IJPSR (2023), Volume 14, Issue 1 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 15 May 2022; received in revised form, 28 June 2022; accepted, 29 July 2022; published 01 January 2023

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NOVEL5, 6-DIHYDRO-3-(SUBSTITUTED PHENYL) [1, 2, 4] TRIAZOLE (3, 4-B) [1, 3, 4] THIADIAZINE-7-ONE DERIVATIVES FOR ANTIMICROBIAL AND FREE RADICAL SCAVENGING ACTIVITY

Kirti Sharma [2], Tinku [*1], Vikas Jogpal [1], Mohit Sanduja [1] and Prabhakar Kumar Verma [2]

School of Medical and Allied Sciences [1], G. D. Goenka University, Sohna Road, Gurgaon - 122103, Haryana, India.
Department of Pharmaceutical Sciences [2], M. D. University Rohtak - 124001, Haryana, India.

Keywords:

Triazole, Fluconazole, Norfloxacin, Tube dilution, Ascorbic acid, Minimum bactericidal concentration (MIC), Minimum fungicidal concentration (MFC)

Correspondence to Author:
Dr. Tinku

School of Medical and Allied Sciences, G. D. Goenka University, Sohna Road, Gurgaon - 122103, Haryana, India.

E-mail: tinkujhajjar87@gmail.com

ABSTRACT: The present research aims to synthesize novel 5, 6-dihydro-3-(substituted phenyl) [1, 2, 4] triazolo (3, 4-b) [1, 3, 4] thiadiazine-7-one derivatives and their physiochemical evaluation for antibacterial and antioxidant activities. Novel synthetic schemes were designed to synthesize compounds (1-6), which were then characterized using physicochemical and spectroscopic methods (IR, 1HNMR). *In-vitro* antimicrobial activity was performed against Gram-positive (*Staphylococcus aureus*, *Bacillius subtilis*), Gram-negative (Escherichia coli) bacterial strains and fungal strains (*Aspergilus niger*, *Candida albicans)* of all synthesized compounds. In addition, Minimum inhibition concentration (MIC) and Minimum fungicidal concentration (MFC) values were determined using tube dilution methods using standards such as norfloxacin and fluconazole. The free radical scavenging activity was also assessed using the DPPH assay, with vitamin C serving as a reference molecule. Compound 3 was discovered to have the best antibacterial activity (IC_{50}- 80.27) of all the compounds, while the rest compounds showed modest scavenging activity.

INTRODUCTION: The incidence of systemic microbial infections has surged due to increased immune-compromised hosts. Furthermore, the rising reports of germ resistance to effective antibiotics are becoming a chief supply of concern. As a result, the excessive value of therapy, toxicities, and drug resistance offer a new dilemma that prompted microbial scientists and chemists to develop novel antimicrobial with extra unique action [9].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(1).444-52

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.14(1).444-52

Hence, the hunt for novel antimicrobial will continue to be a crucial and hard attempt for medicinal chemists. Triazoles and their derivatives are a fascinating family of chemical compounds offering various potential pharmacological activities.

Scaffolds containing 1,2,4 triazole containing ring systems were reported to have anti-bacterial, anti-fungal [16, 18, 19], anti-tubercular [1-15], antihyper-glycemic [17], analgesic, anti-inflammatory [7] free radical scavenging) [3], anti-cancer [11], anticonvulsant (Kamboj *et al.*, 2015), antiviral [10], anti-amoebiosis [15], anti-depressant and other central nervous system (CNS) activities [6]. Treatment of infectious ailments is a critical and challenging task because of the growing infectious and developing range of multi-drug resistant microbial infections.

Despite the availability of a large range of antibiotics and chemotherapeutics for medical use, the upward thrust of old and novel antibiotic resistance evokes the discovery of a new class of antimicrobial drugs [18]. Usually, the 1, 2, 4-triazole moiety appears often in the structure of different natural products and the synthesis of molecules integrating this moiety has picked the interest of chemists and biologists alike, owing to their varied biological activity in pharmacological and agrochemical sectors [9].

MATERIALS AND METHOD: Melting points were obtained using sonar melting point equipment in open capillary tubes and are uncorrected. Thin layer chromatography on a silica gel plate (Merck silica gel G) was used to monitor the completion of the reaction. ^{1}H-NMR spectra were obtained *via* Brucker Avance II 400 NMR spectrometer using suitable deuterated solvents and are represented in parts per million (6 ppm) downfield from tetramethylsilane (TMS-internal standard). IR spectra were acquired on a Brucker 1206-0280 using OPUS 7.2.139.1294 software.

1. Synthesis of 5,6-dihydro-3-(substituted phenyl)[1,2,4]triazolo(3,4-b) [1,3,4] thiadiazine-7-one: Initially, substituted aromatic acid (0.001 mol) and absolute alcohol (50 mL) were simultaneously placed in a 100 mL round bottom flask (RBF). In that mixture, a few drops of concentrated sulfuric acid (H_2SO_4) and a little porcelain chip were added. To maintain the anhydrous environment, a condenser with a calcium chloride guard tube was connected at the top. After refluxing for 6-8 hours, the reaction mixture was concentrated under reduced pressure to yield the ester. After successful completion of first stage, hydrazine hydrate (0.2 mol) and absolute alcohol (50 mL) were added and the reaction mixture was refluxed for 8-10 hours. Subsequently, the concoction was concentrated and poured over crushed ice. The solid substituted benzohydrazides mass was separated, filtered, and dried [13]. Further, the reaction mixture of an ethanolic solution of substituted benzohydrazides (0.01mol), potassium hydroxide (0.015 mol), and carbon disulphide (0.015 mol) was refluxed for 7-8 hours. Following that, the mixture was acidified with dil. HCI, and the resulting solid were collected, washed with distilled water, recrystallized, and dried in a vacuum. Afterward, the product was refluxed with hydrazine hydrate for 6-8 h; this reaction leads to the cyclization of traizoles with the elimination of water molecules. Finally, chloroacetyl chloride is refluxed with the final product to obtain the bicyclic targeted heterocyclic derivative. Thin layer chromatography using mobile phase chloroform: Methanol (8.5:1.5) was used to confirm the completion of the reaction. Eventually, 5, 6-dihydro-3 [substituted, 2,4] triazolo (3, 4b) [1,3,4] thiadiazine-7-one derivatives were synthesized **Fig. 1** washed, and recrystallized using an appropriate solvent.

1.1 *In-vitro* Study:

1.1.1 Free Radical Scavenging Activity: Free radical scavenging activity of synthesized compounds was evaluated using a Shimadzu UV-visible spectrophotometer using DPPH (2, 2-diphenyl-2-picrylhydrazyl hydrate) as standard. Different dilutions (25, 50, 75, and 100 µg/ml of the compounds were prepared using methanol as a diluting agent. From the stock solutions, 0.25, 0.50, 0.75, 0.1 ml were taken in different test tubes. Freshly prepared DPPH solution (1.3 mg/ml) was added to each test tube and kept dark for 30 minutes. The absorbance was measured at 517 nm using UV-spectrophotometer [2]. The percentage inhibition was calculated using the following formula:

$$\%I = A_{control} - A_{sample} / A_{control} \times 100$$

$A_{control}$ equals the absorbance of the control reaction and A_{sample} equals the absorbance of the test chemical (1-6). The IC_{50} of the substances was determined by plotting inhibition against the concentration on a graph. A calibration curve was generated for varying amounts of ascorbic acid, which was utilized as a positive control (standard). All of the experiments were done in triplicate.

1.1.2 Antimicrobial Activity: The synthesized compounds were tested for antimicrobial activity against gram-positive bacteria (*S. aureus, B. subtilis*), gram-negative bacteria (*E. coli*), and fungal strains (*C. albicans, A. niger*) using the tube dilution technique.

Compounds 1–6 and standard samples were dissolved in dimethylsulphoxide (DMSO) to a 100 g/ml concentration. Dilutions of the test and control

chemicals (norfloxacin and fluconazole) were produced in double strength nutritional broth-I.P. for bacteria and Sabouraud dextrose broth I.P. for fungi [5]. The samples were incubated at 37 °C for 24 hours for gram's bacteria, 25 °C for 7 days for fungal stain (*A. niger*) and 37 °C for 48 hours for *Candida albicans*. The results were reported in terms of the lowest inhibitor concentration.

RESULTS AND DISCUSSION:

2.1 Synthesis of 5,6-dihydro-3-(substituted phenyl)[1,2,4]triazolo(3,4-b) [1,3,4]thiadiazine-7-one: A series of 5,6-dihydro-3-(substituted phenyl) [1, 2, 4] triazolo (3, 4-b)[1, 3, 4] thiadiazine-one compounds(1-6) were synthesized as per the above-mentioned scheme in **Fig. 1** for the antimicrobial and free radical scavenging activity concerning the 1, 2, 4 triazole. The physicochemical characteristics of synthesized compounds (1-6) are presented in **Table 1**. IR and 1HNMR characterized the structures of synthesized compounds.

Fig. 2 revealed the spectral details of 5, 6-dihydro-3-(substituted phenyl) [1,2,4] triazolo (3, 4-b) thiadiazine-7-one intermediates and synthesized compounds (1-6) was **Table 2.**

TABLE 1: PHYSICOCHEMICAL PROPERTIES OF THE SYNTHESIZED COMPOUNDS

Compound	Mol. formula	Mol. Wt.	R_f value	M. Pt.	% yield
1	$C_{10}H_8N_4O_2S$	248	0.63	180-182	70.59
2	$C_{11}H_{10}N_4OS$	246	0.56	172-174	56.29
3	$C_{13}H_{14}N_4O_4S$	322	0.43	156-158	62.23
4	$C_{10}H_7N_5O_4S$	293	0.59	98-100	65.30
5	$C_{10}H_7ClN_4OS$	266	0.34	120-122	68.45
6	$C_{10}H_9N_5OS$	247	0.39	136-138	56.10

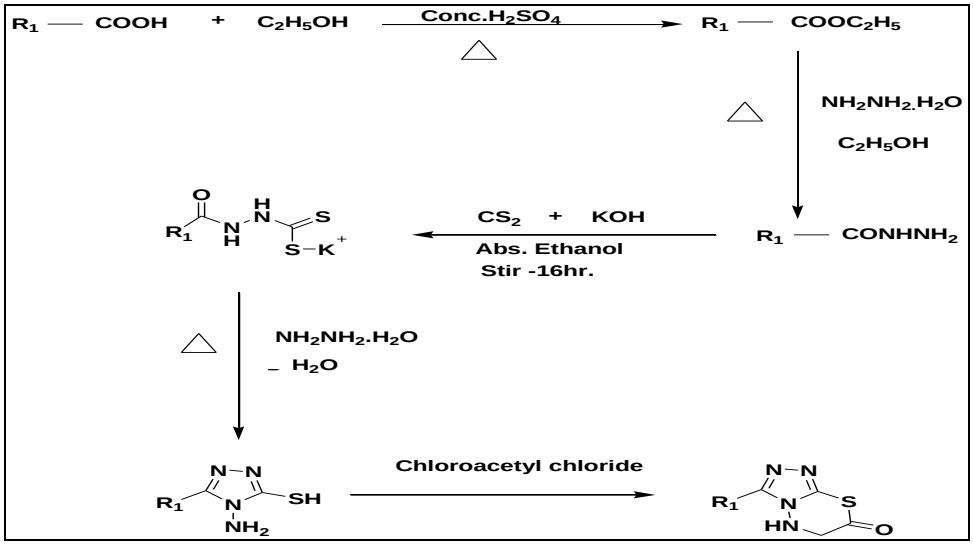


FIG. 1: SYNTHESIS OF 5, 6-DIHYDRO-3-(SUBSTITUTED PHENYL) [1, 2, 4] TRIAZOLO (3, 4-B) [1, 3, 4] THIADIAZINE-7-ONE

Intermediate 1 (cm^{-1}) 3027(C-H str., aromatic), 1707 (C=O str., carbonyl), 1275 (C-O str., ester), 1663 (C=C str., aromatic ring), 1568 (C-C str., aromatic in ring), 1438 (C-H bend, alkane), 3490 (O-H str.)

Intermediate 2 (cm^{-1}) 3017 (C-H str., aromatic), 1751 (C=O str., carbonyl), 1250 (C-O str., ester), 1670 (C=C str., aromatic ring), 1560 (C-C str., aromatic in ring), 1400 (C-H bend, alkane), 3487 (O-H str.), 1098(C-N str.), 3309 (N-H str., hydrazide).

Intermediate 3 (cm^{-1}) 3013 (C-H str., aromatic), 1256 (C-O str., C-OH), 1672 (C=C str., aromatic ring), 1509 (C-C str., aromatic in ring), 1404 (C-H bend, alkane), 3487 (O-H), 1084 (C-N str.), 3348 (N-H str., amino), 2367 (S-H str., thiole).

Compound 1 (cm^{-1}) 2987(C-H str., aromatic), 1707 (C=O str., carbonyl), 1251 (C-O str., ester), 1660 (C=C str., aromatic ring), 1567 (C-C str., aromatic in ring), 3467 (O-H str.), 1063 (C-N str.), 3331 (N-H str.).

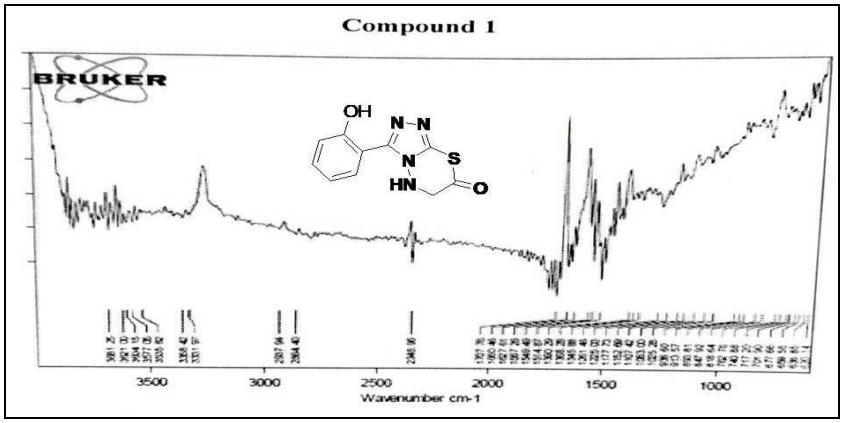
Compound 2 (cm^{-1}) 3000 (C-H str., aromatic), 1717 (C=O str., carbonyl), 1251 (C-O str., ester), 1649 (C=C str., aromatic ring), 1541 (C-C str., aromatic in ring), 1070 (C-N str.), 3335 (N-H str.).

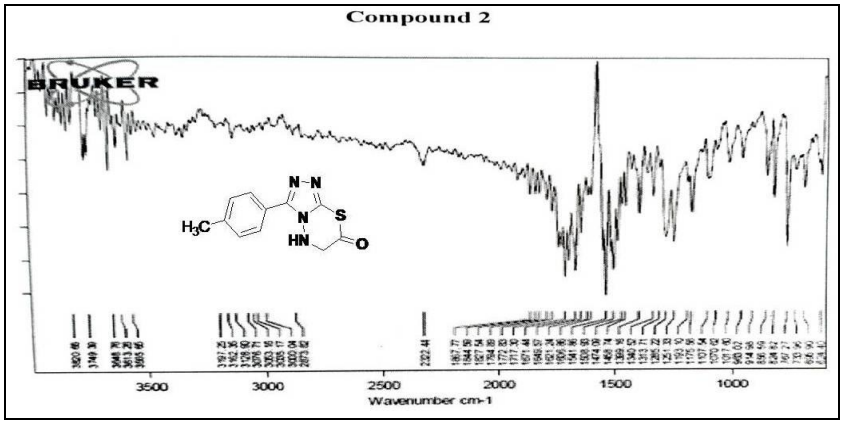
Compound 3 (cm^{-1}) 3034 (C-H str., aromatic), 1731 (C=O str., carbonyl), 1257 (C-O str., ester), 1681 (C=C str., aromatic ring), 1571 (C-C str., aromatic in ring), 1033 (C-O str., ether), 1061 (C-N str.) 3407 (N-H str.).

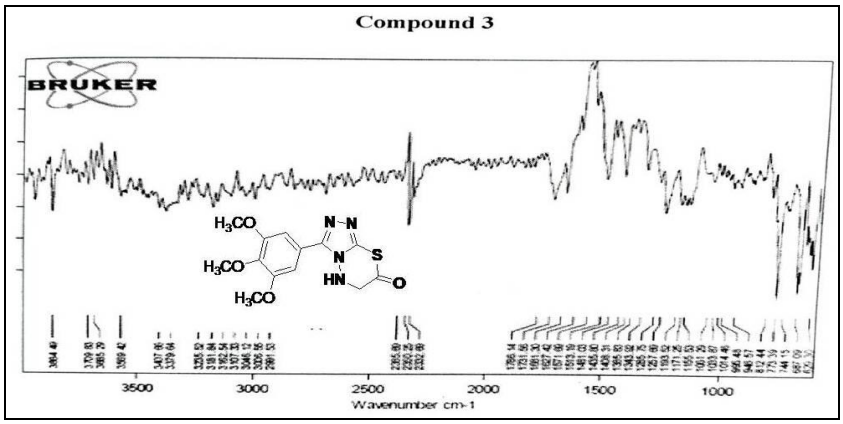
Compound 4 (cm^{-1}) 3046 (C-H str., aromatic), 1730 (C=O str., carbonyl), 1256 (C-O str., ester), 1689 (C=C str., aromatic ring), 1571 (C-C str., aromatic in ring), 1020 (C-O str., ether), 1104 (C-N str.), 3478 (N-H str.)

Compound 5 (cm^{-1})3097 (C-H str., aromatic), 1748 (C=O str., carbonyl), 1680 (C=C str., aromatic ring), 1565 (C-C str., aromatic in ring), 1108 (C-N str.), 3368 (N-H str.), 745 (C-Cl str. halide).

Compound 6 (cm^{-1}) 3064 (C-H str., aromatic), 1730 (C=O str., carbonyl), 1680 (C=C str., aromatic ring), 1571 (C-C str., aromatic in ring), 1125 (C-N str.), 3368 (N-H str. Amine), 1076 (C-N str.).







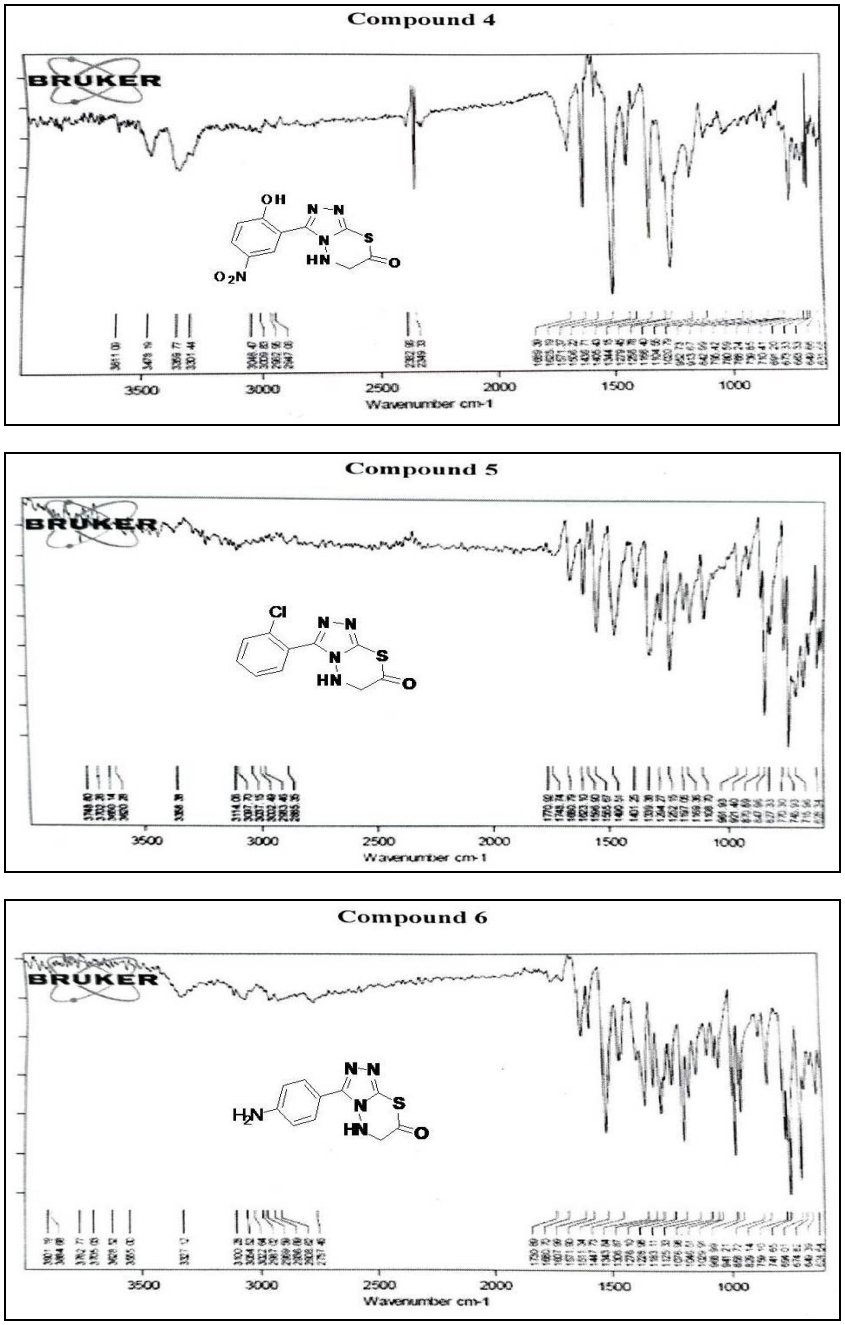


FIG. 2: SPECTRAL DETAILS OF 5, 6-DIHYDRO-3-(SUBSTITUTED PHENYL) [1, 2, 4] TRIAZOLO (3, 4-B) THIADIAZINE-7-ONE INTERMEDIATES AND SYNTHESIZED COMPOUNDS: A) COMPOUND (1), B) COMPOUND (2),C) COMPOUND (3),D) COMPOUND (4),E) COMPOUND (5), F) COMPOUND (6)

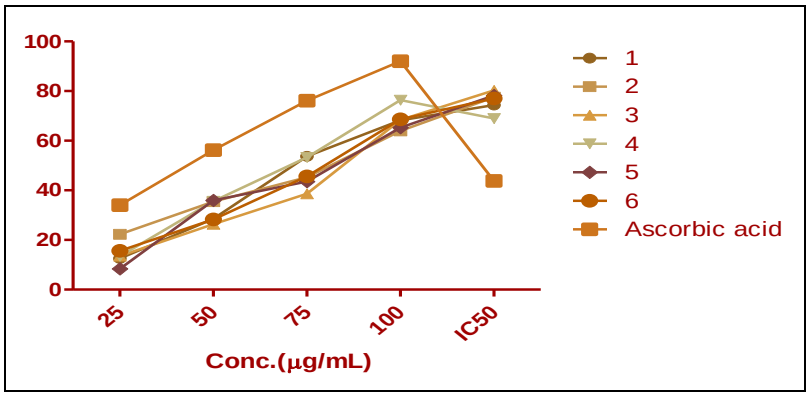


FIG. 3: % AGE INHIBITION VALUE OF ACTIVE ANTIOXIDANT COMPOUNDS

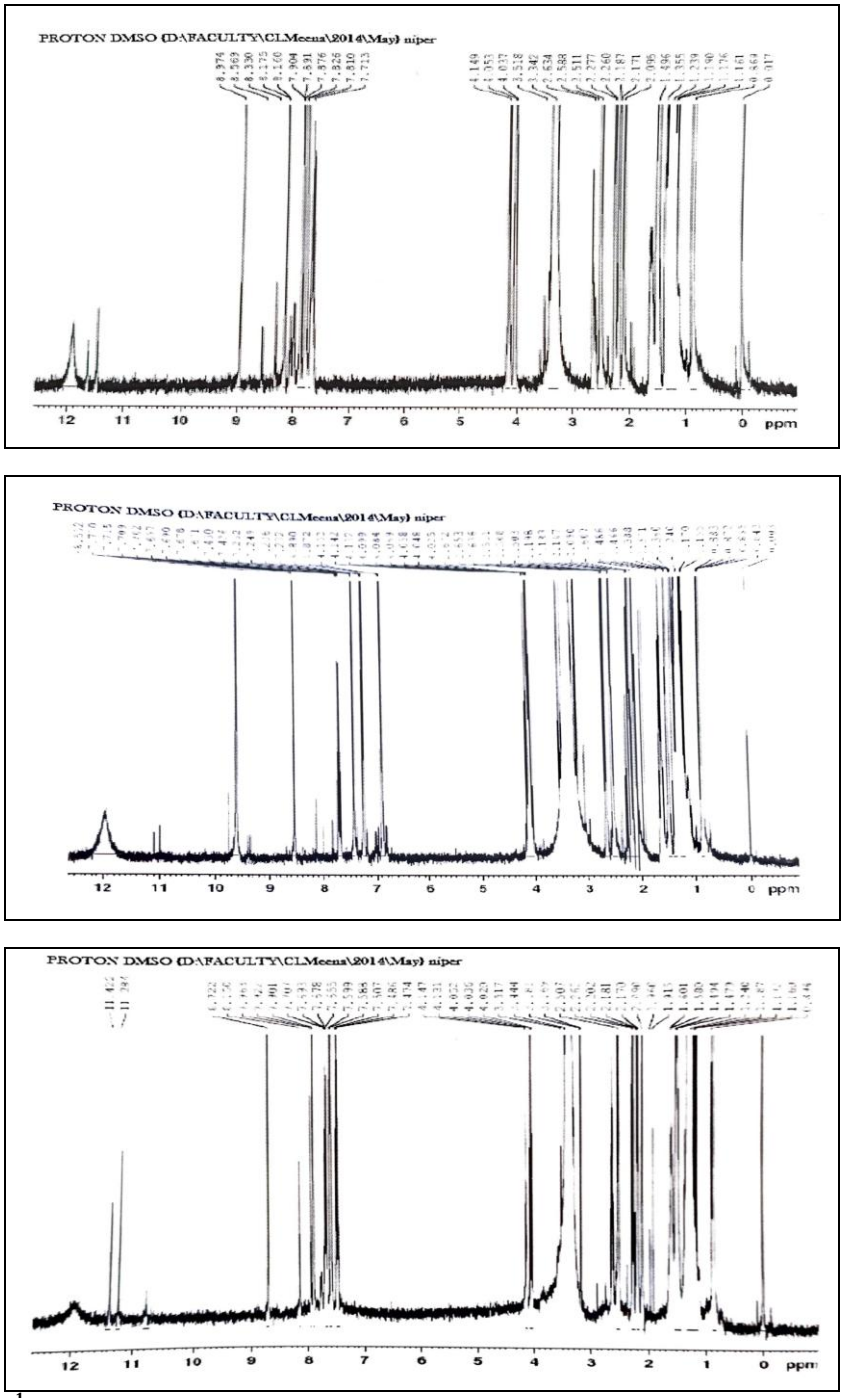


FIG. 4: ^{1}H NMR SPECTRA: A) COMPOUND 1 B) COMPOUND 2 C) COMPOUND 3

2.2 Free Radical Scavenging Activity: Free radical scavenging using DPPH is regarded as a reliable *in-vitro* approach for assessing free radical scavenging activity. The free radical scavenging activity of synthesized compounds (1-6) against DPPH was evaluated and the result in **Table 4** was computed as the inhibition percentage (percent I). The percent inhibition of several substances was shown to vary with concentration. The activity of o-hydroxy phenyl (compound 1) was shown in **Fig. 3** at 75 g/ml and 100 g/ml, with values of 53.69 percent and 68.23 percent, respectively. Compound 3 had the highest activity at 100 g/ml of 3,4, 5-trimethoxy phenyl derivative (68.39 %). At 100 g/ml, 2-hydroxy-5-nitro phenyl (compound4) had the greatest efficacy (76.39 percent).

At 100g/ml, p-amino phenyl (compound 6) has considerable free radical scavenging properties (68.65 percent). The results reveal that most compounds had excellent action at greater concentrations of up to 100 g/ml.

When the concentration is reduced, the free radical scavenging activity decreases in comparison to ascorbic acid, however, the percent inhibition of the produced molecule with ascorbic acid increases with decreasing concentration.

TABLE 2: DETAILS OF 5, 6-DIHYDRO-3-(SUBSTITUTED PHENYL) [1, 2, 4] TRIAZOLO (3, 4-B) THIADIAZINE-7-ONE SYNTHESIZED COMPOUNDS (1-6)

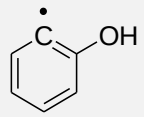
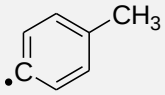
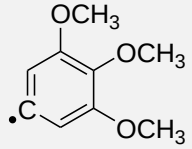
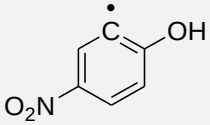
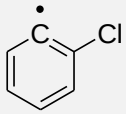
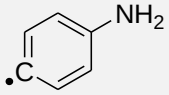
S. no.	R_1	Chemical Name
1.		o-hydroxy phenyl (2-hydroxy phenyl)
2.	 4-methyl phenyl	p- methyl phenyl (4-methyl phenyl)
3.		3,4,5-trimethoxy phenyl
4.		2-hydroxy-5-nitro phenyl
5.		2-chloro phenyl
6.		p-amino phenyl (4-amino phenyl)

TABLE 3: ANTIMICROBIAL ACTIVITY (pMIC in µM/ml) OF SYNTHESIZED COMPOUNDS

Compound	$pMIC_{ec}$	$pMIC_{bs}$	$pMIC_{sa}$	$pMIC_{ca}$	$pMIC_{an}$
1	12.50	06.25	06.25	12.50	12.50
2	12.50	06.25	03.12	06.25	06.25
3	12.50	12.50	06.25	12.50	12.50
4	12.50	12.50	06.25	12.50	12.50
5	25.00	12.50	12.50	12.50	12.50
6	12.50	12.50	06.25	06.25	12.50
Standard	01.56*	01.56*	01.56*	01.56**	01.56**

Norfloxacin* Fluconazole**

TABLE 4: PERCENTAGE INHIBITION (% I) AND IC_{50} VALUE OF THE SYNTHESIZED COMPOUNDS

Compound	Conc.(µg/ml)				
	25	50	75	100	IC_{50}
1	12.56	28.56	53.69	68.23	74.39
2	22.26	35.42	45.26	63.95	77.58
3	13.56	26.35	38.59	68.39	80.27
4	13.46	35.59	53.26	76.39	68.93
5	08.39	35.95	43.56	65.29	78.24
6	15.65	28.25	45.62	68.65	77.06
Ascorbic acid (Standard/+ve control)	34.02	56.22	76.12	92.01	43.78

2.3 Antimicrobial Activity: The antibacterial activity of triazole derivatives was measured using the MIC, and the findings are shown in **Table 3**. Almost all of the synthesized compounds (1-6) outperformed norfloxacin and fluconazole as conventional medications in terms of antibacterial and antifungal activities. The chemicals were efficient against a variety of bacteria types,

including *E. coli, B. subtilis, S. aureus,* and *Candida albicans*. Compound 1 showed excellent activity against *B. subtilis* and *S. aureus* with a MIC value of 06.25, whilst other strains demonstrated action with a MIC value of 06.25 & 12.50. Compound 2 demonstrated the most effective antibacterial action against *S. aureus* with a MIC value (3.12), as well as improved results against *C. albicans, A. niger,* and *B. subtilis* with MIC values 06.25,06.25,06.25, respectively) (6.25). It did not demonstrate satisfactory action against *E. coli*. Compound 3 had no similar antibacterial action against the strains except *S. aureus,* where the MIC was determined to be 06.25. Compound 4 had antibacterial efficacy comparable to compound 3. Compound 5 was not extremely efficient against *E. coli*, with a MIC (25.00) and did not yield statistically significant results compared to the standard. Compound 6 has demonstrated promising effectiveness against S. aureus and *Candida albicans*. As a result, compound 2 was discovered to have the most potent antibacterial activity among the six produced compounds.

The results showed that triazole had high antibacterial action against a variety of bacteria types. As a result, the chemical derivative of substituted p-methyl phenyl (o-hydroxy phenyl) was shown to be more efficient against antibacterial activity than compound 1. Compounds 3(3, 4, 5-trimethoxy phenyl) and 4 (2-hydroxy-5-nitro phenyl) have the same action as compound 2. Compound 6 (p-amino phenyl) showed equivalent efficacy to the o-hydroxy phenyl derivative, whereas the o-chloro phenyl derivative did not outperform the other compounds. Different free radical species are often created and quenched for certain metabolic activities by an effective free radical scavenging pathway in the body. When the production of these species exceeds the free radical scavenging mechanism's capacity, oxidative damage to tissues and biomolecules occurs, leading to disease conditions, particularly degenerative diseases [4] and the pathogenesis of certain human diseases such as cancer, aging, diabetes, and atherosclerosis [12]. Triazole derivatives have already gotten a lot of press because of their wide range of pharmacological properties, including anti-carcinogenic [20], antiviral [14], analgesic, and anti-malarial properties.

CONCLUSION: Most triazole derivatives had moderate to good antibacterial activity, although the free radical scavenging activity of the various compounds varied at different doses. Compound 3 was shown to have the most efficient antibacterial activity (MIC=03.12) against *E. coli, B. subtilis, S. aureus, C. albicans,* and *A. niger,* as well as free radical scavenging activity against DPPH, among the synthesized compounds. We may and conclude from the aforementioned findings that 1, 2, 4-triazole has high antibacterial and free radical scavenging activity and can be employed in the future in the medical area.

ACKNOWLEDGMENT: I'd like to show my gratitude to the Department of Pharmaceutical Sciences, MD University Rohtak, Haryana-India for providing me with all research facilities during the study project.

CONFLICT OF INTEREST: No conflicts of interest were declared by any of the writers.

REFERENCES:

1. Al-Soud YA, Al- Masoudi IA, Saeed B, Beifub U and Al Masoudi NA: Synthesis of new 1H- 1,2,4-triazolylcoumarins and their anti-tumour and anti HIV activities. Chem Heterocycle Comp 2006; 42(5): 583-590.
2. Badarinath AV, Rao KM and Madhusudhana CC: A review on *in-vitro* free radical scavenging methods: comparisons, correlations and considerations. Int J Pharm Tech Res 2010; 2(2): 276-85.
3. Barbuceanu SF, Ilies DC, Saramet G, Uivarosi V, Draghici C and Radulescu V: Synthesis and free radical scavenging activity evaluation of new compounds from hydrazinecarbothioamide and 1,2,4-triazole class containing diarylsulfone and 2,4-difluorophenyl moieties. International J of Mol Sci 2014; 15(6): 10908–10925.
4. Tinku, Mohd. Mujeeb, Abdul Ahad, Mohd. Aqil, Syed Obaidur Rahman, AbulKalamNajmi, Waseem Ahmad Siddiqui. Preparation, optimization and biological evaluation of gymnemic acid loaded niosomes against streptozotocin-nicotinamide-induced diabetic-nephropathy in Wistar rats. Journal of Drug Delivery Science and Technology 2019; 54: 1-10.
5. Kumar S, Kaushik A, Narasimhan B, Shah SAA, Lim SM, Ramasamy K and Mani V: Molecular docking, synthesis and biological significance of pyrimidine analogues as prospective antimicrobial and antiproliferative agents. BMC Chem 2019; 9: 13(1): 85.
6. Deng XQ, Song MX, Wang SB, Quan ZS. Synthesis and evaluation of the anticonvulsant activity of 8-alkoxy-4,5-dihydrobenzo[b] [1,2,4] triazolo [4, 3 d][1,4] thiazepinederivatives. J Enzym Inhib Med Chem 2014; 29: 272–280.
7. Gajanan Khanage S, Raju A, Baban Mohite P and Bhanudas Pandhare R: Analgesic activity of some 1,2,4-triazole heterocycles clubbed with pyrazole, tetrazole,

isoxazole and pyrimidine. Advanced Pharmaceutical Bulletin 2013; 3(1): 13–18.
8. Kamboj VK, Verma PK, Dhanda A and Ranjan S: 1,2,4-triazole derivatives as potential scaffold for anticonvulsant activity. Cent Nerv. Syst Agents Med Chem 2015; 15(1): 17-22.
9. Khalil Nasser: Efficient synthesis of novel 1,2,4-triazole fused acyclic and 21–28 membered macrocyclic and/or lariat macrocyclicoxaazathia crown compounds with potential antimicrobial activity, European Journal of Medicinal Chemistry 2010; 45(11): 5265-5277.
10. Kuçukguzel I, Tatar E, Kuçukguzel SG, Rollas S and De Clercq E: Synthesis of some novel thiourea derivatives obtained from 5-[(4-aminophenoxy)methyl]-4-alkyl/aryl-2,4-dihydro-3H-1,2,4-triazole-3-thiones and evaluation as antiviral/anti-HIV and anti-tuberculosis agents. Eur. J Med Chem 2008; 43(2): 381-392.
11. Liang T, Sun X, Li W, Hou G and Gao F: 1,2,3-Triazole-Containing compounds as anti-lung cancer agents: current developments, mechanisms of action, and structure-activity relationship. Frontie in Pharma 2021; 12: 661173.
12. Moskovitz J, Yim MB and Chock PB: Free radicals and disease. Arch Biochem Biophys 2002; 397(2): 354-359.
13. Hussain S, Sharma J and Amir M: Synthesis and Antimicrobial Activities of 1,2,4-Triazole and 1,3,4-Thiadiazole Derivatives of 5-Amino-2-Hydroxybenzoic Acid", Journal of Chemistry 2008; 5: 924734-40.
14. Selvam P, Chandramohan M, De Clercq E, Witvrouw M and Pannecouque C: Synthesis and anti-HIV activity of 4-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene) amino]-N(4,6-dimethyl-2-pyrimidinyl)-benzene sulfonamide and its derivatives. Eur. J Pharm Sci 2001; 14 (4): 313-316.
15. Siddiqui N and Ahsan W: Triazole incorporated thiazoles as a new class of anticonvulsants: Design Synthesis and in vivo screening, Euro J Med Chem 2010; 45: 1536-43.
16. Sujith KV, Kalluraya B, Adhikari A and Vijayanarayana K: Microwave – mediated synthesis of triazolothiadiazoles as anti-inflammatory, analgesic and free radical scavenging agents. Med Chem Res 2012; 21: 543-551.
17. Taj T, Kamble RR and Kattimani PP: Synthetic utility of sydnones: synthesis of pyrazolinesderivatized with 1, 2, 4-triazoles as anti-hyperglymic, free radical scavenging agents and their DNA cleavage study. Med Chem Res 2012; 21: 3709–3719.
18. Upmanyu N, Gupta J, Shah K and Mishra P: Anti-inflammatory and antinociceptive evaluation of newly synthesized 4-(substituted ethanoyl) amino-3-mercapto-5-(4-methoxy) phenyl-1, 2, 4-triazoles. J Pharm Bio Allied Sci 2011: 3(2): 259–265.
19. Valentina P, Ilango K, Deepthi M, Harusha P, Pavani G. Free radical scavenging activity of some substituted 1,2,4-triazo-5-thione, Schiff base. J Pharm Sci & Res 2009; 1(2): 74-77.
20. Yüksek H, Ocak Z, Alkan M, Bahçeci S and Ozdemir M: Synthesis and determination of pKa values of some new 3,4-disubstituted-4,5-dihydro-1H-1,2,4-triazol-5-one derivatives in non-aqueous solvents. Molecules 2004; 9(4): 232-240.

How to cite this article:
Sharma K, Tinku, Jogpal V, Sanduja M and Verma PK: Synthesis, characterization and biological evaluation of novel 5, 6-dihydro-3-(substituted phenyl) [1, 2, 4] triazole (3, 4-b) [1, 3, 4] thiadiazine-7-one derivatives for antimicrobial and free radical scavenging activity. Int J Pharm Sci & Res 2023; 14(1): 444-52. doi: 10.13040/IJPSR.0975-8232.14(1).444-52.