ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

Research Article

Design and Synthesis of Novel Tetrazole Derivatives with Potential Antimicrobial Activity

Ajay Kumar Yadav[1], Asheesh Kumar Singh[2], Prashant Singh[3]
[1]Department of Pharmaceutical Chemistry, Buddha Institute of Pharmacy, GIDA, Gorakhpur, (U.P.), India-2730209
2Department of Pharmacognosy, Buddha Institute of Pharmacy, GIDA, Gorakhpur, (U.P.), India-273209
3Department of Pharmaceutics, Buddha Institute of Pharmacy, GIDA, Gorakhpur, (U.P.), India-273209
ajayyadavmpharm@gmail.com

Abstract

Tetrazole five membered heterocyclic ring contain four nitrogen and one carbon atom. Tetrazole shows diverse pharmacological activity. A series of tetrazole derivatives A(1-4) were synthesized by reaction between tetrazole aldehyde and aromatic hydrazine by Mannich base reaction mechanism. The Synthesized compounds A(1-4) were confirmed by IR, 'H NMR, mass spectral, and elemental analysis. Synthesized compounds A(1-3) and were screened for antibacterial activity. The compound 2 was highly active against S. aureus in antibacterial screening. It was show that synthesized derivatives show microbial activity against both gram-negative and gram-positive bacterial species. New tetrazole derivatives show significant potential and provide important directions for future antibacterial drug development.

Keywords: Heterocyclic compound, Tetrazole derivatives, Bacterial strain

Introduction

The worldwide rise of antibiotic-resistant organisms is causing infectious diseases to re-emerge as a major threat, undermining the significant advances achieved in modern medicine. [1]. When bacteria are treated with antimicrobial substances, their growth, reproduction, or even death can be inhibited. They come in a variety of types, such as antibiotics [2]. The long-term and widespread use of antibiotics has contributed significantly to the emergence of antimicrobial resistance (AMR) in microorganisms [3,4]. Although microbial infections are commonly treated with antibacterial and antifungal agents, the rapid rise of antibiotic resistance has created a major barrier to effective therapy. This growing resistance has become a critical global concern, posing a serious threat to human health and directly impacting quality of life. Addressing AMR has therefore become an urgent priority, requiring the development of timely and effective solutions.

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

Given this alarming situation, the discovery and development of new antimicrobial agents is essential for managing microbial infections [5–7]. Experts agree that innovative therapeutic strategies are necessary to combat antibiotic-resistant pathogens and prevent their further spread, a task that will demand significant scientific effort and collaboration.

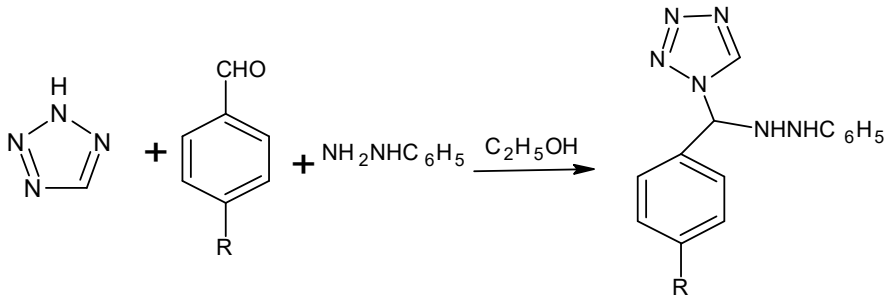
Meanwhile, fungal infections are also increasing worldwide, especially in developing countries where access to appropriate healthcare is limited, placing vulnerable populations at heightened risk. Notably, invasive candidiasis remains a major health challenge, with mortality rates reaching up to 40% [9], and it has become the third most common cause of bloodstream infections [8].

Azoles—including imidazoles, triazoles, and tetrazoles—exhibit a wide range of potent antibacterial properties and are widely used to treat both systemic and topical mycoses, particularly those associated with AIDS-related fungal infections [10]. Tetrazoles, in particular, show a strong affinity for benzodiazepine receptors [2], and various tetrazole derivatives have been identified as effective α-mannosidase inhibitors due to their mannose-mimicking behavior [3,4].Among them, **1,5-disubstituted-1H-tetrazoles** serve as valuable peptide bioisosteres [11], and numerous tetrazole derivatives possess notable medicinal significance, having demonstrated antifungal [12,13], antinociceptive [14,15], antimycobacterial [16], anti-inflammatory [17], antiproliferative [18], anticonvulsant [19], and antibacterial [12] activities.The **Mannich reaction** also plays a crucial role in the synthesis of biologically active compounds [20,21]. Mannich bases are well known for their diverse biological activities, including cytotoxic [22,23], anticonvulsant [24], and antibacterial properties [25]. In light of these findings, we set out to synthesize a new series of tetrazole derivatives and evaluate their **antibacterial activity against dental-plaque-related pathogens** as well as their **cytotoxic potential**.

Material and method

Synthesis of 1-[phenyl(2-phenylhydrazinyl)methyl]-1H-tetrazole A(1-4): A mixture of tetrazole aldehyde and hydrazine of 0.1 mole of each compound were taken in rbf, the mixture was refluxed in ethanol for 3hours. The obtained product was poured in crushed ice. The product was recrystallised using ethanol solvent. [26-27]

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in



Scheme-1

Antimicrobial Activity- A newly synthesized compound were screened for anti bacterial activity by using different bacteria strain. The bacterial strain for the study of antimicrobial activity were E.coli, Pseudmonas aeruginosa and Bacillius subtilis.

Agar Cup Method: Ciprofloxacin was used as the reference standard for evaluating antibacterial activity. The assay was performed using a modified agar cup method. Briefly, 0.2 mL of the test culture suspension was mixed with sterile 1.5% melted top agar cooled to room temperature. The mixture was poured onto sterile base agar medium (autoclaved at 121 °C for 15 minutes) in Petri dishes and allowed to solidify. Three wells were then made in each agar plate using a sterile cup borer. Into these wells, 0.1 ml of the test solution, 0.1 mL of the reference solution, and 0.1 mL of the DMSO solvent (control) were added, respectively. The plates were kept at 4–5 °C for 20 minutes to allow diffusion, followed by incubation in an upright position at 37 °C for 24 hours. After incubation, the presence of a clear zone of inhibition around each well indicated the organism's susceptibility to the antimicrobial agent. Antibacterial activity was quantified by measuring the diameter of the inhibition zones, with larger zones corresponding to higher activity. [28, 29]

Determination of the minimal inhibitory concentration (MIC): Dimethylsulfoxide was used to dissolve the compound at a concentration of 64 µg/mL. The solution was produced in two dilutions (64, 32,..., 0.5 µg/mL). The appropriate wells were infected with the microbe suspensions at doses of 10°CFU/mL (colony forming unit/mL). For 24 hours, the plates were incubated at 36° C. [30]

Result and Discussion

A series of compound 1-3 were synthesized from condensation method and reaction is given in Scheme-1 and physical property in Table-1

Table-1: Physical Characterization of sybthesized drug

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

Derivative	R	M.F	M.W	Yield (%)
1	H	C14H14N6	266.30	60
2	Cl	C14H13ClN6	300.74	70
3	OH	C14H14N6O	282.30	52

The structure of synthesized is characterized by IR, 1H-NMR and Mass Spectroscopy. IR3408, 1660, 1315, and 1512 cm respectively. 'H NMR spectrum of the compound (la) shows that signals obtained at 6 9.60, 6.32, and 2.22 corresponding to NH_2, CH, and NH respectively.

1-[phenyl(2-phenylhydrazinyl)methyl]-1H-tetrazole 1: IR (KBr, cm): 3326 (NH2),2826(CH=Str) 3100 (NH),1530 (N=N), 1364 (C-N), 967(NH), 822 (ArH).NMR (DMSO-d6), H (ppm) 9.40 (2H,s,NH2), 8.67 (IH, s, 5CH-tetrazole), 7.40-7.36 (4H, m, phenyl), 5.42 (IH,s,-CH-), 2.22(IH, s,NH) (Relative intensity % m/z = 265.82 (M, 10%)

1-[(4chlorophenyl)(2-phenylhydrazinyl)methyl]-1H-tetrazole 2: IR (KBr, cm): 3326 (NH2),2826(CH=Str) 3100 (NH),1530 (N=N), 1364 (C-N),816(Ar-Cl) 967(NH), 822 (ArH). NMR (DMSO-d6) H (ppm) - 9.40 (2H,s,NH2), 8.67 (IH, s, 5CH-tetrazole), 7.40-7.36 (4H, m, ph), 5.42 (IH,s,-CH-), 2.22(IH, s,NH) (Relative intensity % m/z = 299.82 (M, 10%)

1-[(4hydroxyphenyl)(2-phenylhydrazinyl)methyl]-1H-tetrazole 3 : 3326(NH2),2826(CH=Str) 3100 (NH),1530 (N=N), 1364 (C-N),726(Ar-OH) 967(NH), 822 (ArH).NMR (DMSO-d6), H (ppm) 9.40 (2H,s,NH2), 8.67 (IH, s, 5CH-tetrazole), 7.40-7.36 (4H, m, ph), 5.42 (IH,s,-CH-), 2.22(IH, s,NH), 9.45(1H,s, Ph-OH) Ms (Relative intensity % m/z = 281.82 (M, 10%)

Antimicrobial activity: The recrystallized product was examined for antibacterial activity in vitro. Out of the three tetrazole compounds, l,3 and 2 shown moderate inhibition against gram-negative bacterial species, particularly Escherichia coli, according to the findings in Table 2, whereas 1 and 3 demonstrated maximum action against the majority of gram-negative organisms. Nearly every molecule in the series demonstrated maximal inhibition against gram-positive organisms.

Table-2 Antimicrobial activity of compound by Zone of Inhibition

Derivative	Zone of Inhibition		
	Bacterial Strain		
	E. coli	Pseudomonas aerugenosa	Bacilius subtilis
1	12	13	15
2	18	20	23

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

3	14	12	17
Std	30	30	30

Antimicrobial activity of compound in 10% DMSO Standard Drug- Ciprofloxacin the antibacterial properties of three synthesized compounds (1-3) when compared to standard drug like ciprofloxacin. Compound 1was highly effective against Pseudomonas aeruginosa (MIC: 8 µg/mL). Compound 3 showed high activity against Escherichia coli when combined with conventional antibiotics (MIC: 4 µg/mL).

Determination of the minimal inhibitory concentration (MIC): Dimethyl sulfoxide (DMSO) was used to dissolve the compound at a concentration of 64 µg/mL. The solution was then prepared in two additional dilutions (32 and 0.5 µg/mL). The corresponding wells were inoculated with microbial suspensions at a concentration of 10° CFU/mL (colony-forming units per milliliter). The plates were incubated at 36 °C for 24 hours. [31]

Table 3 Provides a summary of the data and minimum inhibitory concentrations.

Derivative	MIC		
	Bacterial Strain		
	E.coli	Pseudomonas aerugenosa	Bacilius subtilis
1	60	65	46
2	40	45	30
3	68	12	17
Std	0.5	0.5	32

Antimicrobial activity of compoundin 10% DMSO
Standard Drug- Ciprofloxacin

Conclusion- The text is a conclusion from a research paper on the creation and testing of tetrazole derivatives, which are a class of organic compounds used in medicinal chemistry.

- A synthetic method for develop novel tetrazole derivatives was outlined.
- Compound (1) demonstrated excellent activity against S. aureus (a type of bacteria).
- The presence of a chlorine substituent on the phenyl rings made most compounds active in antibacterial screenings.

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

- The research indicates the potential for these novel derivatives to have antibacterial and cytotoxic (toxic to living cells) activity, guiding future drug development.

References

1. Yapar N. Epidermology and risk factors for invasive candidiasis. Therapeutics and Chimcal Risk Management, 2014, 10:95.
2. Bansal Y. Kaur M., Bansal G. Antimicrobial poumtial of benzimidazole derived molecules. Mini Reviews in Medicinal Chemistry, 2019, 19:624
3. Keri R.S. Rapappa CK. Patil SA, Nagaraja B.M. Benzimidazole-core as an antimycobacterial agent. Pharmacological Reports, 2016, 68: 1254
4. 4.Friedberg I W., Cohen P, Chen L., Robinson KS, Forero-Torres A, La Caice AS, Fayad LE,
5. Beunde A, Camacho ES, Williams M.E. Bendamustine in patients with rituximabrefractory indolent and transformed sonHodgkin's lymphoma results from a phase II multicenter, single-agent study Journal of Clinical Oncology, 2008, 26:204
6. Vatolkina O. Plotkia A., Libinzon R. Analysis of the relationship between the inhibition of the cyclic AMP phosphodiesterase activity and pharmacological action of drugs Pharmaceutical Chemistry Journal, 1985, 19 172.
7. Kearns GL, Andersson T., James L.P., Gaedigk A. Kraynak RA, Abdel Rahman S M., Ramabadran K. van den Anker IN, Network P.P.RU. Omeprazole disposition in children following single-dose administration. The Journal of Clinical Pharmacology, 2003, 43:840
8. Elahi RH, Osman A.G., Sherif A.M., Elhussein A.A. Comparative study of the fungicide Benomyl toxicity on some plant growth promoting bacteria and some fungi pure cultures. Interdisciplinary Toxicology, 2014, 7:12
9. Gupta P.K. Toxicity of fungicides. Veterinary Toxicology (Third Edition), 2018, 569
10. Citardia A., Moi D., Pedrini M., Pérez-Peña II., Pieraccini 5., Dimasi A., Stagno C. Micale N., Schirmeater T., Sibille G. Synthesis of SARSCOV-2 M pro inhibitors bearing a cinnamic ester warhead with in vitro activity against human coronaviruses. Organic & Biomolecular Chinmistry, 2023, 21:3811
11. Vishvakrama P. Sharnas 5. Liposomes an overview. Journal of Drug Delivery and Therapeutics. 2014 Jius 24:47-55.
12. Vishvakarma P. Design and development of montelukast sodan fast dissolving films for better therapeutic efficacy. Journal of the Chilean Chemical Society 2018 Jun;63(2):3988-93

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

13. Visvakarma P. Mandal 5. Verma A. A review on current aspects of nutraceuticals and dietary supplements. International Journal of Pharma Professional's Research (UPPR). 2023;14(1):78-91.
14. Prabhakar V, Agarwal S, Chauhan R, Sharma S. Fast dissolving tablets an overview. International Journal of Pharmaceutical Sciences: Review and Research, 2012.16(1)1:17.
15. Mandal S. Vahvakarma P. Verma M, Alam MS, Agrawal A. Mishra A. Solzevn Nigrun Linn: an analysis of the Medicinal properties of the plant Journal of Pharmaceutical Negative Results 2023 Jan 1:1595-600.
16. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis of The Most Recent Trends in Flavoring Herbal Medicines in Today's Market. Journal of Pharmaceutical Negative Results. 2022 Dec 31:9189-98
17. Mandal S, Vishvakarma P. Mandal S. Future Aspects and Applications of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. European Journal of Molecular & Clinical Medicine. 2023:10(01):2023
18. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier Indian J of Pharmaceutical Education and Research. 2023;57(38):5481-98.
19. Prabhakar V. Agarwal 5, Chauhan R, Sharma 5. Fast disolving tablets an overview. International Journal of Pharmaceutical Sciences: Review and Research, 2012.16(1):17.
20. Push RH. Dixit HC. Synthesis characterization and anti-microbial activity of imidazole derivatives based on 2-chloro-7-methyl-3-formylquinoline. J Chem 2012:9:1188-95.
21. Mishra R, Oanguly S, Sethi KK, Mazumder PM. Synthesis and anticonvulsant activity of some novel 2-methyl inidazole derivatives. Lett Drug Des Diacov 2012,9, 402-8.
22. Khaliullin F. Näitias L. Valirva A. Miftakhova A. Khalilov L. Mescheryakova E. Synthesis and Antidepressant activity of 2-bromo-1- (thien-3-yl) imidazole 4, 5-dicarboxylic acid derivatives. Int J Pharm Pharm S 2017,9,154.
23. LiY. F. Wang O. F. He P. L., Huang W. G., Zhu F. H., Gao H. Y., Tang W., Luo Y., Feng C. L. ShiL. P. Rem V. D. La W., Zuo 1. P., Synthesis and anti-hepatitis Bvirus activity of novel benzimidazole derivatives 2. Med. Chem, 2006, 49, 479.
24. Varvarsson A., Tantili-Kakoulidou A., Siatra-Papastasikoudi T., Tiligada E., Syathesis and biological evahandson of indole comaining derivatives of thiosemicarbaride and their cyclic 1, 2, 4-triazole and 1.3,4-thiadiazole analogs, Armeim Forsch, 2000, 50, 48.
25. Gokce M., Cak B., Earli K., Satun M., Synthesis and antimicrobial activity of [(2-oxabenzothiazolin 3-yl)-methyl)-4-alkyaryl-1, 2, 4-mazoline-5-thiones, Arch. Pharm, 2001, 334, 279,

ISSN: xxxx-xxxx
Buddha Journal of Pharmaceutical Science and Research (BJPSR)
Volume 1 | Issue 1 | August 2025 Website: www.bip.ac.in/journal/index.php Email: bjpsr2025@bip.ac.in

26. Pintilie O., Protire 1, Sunel V Popa M., Pa A., Synthesis and antimicrobial activity of some new 1. 3.4-thiadiazole and 1,2,4-triazole compounds having a D.L-methionine moiety, Molecules, 2007, 12,105
27. Faroumadi A. Mirzani M., Shalice A., Syntheses and antituberculosis activity of 2-aryl-1, 3, thandianole derivatives, Pharmarse, 2001, 56, 610.
28. 27.Nikam Anil Ishwar, Vikas Kumar Pal, Preeti, Ajay kumar Yadav, Design, Synthesis, Molecular Docking. And Biological Evaluation of Tetrazole Derivatives For Antimicrobial Potential, Frontiers in Health Informatics, 2676-7104, 2024,13,3:5446.
29. Zan X3 Lai L. H. JmGY. Zhong Z. X. Synthesis, fungicide activity and 3D-QSAR of 1, 3, 4 exadiazules and 1, 3, 4-thiadiazoles, 1. Agric Food Chem, 2002, 50, 3747.
30. Chem II. Li Z. Ban Y. Systhesis and fungicidal activity (alicylthio)-5-pyrazolyl-1, 3, 4-otadiaroles (thiadiazoles), J. Agric. Food Chem, 2000, 48, 5312.
31. Clanski F. Fox D. Guide M. Loche A, Perlas V., Brudoni M., Synthesis of Jamino-3 phomyti,3,4-thiadiazole derivatives and evaluation of their antidepressant and anxiolytic activity, J Med Chem, 2001, 44, 931.
32. Okol T. Cakir R. Sabir M. F. Synthesis and antociceptive activity of 2-[(2-oxabenzothiazole-3-yl)-methyl]-5-aminoalkyl/aryl-1.3.4 thiadiazole, Turk J. Chem, 2004, 28, 461