1	0.2	0.1	0.1	0.1
3h	IZ	9mm	14mm	12mm	10mm	15mm	13mm	14mm	8mm
	AI	0.1	0.1	0.1	0.1	0.2	0.1	0.2	0.09
3i	IZ	11mm	14mm	13mm	10mm	13mm	10mm	12mm	11mm
	AI	0.1	0.1	0.1	0.1	0.2	0.1	0.1	0.1
5b	IZ	12mm	13mm	14mm	7mm	7mm	10mm	13mm	11mm
	AI	0.2	1.5	0.2	0.1	0.1	0.1	0.2	0.1

I.Z=Inhibition zone (I.Z.) produced against microorganism by extract in mm; AI= Activity index of extract; EF=*Enterococcus faecalis* (ATCC29212); PA=*Pseudomonas aeruginosa*; EC=*Escherichia coli*; KP=*Klebsiella pneumoniae*; CA=*Candida albicans*; BA=*Bacillus anthracis*; PM=*Proteus mirabilis*;; SAB=*Staphylococcus aureus*

CONCLUSION

A new series of molecular hybrids i.e., urea derivatives carrying 1,2,4-triazole molecular hybrid scaffolds were synthesized via reaction of carbamates of 4-amino-1,2,4-triazoles with amines in DMF for 15 h using trimethyl amine. The approach was further expanded to produce urea derivatives of 3-(methylthio)-4-amino-1,2,4-triazoles. Antibacterial activity for all synthesized derivatives were evaluated against *Enterococcus faecalis, Pseudomonas, E. Coli, Klebsiella pneumonia, Candida albicans, Bacillus anthracis, Proteus mirabilis*, and *Staphylococcus aureus*. All the synthesized compounds found promising antibacterial activity in the test.

ACKNOWLEDGEMENT

Thanks are due to MNIT, Jaipur (India) for instrumental facilities.

REFERENCES

1. Othman. E. M.; Fayed. E. A.; Husseiny. E. M.; Abulkhair H S.; *New J Chem.*, **2022**.
2. Turky. A.; Bayoumi. A. H.; Sherbiny. F. F.; El-Adl K.; Abulkhair H S.; *Mol Divers.*, **2021**, *25,* 403.
3. El-Shershaby. M. H.; El-Gamal. K. M.; Bayoumi. A. H.; El-Adl. K.; Alswah. M.; Ahmed H E.; Al-Karmalamy. A. A.; Abulkhair. H. S.; *New J Chem.*, **2021**, *45*, 13986.
4. Holla. B. S.; Mahalinga. M.; Karthikeyan. M. S.; Poojary. B.; Akberali. P. M.; Kumari. N. S.; *Eur J Med Chem.*, **2005**, *40,* 1173.
5. Thomas. K.; Adhikari. A. V.; Shetty. N. S.; *Eur J Med Chem.*, **2010**, *45*, 3803.
6. Mishra. D. R.; Nayak. S.; Raiguru. B. P.; Mohapatra. S.; Podh. M. B.; Sahoo. C. R.; Pandey. R. N.; *J Het Chem.*, **2021**, *58,* 111.
7. Shalini. K.; Kumar. N.; Drabu. S.; Sharma. P. K.; *Beilstein J Org Chem.*, **2011**, *7,* 668.
8. Cao. X.; Sun. Z.; Cao. Y.; Wang. R.; Cai. T.; Chu. W.; Hu. W.; Yang. Y.; *J. Med. Chem.*, **2014**, *57,* 3687.
9. Kocyigit-Kaymakcioglu. B.; Celen. A. O.; Tabanca. N.; Ali. A.; Khan. S. I.; Khan. I. A.; Wedge. D. E.; *Molecules.*, **2013**, *18*, 3562.
10. Quan. X-J.; Ren. Z-H.; Wang. Y-Y.; Guan. Z-H.; *Organic lett.*, **2014**, *16*, 5728.
11. Sheng. C.; Zhang. W.; *Current Med Chem.*, **2011**, *18*, 733.

12. Matesanz. A. I.; Joie. C.; Souza. P.; *Dalton Transactions*., **2010**, *39*, 7059.
13. Souza. P.; Matesanz. A. I.; Pastor. C.; *Inorg Chem Commun*., **2002**, *5,* 344.
14. Holm. S. C.; Straub. B. F.; *Org Prep Proced Int*., **2011**, *43,* 319.
15. Yang. L.; Bao. X-P.; *RSC Adv*., **2017**, *7,* 34005.
16. Li. C.; Liu. J-C.; Li. Y-R.; Gou. C.; Zhang. M-L.; Liu. H-Y.; Li. X-Z.; Zheng. C-J.; Piao. H-R.; *Bioorg Med Chem Lett*., **2015**, *25*, 3052.
17. Vijesh. A.; Isloor. A. M.; Shetty. P.; Sundershan. S.; Fun. H. K.; *Eur J Med Chem*., **2013**, *62*, 410.
18. Ley. C.; Elvers. B.; Bellussi. G.; Bus. J.; Drauz. K.; Greim. H.; Hessel. V.; Kleemann. A.; Kutscher. B.; Meijer. G.; Ullmann's encyclopedia of industrial chemistry; Wiley Online Library., **2010**.
19. Lam. P. Y.; Jadhav. P. K.; Eyermann. C. J.; Hodge. C. N.; Ru. Y.; Bacheler. L. T.; Meek. J. L.; Otto. M. J.; Rayner. M. M.; Wong. Y. N.; *Science*., **1994**, *263,* 380.
20. Li. H-Q.; Lv. P-C.; Yan. T.; Zhu. H-L.; *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents)*., **2009**, *9,* 471.
21. Upadhayaya. R. S.; Kulkarni. G. M.; Vasireddy. N. R.; Vandavasi. J. K.; Dixit. S. S.; Sharma. V.; *Chattopadhyaya J, Bioorg Med Chem*., **2009,** *17,* 4681.
22. Khan. S. A.; Singh. N.; Saleem. K.; *Eur J Med Chem*., **2008**, *43,* 2272.
23. Seth. P. P.; Ranken. R.; Robinson. D. E.; Osgood. S. A.; Risen. L. M.; Rodgers. E. L.; Migawa. M. T.; Jefferson. E. A.; Swayze. E. E.; *Bioorg Med Chem Lett*., **2004**, *14,* 5569.
24. Kaymakçıolu. B. K.; Rollas. S.; Körceez. E.; Arıcıolu. F.; *Eur J Pharmaceut Sci*., **2005,** *26* 97.
25. Bladin. J., *Berichte der deutschen chemischen Gesellschaft*., **1885**, *18,* 1544.
26. Potts K.; *Chem Rev*., **1961**, *61,* 87.
27. Krassig. H.; Stannett. V.; Funke. W.; Cantow, Institut fur makromolekulare Chemie der Universitiit, 7 8 Freiburg i. Br., Stefan-M eier-Str. 31. Prof. Dr.]. D. Ferry, Department of Chemistry, The University of Wisconsin, Madison 6, Wisconsin/USA. Prof. Dr. W. Kern, Institut fur Organische Chemie der Universitiit, 65 Mainz.
28. Ainsworth. C.; Jones. R.; *J Am Chem Soc*., **1955**, *77,* 621.