Advances in Bioresearch
Adv. Biores., Vol 16 (4) July 2025: 23-32
©2025 Society of Education, India
Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.4.2332

Advances in Bioresearch

ORIGINAL ARTICLE

Microwave Irradiated Synthesis, Characterization, Biological Screening and *In Silico* Pharmacokinetics of Fused Oxazolo and Imidazo [1,8] Naphthyridines

Shabhari Prasad Suggula [1,2], **Jagadeesh Kumar Ega**[1*], **P. Muralidhar Reddy**[2*], **Nageswara Rao Ambala**[3]

[*1] Department of Chemistry Chaitanya (Deemed to be University), Himayathnagar, Hyderabad 500075, Telangana, India

[*2] Department of Chemistry, University College of Science, Osmania University, Hyderabad 500007, Telangana, India

[3] Department of Chemistry, Sri Chaitanya Degree College, Wyra, Khammam 507165, Telangana, India

***Corresponding author's email:** jkjagadeeshkumare@gmail.com & pmdreddy@gmail.com

ABSTRACT

Herein, we report the microwave assisted synthesis of 4-phenylbenzo[b]oxazolo[5,4-f] [1,8] naphthyridines 3a-l shown in Scheme-I,Fig.1 & 4-phenylbenzo[b] imidazole [5,4-f] [1,8] naphthyridine 5a-l shown in Scheme-II,Fig.2 from series of aldehydes , 3-(oxazol-5-yl) quinolin-2-amine 1 /3-(1H-imidazol-5-yl) quinolin-2-amine 4 to yield promising yields, and also screened for anti-bacterial evaluation. Among them 3f, 3g, 5h, 5f, 5g, and 5h established more efficient bacterial inhibitory action against B. subtilis, with MICs of 3.12, 3.12, and 1.56 μg/mL, respectively, whereas typical streptomycin MICs were 6.25 μg/mL. Compound 3h and 5h have showed more potent activity against S. aureus, with MIC value of 3.12 μg/mL, whereas compound 3f and 5f has shown equipotent activity against the S. aureus, with MIC value of 6.25 μg/mL. Compound 3k and 5k shown equipotent activity against B. subtilis and good activity against S. aureus with MIC values of 3.12 μg/mL and 6.25 μg/mL, and also Physicochemical properties with SwissADME tool, Pharmacokinetics with pkCSM tool evaluated and depicted in Table 1 to 6.

Keywords: *Oxazolo- naphthyridines, Imidazole - naphthyridine, MWI, SwissADME, pkCSM*

Received 21.05.2025 Revised 28.06.2025 Accepted 04.07.2025

How to cite this article:
Shabhari Prasad S, Jagadeesh K E, P. Muralidhar R, Nageswara R A. Microwave Irradiated Synthesis, Characterization, Biological Screening and *In Silico* Pharmacokinetics of Fused Oxazolo and Imidazo [1,8] Naphthyridines. Adv. Biores. Vol 16 [4] July 2025.23-32

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a significant threat to global public health, reducing the effectiveness of standard antibiotics and leading to persistent infections and higher mortality rates [1,2]. The World Health Organization has recognized AMR as one of the top ten global public health threats facing humanity [1]. In response to this crisis, there is an urgent need to discover and develop novel antimicrobial agents capable of combating multidrug-resistant strains [2,3].

In the search for newer therapeutic scaffolds, heterocyclic compounds have shown immense promise due to their broad spectrum of biological activity and structural versatility [4,5]. Among them, fused oxazolo[4,5-c] quinolines and imidazo [1,8] naphthyridines have gained considerable attention owing to their significant antimicrobial, anticancer, and anti-inflammatory activities [6,7]. Furthermore, the fusion of aromatic and heterocyclic units enhances molecular rigidity and planarity, thereby improving interactions with biological targets and increasing cell permeability [6,8,9].

Microwave-assisted organic synthesis (MAOS) has revolutionized green chemistry by significantly enhancing reaction efficiency, selectivity, and product yield while reducing reaction time and energy consumption [10,11]. Several solvent-free and catalyst-supported methods, such as reactions using clayzic, alumina, or iodobenzene diacetate, have been reported to facilitate environmentally benign

synthesis of functional heterocycles [12–14]. These methods represent a shift toward sustainable chemistry approaches that are aligned with eco-friendly principles [13].

The structural diversity and potential drug-likeness of such heterocycles can be further evaluated using in silico tools. Web platforms like SwissADME allow for predictive evaluation of pharmacokinetic properties, medicinal chemistry friendliness, and overall drug-likeness of newly synthesized molecules [15]. Such computational evaluations support early-stage screening of compounds for ADMET (absorption, distribution, metabolism, excretion, toxicity) properties, thereby optimizing the drug discovery pipeline [15,16].

Another important motif explored in current heterocyclic research is the benzene-centered tripodal imidazolium (BTI) system, which has demonstrated potential in various interdisciplinary fields, including catalysis, coordination chemistry, and drug development [17–19]. Incorporating such motifs within biologically active scaffolds may lead to multifunctional therapeutics with improved efficacy and selectivity [19–21].

Recent studies have highlighted the value of synthetic derivatives like 2-arylquinoline-fused thiazolotriazoles and phenanthrene-linked oxadiazoles for their promising antimicrobial and anticancer activities [22,23]. Furthermore, bio glycerol-based green catalysts have enabled the development of highly active indole derivatives with enhanced anticancer properties [23]. Molecular docking and spectral characterization continue to guide structure–activity relationship (SAR) analyses in drug design [24–27].

Based on these insights, the present study focuses on the microwave-assisted synthesis of novel fused oxazolo and imidazo [1,8] naphthyridines, their characterization via spectral techniques, biological evaluation against microbial strains, and pharmacokinetic profiling using in silico tools. By integrating green chemistry with computational modeling and biological screening, this research aims to identify new lead molecules with drug-like potential.

MATERIAL AND METHODS

Chemistry

All reagents were procured from Sigma-Aldrich, and are of laboratory grade. The melting points reported here-in are uncorrected and were determined in open capillaries using Thiele's melting point apparatus. Reactions were monitored by thin layer chromatography (TLC), which were performed on coated Silica gel G plates activated for 30 min.(120ºC) and spots were visualized by exposure to iodine vapours. 1H NMR spectra were determined on Mercury Plus 400MHz NMR Spectrometer in DMSO-d6 with TMS, δ 0 ppm as an internal standard. 13C NMR spectra were recorded with DMSO-d6 at100MHz on a Mercury Plus NMR Spectrometer. Mass spectra were collected using a Jeol JMC-300 spectrometer (ESI, 70 eV). The Carlo Erba 106 and PerkinElmer model 240 analysers were used to analyse the elements.

GENERAL PROCEDURE

Synthesis of oxazolo[5,4-f] [1,8] naphthyridines 3a-l & imidazole [5,4-f] [1,8] naphthyridine 5a-l

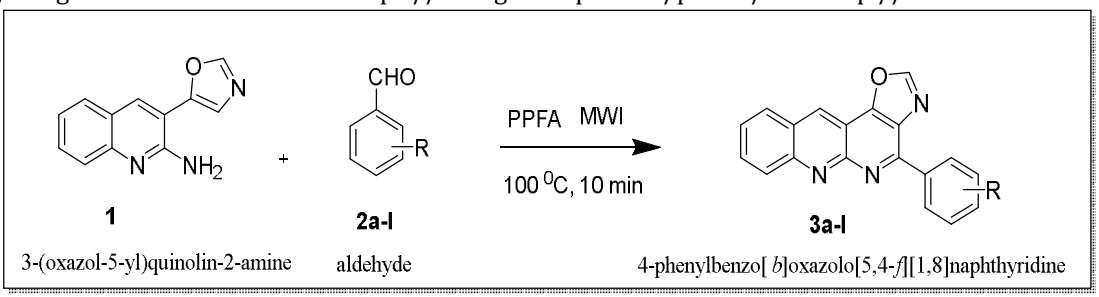
Phenethyl Phenol Formaldehyde Resin Polyoxyethylene Ether (PPFA) is a non-ionic surfactant derived from a modified phenolic resin, combined with polyoxyethylene (PEO) chains (10 mol%) with various aldehydes 2a-l and, 3-(oxazol-5-yl) quinolin-2-amine 1 to give 4-phenylbenzo[b]oxazolo[5,4-f] [1,8] naphthyridines 3a-l derivatives are shown in Scheme-I and Fig. 1. transferred into a microwave vial. The vial sealed with caps and vials was subjected to microwave irradiation (300 Watt) at 100˚C for 10 min. with promising yields [28] Shown in Scheme-I Another hand aldehydes 2a-l with 3-(1H-imidazol-5-yl) quinolin-2-amine 4 to give 4-phenylbenzo[b] imidazole [5,4-f] [1,8] naphthyridine 5a-l Shown in Scheme-II and Fig.2. with excellent yields. PPFA resins have a number of desirable properties, including good adhesion, high temperature resistance, and resistance to chemicals and solvents.

Antibacterial activity

Using the conventional broth microdilution method, the title compounds (3a-3l) & (5a-5l) were tested for in vitro antibacterial activity against gram-positive (G+ve) bacterial strains *B. subtilis*, *S. aureus*, and *S. epidermidis* with streptomycin serving as a positive control [14]. All derived compounds' minimum inhibitory concentrations (MICs) were indicated in μg/mL. The results are shown in Table 1 and 2. Table 1 and 2 demonstrates that 4f, 4g, and 4h demonstrated more efficient bacterial inhibitory action against B. subtilis, with MICs of 3.12, 3.12, and 1.56 μg/mL, respectively, whereas typical streptomycin MICs were 6.25 μg/mL. Compound 3h ,5h have showed more potent activity against *S. aureus*, with MIC value of 3.12 μg/mL, whereas compound 3f ,5f have shown equipotent activity against the *S. aureus*, with MIC value of 6.25 μg/mL. Compound 4k shown equipotent activity against *B. subtilis* and good activity against *S. aureus* with MIC values of 3.12 μg/mL and 6.25 μg/mL, and compounds 3e,5e,3i and 5i similarly demonstrated moderate activity against *B. subtilis* and *S. aureus* (with MIC values 6.25 μg/mL).

***In silico* pharmacokinetic profile**

It is well known that the nitrogen and oxygen-heterocycles are key frameworks of several drugs. The combination of these heterocycles lead to change numerous properties of bioactive compounds which includes lipophilicity, polarity, solubility and hydrogen bonding ability etc. These properties consequently led to the progress of ADMET properties of the intended compounds and drugs [15]. Therefore, we carried out in silico SwissADME (Table 4,6) and pkCSM (Table 3,5) Water solubility (log mol/L), Human Intestinal absorption HIA (%), CYP2D6 inhibition and MLogP, TPSA and GI absorption of 3a-3i & 5a-5l were calculated. *In silico* in silico SwissADME and pkCSM for the compounds 3a-3l, 5a-5l and Erlotinib drug using the standard. web links https://biosig.lab.uq.edu.au/pkcsm/. and http://www.swissadme.ch/.



Scheme -I Synthesis of 4-phenylbenzo[b]oxazolo[5,4-f] [1,8] naphthyridines 3a-l

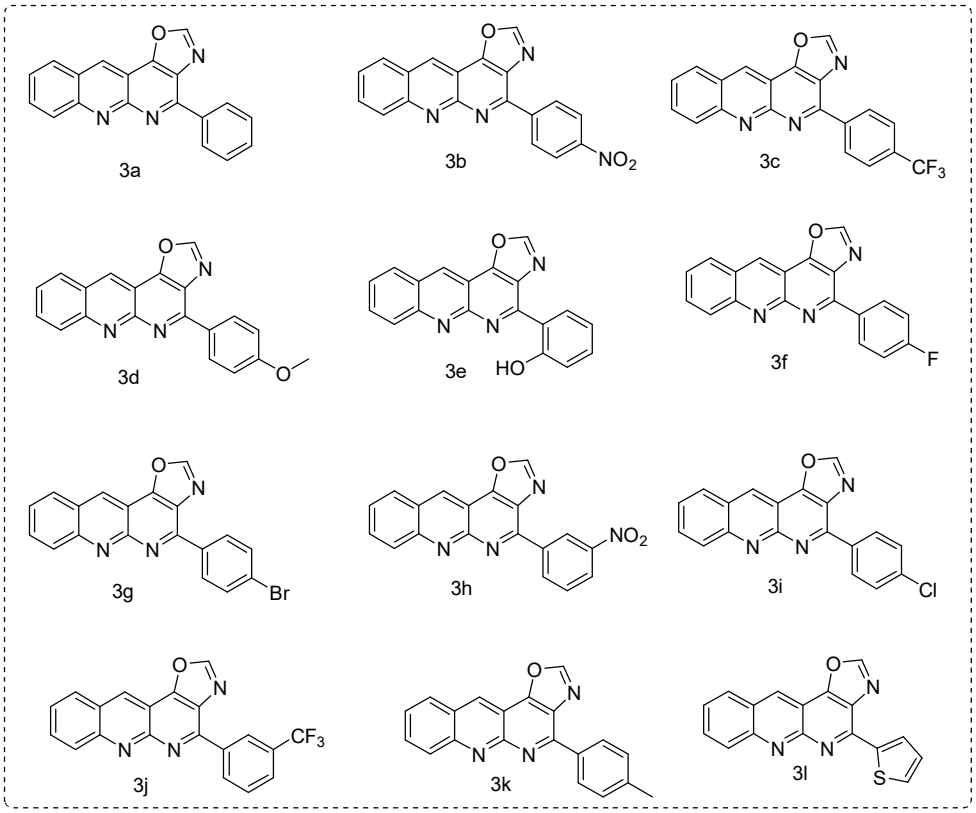


Fig. 1. Structures of designed target oxazolo[5,4-f] [1,8] naphthyridines 3a-l

RESULTS

4-phenylbenzo[b]oxazolo[5,4-f][1,8] naphthyridine (3a)

Yellow - orange, Yield 84 %. 1H NMR (DMSO-d6): δ 8.78 (d, J = 1.4 Hz, 1H), 8.06 (dd, J = 7.1, 5.6, 1.3 Hz, 3H), 7.95 (s, 1H), 7.78 (dt, J = 7.5, 1.6 Hz, 1H), 7.59 (td, J = 7.5, 1.5 Hz, 1H), 7.47 – 7.41 (m, 3H), 7.39 – 7.34 (m, 1H); 13C NMR (DMSO-d6): δ 157.94, 155.66, 150.51, 146.98, 139.85, 134.86 , 133.00 , 131.94 , 131.33 , 130.46 , 129.16, 127.61, 127.37, 124.33, 117.88, 110.74; ESI-MS: 294 [M+H]+, Found: C, 76.77; H, 3.75; N, 14.10; calcd for C19H11N3O: C, 76.76; H, 3.73; N, 14.13.

4-(4-nitrophenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3b)

Yellow, Yield 86 %.1H NMR (DMSO-d6): δ 8.79 (s, 1H), 8.37 – 8.27 (m, 4H), 8.07 (s, 1H), 7.95 (s, 1H), 7.78 (s, 1H), 7.59 (s, 1H), 7.44 (s, 1H); 13C NMR (DMSO-d6): δ 157.94, 155.66, 150.34, 146.98, 139.85, 133.00, 131.94, 130.46, 127.61, 124.33, 117.88, 110.74; ESI-MS: 343[M+H]+, Found: C, 67.72; H, 2.95; N, 16.10; calcd for C19H10N4O3: C, 66.67; H, 2.94; N, 16.37.

4-(4-(trifluoromethyl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3c)

Pale yellow, Yield 84 %.1H NMR (DMSO-d6): δ 8.78 (d, J = 1.4 Hz, 1H), 8.08 (s, 1H), 8.04 (d, J = 7.5 Hz, 2H), 7.95 (s, 1H), 7.78 (dt, J = 7.5, 1.4 Hz, 1H), 7.69 (d, J = 7.5 Hz, 2H), 7.59 (td, J = 7.5, 1.4 Hz, 1H), 7.44 (td, J = 7.4, 1.5 Hz, 1H); 13C NMR (DMSO-d6): δ 157.94, 155.66 , 150.51, 146.98 , 139.85, 135.72, 131.94, 131.65, 130.46, 127.61, 127.31, 125.51, 124.33, 123.41, 121.32, 117.88, 110.74; ESI-MS: 366[M+H]+ , Found: C, 66.67; H, 2.77; N, 11.43; calcd for C20H10F3N3O: C, 65.76; H, 2.76; FN, 11.50

4-(4-methoxyphenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3d)

Off-white, Yield 86 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.05 (d, J = 22.1 Hz, 3H), 7.95 (s, 1H), 7.76 (s, 1H), 7.61 (s, 1H), 7.41 (s, 1H), 7.05 (s, 2H), 3.82 (s, 3H); 13C NMR (DMSO-d6): δ 161.61 , 157.94, 155.66, 150.51, 146.98, 139.85, 133.00, 131.96, 130.46, 127.37, 125.81, 124.33, 117.88, 114.17, 110.74, 56.03; ESI-MS: 328[M+H]+, Found: C, 73.76; H, 3.83; N, 12.13; calcd for C20H13N3O2: C, 73.38; H, 4.00; N, 12.84

2-(benzo[b]oxazolo[5,4-f] [1,8] naphthyridin-4-yl) phenol (3e)

Yellow-orange, Yield 88 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.07 (s, 1H), 7.95 (s, 1H), 7.92 (dd, J = 7.5, 1.4 Hz, 1H), 7.77 (s, 1H), 7.57 (s, 1H), 7.41 (s, 1H), 7.19 (s, 1H), 7.01 (s, 1H), 6.94 (s, 1H); 13C NMR (DMSO-d6): δ 158.14 , 156.68, 155.66, 150.51, 147.71, 137.11, 133.08, 132.50, 131.94, 131.20 , 130.46, 121.58, 120.53, 117.88, 106.40; ESI-MS: 314[M+H]+, Found: C, 73.01; H, 3.63; N, 13.21; calcd for C19H11N3O2: C, 72.84; H, 3.54; N, 13.41

4-(4-fluorophenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3f)

Pale yellow, Yield 87 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.07 (s, 3H), 7.95 (s, 1H), 7.79 (s, 1H), 7.58 (s, 1H), 7.45 (s, 1H), 7.18 (d, J = 15.5 Hz, 2H); 13C NMR (DMSO-d6): δ 166.83, 164.73, 157.94, 155.66, 150.51, 146.98, 139.85, 133.00, 130.46, 129.22, 127.61, 127.37, 124.33, 117.88, 115.84, 110.74; ESI-MS: 316 [M+H]+ , Found: C, 72.76; H, 3.25; N, 13.01; calcd for C19H10FN3O: C, 72.38; H, 3.20; N, 13.33

4-(4-bromophenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3g)

Pale yellow, Yield 84 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.07 (s, 1H), 7.96 (s, 3H), 7.77 (s, 1H), 7.62 (s, 2H), 7.58 (dd, J = 7.5, 1.6 Hz, 1H), 7.42 (s, 1H); 13C NMR (DMSO-d6): δ 157.94, 155.66, 150.51, 146.98, 139.85, 133.59, 133.00, 132.36, 131.94, 131.14, 130.46, 127.61, 124.33, 117.88, 110.74; ESI-MS:377[M+H]+,Found: C, 60.68; H, 2.71; N, 11.14; calcd for C19H10BrN3O: C, 60.66; H, 2.68; N, 11.17

4-(3-nitrophenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3h)

Bright yellow, Yield 86 %.1H NMR (DMSO-d6): δ 9.04 (s, 1H), 8.79 (s, 1H), 8.40 (d, J = 10.2 Hz, 1H), 8.26 (s, 1H), 8.08 (s, 1H), 7.95 (s, 1H), 7.79 (s, 1H), 7.69 (s, 1H), 7.61 (s, 1H), 7.42 (s, 1H); 13C NMR (DMSO-d6): δ 158.21, 155.66, 150.51, 149.23, 147.09, 139.72, 137.28, 136.42, 133.39, 131.94, 130.46, 128.95, 127.61, 127.37, 126.55, 124.33, 117.88, 111.17; ESI-MS:343[M+H]+,Found: C, 66.70; H, 2.96; N, 16.34; calcd for C19H10N4O3: C, 66.67; H, 2.94; N, 16.37

4-(4-chlorophenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3i)

Pale yellow, Yield 81 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.06 (s, 1H), 8.00 (d, J = 7.5 Hz, 2H), 7.95 (s, 1H), 7.77 (s, 1H), 7.58 (s, 1H), 7.42 (s, 3H); 13C NMR (DMSO-d6): δ 157.94, 155.66, 150.51, 146.98, 139.85, 136.93, 133.00, 131.91 (d, J = 8.6 Hz), 131.30, 130.46, 130.08, 127.61, 124.33, 117.88, 110.74; ESI-MS: 332[M+H]+, Found: C, 68.81; H, 3.08; N, 12.63; calcd for C19H10ClN3O: C, 68.79; H, 3.04; N, 12.67

4-(3-(trifluoromethyl) phenyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3j)

Deeper yellow, Yield 82 %.1H NMR (DMSO-d6): δ 8.80 (s, 1H), 8.12 (s, 1H), 8.06 (d, J = 8.9 Hz, 1H), 7.95 (s, 1H), 7.87 (d, J = 7.5 Hz, 1H), 7.77 (d, J = 2.7 Hz, 1H), 7.66 (d, J = 10.5 Hz, 1H), 7.59 (s, 1H), 7.40 (t, J = 14.8 Hz, 2H); 13C NMR (DMSO-d6): 158.21, 155.66, 150.51, 147.09, 139.72 , 136.13 , 133.39 , 132.39, 131.94, 131.38, 131.17, 130.95, 130.46, 128.59, 127.61, 127.37, 126.45, 125.19, 124.33, 123.09, 121.00, 117.88, 111.17; ESI-MS: 366[M+H]+,Found: C, 65.80; H, 2.79; N, 11.47; calcd for C20H10F3N3O: C, 65.76; H, 2.76; N, 11.50

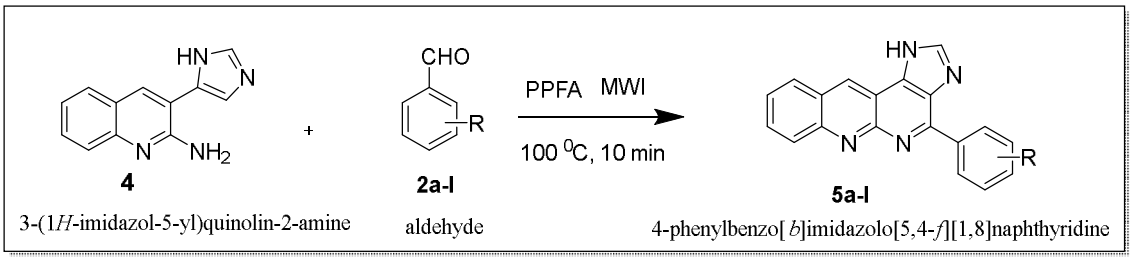
4-(p-tolyl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3k)

Off-white, Yield 89 %.1H NMR (DMSO-d6): δ 8.78 (s, 1H), 8.06 (d, J = 7.5 Hz, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.95 (s, 1H), 7.77 (d, J = 7.3 Hz, 1H), 7.59 (s, 1H), 7.44 (d, J = 6.1 Hz, 1H), 7.31 (d, J = 7.3 Hz, 2H), 2.36 (s, 3H); 13C NMR (DMSO-d6): δ 157.94, 155.66, 150.51, 146.98, 141.24, 139.85, 133.00, 132.66, 130.30, 129.54, 127.37, 124.33, 117.88, 110.74, 21.12; ESI-MS: 312[M+H]+ , Found: C, 77.19; H, 4.24; N, 13.46; calcd for C20H13N3O: C, 77.16; H, 4.21; N, 13.50

4-(thiophen-2-yl) benzo[b]oxazolo[5,4-f] [1,8] naphthyridine (3l)

Deeper yellow, Yield 90 %.1H NMR (DMSO-d6): δ 8.72 (s, 1H), 8.10 (d, J = 7.5 Hz, 1H), 7.95 (s, 1H), 7.92 (d, J = 8.9 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.62 (d, J = 6.1 Hz, 1H), 7.48 (d, J = 7.5 Hz, 2H), 7.35 (d, J = 7.5 Hz,

1H); 13C NMR (DMSO-d6): δ 158.82, 155.66, 150.93, 147.43, 143.09, 136.14, 132.42, 131.98 (d, J = 9.5 Hz), 130.39 (d, J = 19.1 Hz), 128.79, 127.37, 124.33, 117.88, 109.16; ESI-MS: 304[M+H]+ , Found: C, 67.35; H, 3.02; N, 13.81; calcd for C17H9N3OS: C, 67.31; H, 2.99; N, 13.85



Scheme -II Synthesis of 4-phenylbenzo[b] imidazole [5,4-f] [1,8] naphthyridine 5a-l

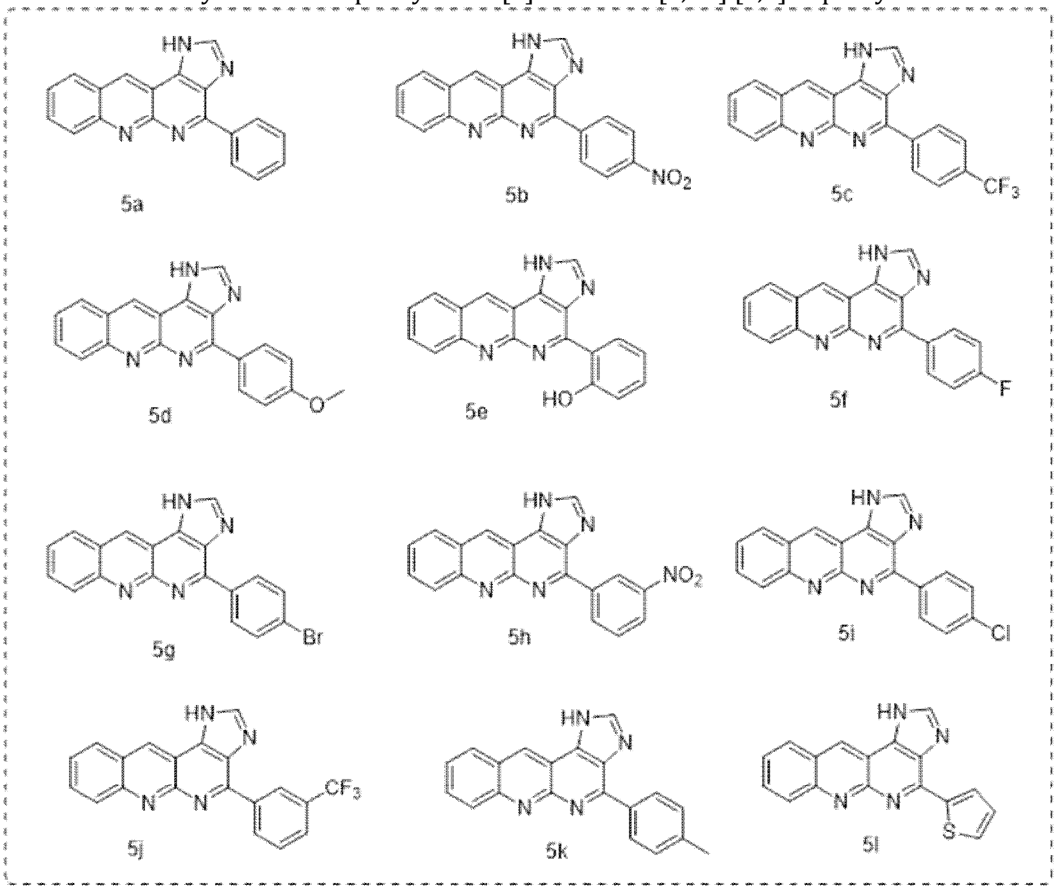


Fig.2. Structures of designed target imidazole [5,4-f] [1,8] naphthyridine 5a-l

4-phenyl-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5a)

Yellow, Yield 90 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.09 – 8.04 (m, 3H), 7.99 (s, 1H), 7.77 (t, J = 3.8 Hz, 1H), 7.67 (s, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.5 Hz, 3H), 7.36 (s, 1H); 13C NMR (DMSO-d6): δ 156.84, 147.95, 145.55, 139.54, 136.26, 134.86, 133.3, 131.33, 130.47, 129.33, 127.61, 127.38, 124.33, 119.16, 112.90; ESI-MS: 297 [M+H]+, Found: C, 77.04; H, 4.11; N, 18.88; calcd for C19H12N4: C, 77.01; H, 4.08; N, 18.91

4-(4-nitrophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5b)

Orange, Yield 86 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.33 (s, 4H), 8.08 (s, 1H), 8.00 (s, 1H), 7.78 (s, 1H), 7.68 (s, 1H), 7.57 (s, 1H), 7.44 (s, 1H); 13C NMR (DMSO-d6): δ 156.84, 150.34, 147.95, 145.55, 139.89, 139.54, 136.26, 133.31, 130.57, 127.61, 127.38, 124.37, 119.16, 112.90; ESI-MS: 342 [M+H]+, Found: C, 66.89; H, 3.28; N, 20.49; calcd for C19H11N5O2: C, 66.86; H, 3.25; N, 20.52

4-(4-(trifluoromethyl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5c)

Off-white, Yield 88 %.1H NMR (DMSO-d6): δ 8.70 (s, 1H), 8.19 – 7.90 (m, 4H), 7.76 (s, 1H), 7.69 (d, J = 13.9 Hz, 3H), 7.57 (s, 1H), 7.42 (s, 1H); 13C NMR (DMSO-d6): δ 156.84, 147.95, 145.55, 139.54, 136.26, 135.72,

133.31, 132.62, 131.84, 130.47, 127.61, 127.51, 124.40, 119.16, 112.90; ESI-MS:365 [M+H]+, Found: C, 65.96; H, 3.07; N, 15.35; calcd for C20H11F3N4: C, 65.93; H, 3.04; N, 15.38

4-(4-methoxyphenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5d)

Pale yellow, Yield 84 %.1H NMR (DMSO-d6): δ 8.68 (s, 1H), 8.06 (d, J = 5.9 Hz, 1H), 8.04 (d, J = 7.5 Hz, 2H), 8.00 (s, 1H), 7.76 (s, 1H), 7.67 (s, 1H), 7.57 (s, 1H), 7.43 (s, 1H), 7.04 (s, 2H), 3.82 (s, 3H); 13C NMR (DMSO-d6): δ 161.61, 156.84, 147.95, 145.55, 139.54 136.26, 133.31, 132.16, 130.47, 127.61, 127.38, 125.81, 124.33, 119.16, 114.27, 112.90, 56.04; ESI-MS:327 [M+H]+, Found: C, 73.64; H, 4.35; N, 17.14; calcd for C20H14N4O: C, 73.61; H, 4.32; N, 17.17

2-(1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridin-4-yl) phenol (5e)

Orange-yellow, Yield 88 %.1H NMR (DMSO-d6): δ 8.68 (s, 1H), 8.06 (d, J = 7.5 Hz, 1H), 7.99 (s, 1H), 7.92 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 10.2 Hz, 1H), 7.67 (s, 1H), 7.59 (d, J = 7.3 Hz, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.19 (d, J = 7.5 Hz, 1H), 7.01 (s, 1H), 6.93 (d, J = 6.1 Hz, 1H); 13C NMR (DMSO-d6): δ 158.15, 156.84, 149.65, 145.55, 140.99, 136.26, 133.44, 132.50, 132.23, 131.21, 130.47, 127.61, 127.38, 124.33, 121.58, 120.53, 119.16, 118.04, 109.45; ESI-MS: 313[M+H]+, Found: C, 71.00; H, 3.90; N, 17.91; calcd for C19H12N4O: C, 73.07; H, 3.87; N, 17.94

4-(4-fluorophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5f)

Bright- yellow, Yield 84 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.06 (t, J = 7.2 Hz, 3H), 8.00 (s, 1H), 7.77 (d, J = 10.3 Hz, 1H), 7.67 (s, 1H), 7.59 (s, 1H), 7.44 (s, 1H), 7.19 (d, J = 7.8 Hz, 2H); 13C NMR (DMSO-d6): δ 161.31, 147.95, 145.55, 139.54, 133.31, 131.74, 130.47, 129.21, 127.61, 127.38, 124.33, 119.16, 117.08, 112.90; ESI-MS: 315[M+H]+, Found: C, 72.63; H, 3.56; N, 17.79; calcd for C19H11FN4: C, 72.60; H, 3.53; N, 17.82

4-(4-bromophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5g)

Pale-yellow, Yield 87 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.07 (d, J = 8.9 Hz, 1H), 7.98 (s, 1H), 7.95 (d, J = 7.5 Hz, 2H), 7.77 (d, J = 8.9 Hz, 1H), 7.67 (s, 1H), 7.60 (dd, J = 17.4, 6.8 Hz, 3H), 7.44 (d, J = 7.5 Hz, 1H); 13C NMR (DMSO-d6): δ 156.84, 147.95, 145.55, 139.54, 136.26, 133.60, 133.31, 132.46, 131.03, 130.47, 127.61, 127.38, 127.17, 124.33, 119.16, 112.90; ESI-MS: 376[M+H]+ , Found: C, 60.85; H, 2.98; N, 14.89; calcd for C19H11BrN4: C, 60.82; H, 2.95; N, 14.93

4-**(3-nitrophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5h)**

Orange-yellow, Yield 90 %.1H NMR (DMSO-d6): δ 9.04 (s, 1H), 8.70 (s, 1H), 8.40 (d, J = 10.2 Hz, 1H), 8.24 (d, J = 7.3 Hz, 1H), 8.07 (d, J = 8.9 Hz, 1H), 8.00 (s, 1H), 7.77 (d, J = 10.5 Hz, 1H), 7.69 (d, J = 7.4 Hz, 2H), 7.58 (d, J = 7.5 Hz, 1H), 7.44 (d, J = 5.9 Hz, 1H); 13C NMR (DMSO-d6): δ 156.84, 149.23, 147.90, 145.55, 139.74, 139.53, 137.29, 136.42, 136.26, 134.31, 130.47, 128.95, 127.61, 127.38, 124.33, 119.16, 113.14; ESI-MS:342 [M+H]+,Found: C, 66.89; H, 3.28; N, 20.49; calcd for C19H11N5O2: C, 66.86; H, 3.25; N, 20.52

4-(4-chlorophenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5i)

Crystalline-yellow, Yield 84 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.07 (d, J = 7.5 Hz, 1H), 8.03 – 7.95 (m, 3H), 7.77 (d, J = 10.2 Hz, 1H), 7.67 (s, 1H), 7.60 (d, J = 7.5 Hz, 1H), 7.44 (dd, J = 15.5, 7.5 Hz, 3H); 13C NMR (DMSO-d6): δ 156.84, 147.95, 145.55, 139.54, 136.93, 136.26, 133.31, 131.87, 131.49, 130.47, 130.19, 127.61, 127.38, 124.33, 119.16, 112.90; ESI-MS:331[M+H]+,Found: C, 69.02; H, 3.38; N, 16.91; calcd for C19H11ClN4: C, 68.99; H, 3.35; N, 16.94

4-(3-(trifluoromethyl) phenyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5j)

Golden-yellow, Yield 86 %.1H NMR (DMSO-d6): δ 8.71 (s, 1H), 8.11 (t, J = 1.4 Hz, 1H), 8.06 (d, J = 7.5 Hz, 1H), 7.96 (s, 1H), 7.86 (d, J = 8.9 Hz, 1H), 7.78 (d, J = 10.5 Hz, 1H), 7.66 (s, 2H), 7.60 (d, J = 6.1 Hz, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H); 13C NMR (DMSO-d6): δ 156.84, 147.90, 145.55, 139.74, 139.53, 136.22, 134.31, 132.40, 131.28, 130.47, 128.55, 127.61, 127.32 126.43, 124.33, 124.14, 119.16, 113.14; ESI-MS:365[M+H]+, Found: C, 65.96; H, 3.07; N, 15.35; calcd for C20H11F3N4: C, 65.93; H, 3.04; N, 15.38

4-(p-tolyl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5k)

Creamy yellow, Yield 88 %.1H NMR (DMSO-d6): δ 8.69 (s, 1H), 8.07 (d, J = 8.9 Hz, 1H), 8.03 – 7.98 (m, 3H), 7.78 (d, J = 2.9 Hz, 1H), 7.67 (s, 1H), 7.59 (s, 1H), 7.41 (s, 1H), 7.31 (d, J = 7.5 Hz, 2H), 2.36 (s, 3H); 13C NMR (DMSO-d6): δ 156.84, 147.95, 145.55, 141.24, 139.54 136.26, 133.31, 132.66, 130.11, 129.43, 127.61, 127.38, 124.33, 119.16, 112.9, 21.13; ESI-MS:311[M+H]+, Found: C, 77.43; H, 4.57; N, 18.02; calcd for C20H14N4: C, 77.40; H, 4.55; N, 18.05

4-(thiophen-2-yl)-1H-benzo[b]imidazo[4,5-f] [1,8] naphthyridine (5l)

Golden-yellow, Yield 90 %.1H NMR (DMSO-d6): δ 8.63 (s, 1H), 8.10 (d, J = 7.5 Hz, 1H), 8.02 (s, 1H), 7.92 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 10.2 Hz, 1H), 7.67 (s, 1H), 7.63 (d, J = 7.4 Hz, 1H), 7.48 (d, J = 7.3 Hz, 2H), 7.34 (d, J = 15.0 Hz, 1H); 13C NMR (DMSO-d6): δ 156.84, 148.60, 145.69, 143.09, 137.94, 136.26, 136.03, 135.56, 132.43, 132.02, 130.47, 128.80, 127.61, 127.38, 124.33, 119.16, 111.07; ESI-MS: 303[M+H]+, Found: C, 67.56; H, 3.36; N, 18.50; calcd for C17H10N4S: C, 67.53; H, 3.33; N, 18.53

Table 1: *In vitro* antibacterial activity data of compounds 3a-3l

Entry	MIC(μg/mL)		
	B. subtilis	***S. aureus***	***S. epidermidis***
3a	50	50	-
3b	25	25	50
3c	-	50	-
3d	25	50	25
3e	12.5	12.5	25
3f	3.12	6.25	12.5
3g	3.12	12.5	12.5
3h	1.56	3.12	6.25
3i	12.5	12.5	25
3j	25	25	50
3k	6.25	12.5	25
3l	25	25	50
Streptomycin	6.25	6.25	3.12

Note: "-" indicates concentration > 50 μg/mL

Table 2: *In vitro* antibacterial activity data of compounds 5a-5l.

Entry	MIC(μg/mL)		
	B. subtilis	***S. aureus***	***S. epidermidis***
5a	50	50	-
5b	25	25	50
5c	-	50	-
5d	25	50	25
5e	12.5	12.5	25
5f	3.12	6.25	12.5
5g	3.12	12.5	12.5
5h	1.56	3.12	6.25
5i	12.5	12.5	25
5j	25	25	50
5k	6.25	12.5	25
5l	25	25	50
Streptomycin	6.25	6.25	3.12

Note: "-" indicates concentration > 50 μg/mL

Table 3: Pharmacokinetics of compounds 3a-3l and Erlotinib using pkCSM tool.

Entry	Water solubility log mol/L	Human Intestinal absorption HIA (%)	CYP2D6 inhibition
3a	-4.794	99.67	No
3b	-3.345	100	No
3c	-3.326	96.13	No
3d	-3.091	99.68	No
3e	-3.146	97.28	No
3f	-3.263	98.65	No
3g	-3.322	97.68	No
3h	-3.098	100	No
3i	-3.308	97.75	No
3j	-3.063	97.15	No
3k	-3.293	99.21	No
3l	-4.601	97.84	No
Erlotinib	-4.411	93.97	No

Table 4: Physicochemical properties of compounds 3a-3l and Erlotinib using SwissADME tool

Entry	M. wt (g/mol)	MLogP	No. of rotatable bonds	No. of HBA	No. of HBD	TPSA (Å²)	GI absorption
3a	297.31	3.14	1	4	0	51.81	High
3b	342.31	3.00	2	6	0	97.63	High
3c	365.31	3.97	2	7	0	51.81	High
3d	327.34	2.81	2	5	0	61.04	High
3e	313.31	2.58	1	5	1	72.04	High
3f	315.30	3.52	1	4	0	51.81	High
3g	376.21	3.75	1	4	0	51.81	High
3h	342.31	3.00	2	6	0	97.63	High
3i	331.76	3.64	1	4	0	51.81	High
3j	365.31	3.97	1	4	0	51.81	High
3k	311.34	3.37	1	4	0	51.81	High
3l	303.34	2.70	1	5	0	80.05	High
Erlotinib	393.44	1.62	10	6	1	74.73	High

Table 5: Pharmacokinetics of compounds 5a-5l and Erlotinib using pkCSM tool.

Entry	Water solubility log mol/L	Human Intestinal absorption HIA (%)	CYP2D6 inhibition
5a	-2.892	85.784	No
5b	-2.892	96.197	No
5c	-2.892	82.711	No
5d	-2.892	86.256	No
5e	-2.892	83.418	No
5f	-2.892	85.225	No
5g	-2.892	84.256	No
5h	-2.892	97.091	No
5i	-2.892	84.323	No
5j	-2.892	85.346	No
5k	-2.892	85.781	No
5l	-2.892	84.383	No
Erlotinib	-4.411	93.971	No

Table 6: Physicochemical properties of compounds 5a-5l and Erlotinib using SwissADME tool.

Entry	M. wt (g/mol)	MLogP	No. of rotatable bonds	No. of HBA	No. of HBD	TPSA (Å²)	GI absorption
5a	296.33	3.14	1	3	1	54.46	High
5b	341.32	3.00	2	5	1	100.28	High
5c	364.32	3.97	2	6	1	54.46	High
5d	326.35	2.81	2	4	1	63.69	High
5e	312.33	2.58	1	4	2	74.69	High
5f	314.32	3.52	1	3	1	54.46	High
5g	375.22	3.75	1	3	1	54.46	High
5h	341.32	3.00	2	5	1	100.28	High
5i	330.77	3.64	1	3	1	54.46	High
5j	364.32	3.97	2	6	1	54.46	High
5k	310.35	3.37	1	3	1	54.46	High
5l	302.35	2.70	1	3	1	82.70	High
Erlotinib	393.44	1.62	10	6	1	74.73	High

DISCUSSION

We discussed the Synthesis , anti-bacterial and, *in silico* studies of oxazolo[5,4-f] [1,8] naphthyridines 3a-l ,imidazole [5,4-f] [1,8] naphthyridine 5a-l The microwave vial sealed with caps and vials was subjected to Phenethyl Phenol Formaldehyde Resin Polyoxyethylene Ether is a non-ionic surfactant derived from a modified phenolic resin, combined with polyoxyethylene chains (10 mol%) with various aldehydes 2a-l and, 3-(oxazol-5-yl) quinolin-2-amine 1 to give 4-phenylbenzo[b]oxazolo[5,4-f] [1,8] naphthyridines 3a-l derivatives under microwave irradiation (300 Watt) at 100˚C for 10 min. with promising yields from Scheme-I and Fig.1 Similarly, aldehydes 2a-l with 3-(1H-imidazol-5-yl) quinolin-2-amine 4 to give 4-phenylbenzo[b] imidazole [5,4-f] [1,8] naphthyridine 5a-l Shown in Scheme-II and Fig.2. with excellent

yields of 80-90%. The title compounds 3a-3l & 5a-5l were tested for in vitro antibacterial activity against gram-positive bacterial strains *B. subtilis*, *S. aureus*, and *S. epidermidis* with streptomycin serving as a positive control The compounds minimum inhibitory concentrations (MICs) were indicated in μg/mL. 4f, 4g, and 4h demonstrated more efficient bacterial inhibitory action against B. subtilis, with MICs of 3.12, 3.12, and 1.56 μg/mL, respectively, whereas typical streptomycin MICs were 6.25 μg/mL. Compound 3h ,5h have showed more potent activity against *S. aureus*, with MIC value of 3.12 μg/mL, whereas compound 3f ,5f have shown equipotent activity against the *S. aureus*, with MIC value of 6.25 μg/mL. Compound 4k shown equipotent activity against *B. subtilis* and good activity against *S. aureus* with MIC values of 3.12 μg/mL and 6.25 μg/mL, and compounds 3e,5e,3i and 5i similarly demonstrated moderate activity against *B. subtilis* and *S. aureus* (with MIC values 6.25 μg/mL) in silico Swiss ADME (Table 4,6) and pkCSM (Table 3,5) Water solubility (log mol/L), Human Intestinal absorption HIA (%), CYP2D6 inhibition and MLogP, TPSA and GI absorption of 3a-3i & 5a-5l were calculated. *In silico* in silico SwissADME and pkCSM for the compounds 3a-3l, 5a-5l and Erlotinib drug using the standard.

CONCLUSION

We synthesized the microwave assisted synthesis of 4-phenylbenzo[b]oxazolo[5,4-f] [1,8] naphthyridines 3a-l & 4-phenylbenzo[b] imidazole [5,4-f] [1,8] naphthyridine 5a-l from series of aldehydes, 3-(oxazol-5-yl) quinolin-2-amine 1 /3-(1H-imidazol-5-yl) quinolin-2-amine 4 to yield promising yields, and also screened for anti-bacterial evaluation. Among them 3f, 3g, 5h, 5f, 5g, and 5h established more efficient bacterial inhibitory action against B. subtilis, with MICs of 3.12, 3.12, and 1.56 □g/mL, respectively, whereas typical streptomycin MICs were 6.25 □g/mL. Compound 3h and 5h have showed more potent activity against S. aureus, with MIC value of 3.12 □g/mL, whereas compound 3f and 5f has shown equipotent activity against the S. aureus, with MIC value of 6.25□□g/mL. Compound 3k and 5k shown equipotent activity against B. subtilis and good activity against S. aureus with MIC values of 3.12 □g/mL and 6.25 □g/mL, and also Physicochemical properties with SwissADME tool, Pharmacokinetics with pkCSM tool evaluated and correlation tables are mentioned.

ACKNOWLEDGEMENTS

Authors like to acknowledge management of the institute for providing facilities to carry out the work.

CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

REFERENCES

1. Antimicrobial Resistance. Available online: https://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance (on 27 February 2019).
2. Crofts T.S., Gasparrini A.J., Dantas G. (2017). Next-generation approaches to understand and combat the antibiotic resistome. Nat. Rev. Microbiol., 15: 422–434.
3. Kularkar A., Chaudhari S.D., Rohilla G., et al. (2023). An insight into mimic of photo-Fenton degradation of ciprofloxacin and tetracycline. Sep. Purif. Technol., 319: 124100.
4. Rohini R., Reddy P.M., Shanker K., Ravinder V. (2009). New mono, bis-2,2-(arylidineaminophenyl) benzimidazoles: synthesis and antimicrobial investigation. Acta Chim. Slov., 56:900–907.
5. Rohini R., Shanker K., Hu A. (2010). Synthesis of some new mono, bis-indolo[1,2-c] quinazolines: evaluation of their antimicrobial studies. J. Braz. Chem. Soc., 21: 897–904.
6. Akula M., Thigulla Y., Davis C., Bhattacharya A. (2015). Synthesis of 4-substituted oxazolo[4,5-c] quinolines by direct reaction at the C-4 position of oxazoles. Org. Biomol. Chem., 13: 2600–2605.
7. Ramesh P., Reddy C.S., Suresh Babu K., et al. (2015). Synthesis, characterization and molecular docking studies of novel 2-amino 3-cyano pyrano[2,3 H] chrysin derivatives. Med. Chem. Res., 24: 3696–3709.
8. Ramesh P., Rao V.S., Reddy P.M., et al. (2020). Synthesis, biological evaluation and molecular modeling studies of novel C (7)-modified analogues of chrysin. Lett. Drug Des. Discov., 17: 873–883.
9. Dhanavath R., Dharavath R., Kothula D., et al. (2022). Synthesis and biological evaluation of novel 2-arylquinoline-3-fused thiazolo[2,3-c] [1,2,4] triazole heterocycles. J. Heterocycl. Chem., 59: 1198–1212.
10. Reddy P.M., Huang Y.-S., Chen C.-T., et al. (2013). Evaluating the potential nonthermal microwave effects of microwave-assisted proteolytic reactions. J. Proteomics, 80: 160–170.
11. Chen C.-C., Reddy P.M., Devi C.S., Chang P.-C., Ho Y.-P. (2016). Study of microwave effects on the lipase-catalyzed hydrolysis. Enzyme Microb. Technol., 82: 164–172.
12. Clark J.H., Cullen S.R., Barlow S.J., Bastock T.W. (1994). Environmentally friendly chemistry using supported reagent catalysts: structure–property relationships for clayzic. J. Chem. Soc., Perkin Trans., *2*, 1994: 1117–1130.
13. Villemin D., Hammadi M. (1996). Environmentally desirable synthesis without use of organic solvent. Synthesis of aryloxy acetic acids. Synth. Commun., 26: 4337–4341.

14. Varma R.S., Dahiya R., Saini R.K. (1997). Iodobenzene diacetate on alumina: Rapid oxidation of alcohols to carbonyl compounds in solventless system using microwaves. *Tetrahedron Lett.*, 386: 7029–7032.
15. Daina A., Michielin O., Zoete V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci. Rep., 7: 42717.
16. Reddy N.N., Hung S.-J., Swamy M.K., et al. (2021). Synthesis and rational design of new appended 1,2,3-triazole–uracil ensembles via in silico VEGFR-2 inhibition. Molecules, 26: 1952.
17. Rondla R. (2018). Benzene centered tripodal imidazolium (BTI) system: Emerged towards multidisciplinary research and development. Inorg. Chim. Acta, 477: 183–191.
18. Rohini R., Rao L.S.P., Ramatenki V., et al. (2017). Benzene centered tripodal imidazolium (BTI) system: emerged towards multidisciplinary research and development. J. Mol. Struct., 1134: 482–491.
19. Shanker K., Reddy P.M., Rohini R., Ho Y.-P., Ravinder V. (2009). Encapsulation of Pd(II) by N_4 and N_2O_2 macrocyclic ligands: their use in catalysis and biology. J. Coord. Chem., 62: 3040–3049.
20. Reddy P., Ho Y.-P., Shanker K., et al. (2009). Physicochemical and biological characterization of novel macrocycles derived from o-phthalaldehyde. Eur. J. Med. Chem., 44: 2621–2625.
21. Reddy P.M., Shanker K., Srinivas V., et al. (2015). Hydrolysis of Letrozole catalyzed by macrocyclic Rhodium(I) Schiff-base complexes. Spectrochim. Acta A Mol. Biomol. Spectrosc., 139:43–48.
22. Thongolla R., Pulabala R., Gogula S.S., et al. (2024). Design, synthesis, and molecular docking studies of new phenanthrene-linked oxadiazoles as potential antimicrobial agents. J. Mol. Struct., 1300; 137260.
23. Gogula S.S., Prasanna D.V., Thumma V., et al. (2023). Efficient green synthesis, anticancer activity, and molecular docking studies of indolemethanes using a bioglycerol-based carbon sulfonic acid catalyst. ACS Omega, 8: 36401–36411.
24. Reddy P.M., Maurya N., Velmurugan B.K. (2019). Medicinal use of synthetic cannabinoids—a mini review. Curr. Pharmacol. Rep., 5: 1–13.
25. Ho Y.-P., Reddy P.M. (2011). Advances in mass spectrometry for the identification of pathogens. Mass Spectrom. Rev., 30: 1203–1224.
26. Huang C.-Y., Ju D.-T., Chang C.-F., et al. (2017). A review on the effects of current chemotherapy drugs and natural agents in treating non-small cell lung cancer. Biomedicine, 7, 23.
27. Reddy K.S., Siva B., Reddy S.D., et al. (2020). In situ FTIR spectroscopic monitoring of the formation of the arene diazonium salts and its applications to the Heck–Matsuda reaction. Molecules, 25: 2199.
28. . Akula M, Thigulla Y, Davis C, Bhattacharya A (2015). Synthesis of 4-substituted oxazolo [4, 5-c] quinolines by direct reaction at the C-4 position of oxazoles. Organic & Biomolecular Chemistry, 13: 2600-2605.