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New Schiff Base Derivatives of Norfloxacin with *s*-Triazole Core: Design, Computational Study and Antimicrobial Activity

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Norfloxacin, a fluoroquinolone, acts against many Gram-negative and Gram-positive bacteria by inhibiting DNA gyrase and topoisomerase IV, enzymes essential for DNA replication and repair. Despite many available antibiotics, antimicrobial resistance remains a major global health challenge, highlighting the need for new therapies. The present work focused on the synthesis of a new series of norfloxacin derivatives (**D13-D24**). Their structures were confirmed through IR, NMR, mass spectrometry and elemental analysis. The molecular docking studies of the synthesized compounds were carried out against targets 3FV5, 5IMW and 5ESE to evaluate possible binding interactions. Among the tested molecules, compound **D20** demonstrated notable antibacterial activity against Gram-positive *S. aureus*, while compound **D13** exhibited promising activity against Gram-negative *E. coli* along with appreciable antifungal efficacy against *S. cerevisiae*, compared with reference drugs norfloxacin and fluconazole. The antimicrobial potential was further assessed using zone of inhibition and minimum inhibitory concentration (MIC) studies.

Keywords: Norfloxacin, Fluconazole, DNA gyrase, Topoisomerase-IV, Docking studies.

INTRODUCTION

Norfloxacin is a synthetic antibacterial drug [1,2] classified under the fluoroquinolone group of antibiotics. It has been widely employed in the management of urinary tract infections, gynaecological infections, prostatitis, gonorrhoea and bladder associated infections [3-5]. Earlier quinolone agents, such as nalidixic acid, possessed comparatively lower antibacterial potency and were mainly prescribed for urinary tract infections because of their renal elimination and high urinary concentrations [6,7].

It was demonstrated that specific structural modifications, particularly the introduction of a fluorine atom into the quinolone nucleus, markedly improved antibacterial activity [8,9]. Although fluoroquinolones have been used in the treatment of typhoid and paratyphoid fever, norfloxacin has shown higher rates of clinical failure than several other agents in this class (417 participants, 5 trials) [10]. In ophthalmic practice, its approved use is mainly restricted to bacterial conjunctival infections caused by susceptible organisms [11]. Norfloxacin is also administered prophylactically to prevent spontaneous bacterial peritonitis in cirrhotic patients presenting with low ascitic fluid protein, renal dysfunction, advanced liver disease, previous spontaneous bacterial peritonitis or oesophageal variceal bleeding [12-15].

Staphylococcus aureus is an opportunistic, facultatively anaerobic, Gram-positive coccus commonly colonising human skin and mucosal surfaces and is well-known for its rapid adaptation to antibiotic pressure [16-18]. *Escherichia coli* is a Gram-negative, facultatively anaerobic, rod-shaped bacterium that normally inhabits the lower intestine of warm-blooded animals [19,20]. While many strains are harmless commensals, certain pathogenic serotypes are capable of causing severe foodborne illness and are frequently linked with food contamination events [21,22].

Norfloxacin exhibits broad-spectrum antibacterial activity against both Gram-positive and Gram-negative microorganisms. Its mechanism of action involves inhibition of bacterial DNA gyrase (topoisomerase II) and topoisomerase IV [23-25], enzymes essential for DNA replication, segregation and cell

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division [26,27]. Rather than directly binding to DNA gyrase alone, norfloxacin primarily stabilises the enzyme-DNA complex through interaction with substrate DNA [28]. Keeping these facts in mind, the present study aimed to design and synthesize new Schiff base derivatives of norfloxacin incorporating an *s*-triazole core, followed by structural characterization using spectral and analytical techniques. Furthermore, the synthesized compounds were evaluated through molecular docking and antimicrobial studies to identify potent candidates against bacterial and fungal pathogens.

EXPERIMENTAL

All reagents and solvents used in the present investigation were of analytical grade and employed without further purification unless otherwise specified. Norfloxacin intermediates and final Schiff base derivatives were synthesized using commercially available chemicals including substituted aromatic aldehydes, 3-chloro-4-fluoroaniline, diethyl ethoxymethylene malonate, benzene, aqueous sodium hydroxide, ethyl iodide, *N*,*N*-dimethylformamide (DMF), triethylamine, pyridine, piperazine, imidazole, hydrazine hydrate, carbon disulfide, ethanol, glacial acetic acid, *etc*.

Microwave-assisted synthesis was carried out using a domestic microwave reactor (Kenstar OM 20 DGQ) operated at controlled power levels ranging from 455 to 750 W. The melting points of the synthesized compounds were determined in open capillary tubes and are uncorrected. The reaction progress and purity were monitored by thin-layer chromatography (TLC) using suitable solvent systems on silica gel plates. Infrared spectra were recorded using ATR-FTIR spectroscopy. ^{1}H NMR spectra were obtained at 300 MHz using DMSO-d_6 as solvent and TMS as internal reference. Mass spectra were recorded using electrospray ionization mass spectrometry (ESI-MS).

Synthesis of ethyl 7-chloro-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylate (step-1): The intermediate was synthesized *via* a Gould-Jacobs reaction using equimolar amounts of 3-chloro-4-fluoroaniline (0.01 mol) and diethyl ethoxymethylene malonate (0.01 mol) under solvent-free conditions. The mixture was irradiated under microwave conditions at 540-750 W for 1.0-1.5 min, yielding a white to pale yellow semi-solid mass [29]. The product was washed with acetone, recrystallized from DMF and its purity confirmed by TLC using petroleum ether:chloroform:ether (85:15:5). Yield: 92%.

Synthesis of 7-chloro-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (step-2): The ethyl ester obtained in step-1 (2.7 g, 0.01 mol) was dissolved in benzene (50 mL) and hydrolysed with aqueous NaOH (5 N, 50 mL) to yield the corresponding carboxylic acid. The reaction mixture was refluxed with stirring for 5-6 h, during which a white solid precipitated. The precipitate was filtered, washed with water until neutral, dried and recrystallized from acetone to afford the purified product.

Synthesis of 7-chloro-1-ethyl-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid (N_1-substitution) (step-3): The product obtained from step-2 (0.01 mol) was suspended in DMF (10 mL), followed by the addition of ethyl iodide (0.01 mol). The mixture was heated to achieve dissolution, after which anhydrous potassium carbonate (0.02 mol) was added. The reaction mass was stirred at 120-140 ºC for 5-8 h. Upon completion, the mixture was poured onto crushed ice or ice-cold water, and the precipitated solid was washed with cold water to remove residual DMF and potassium carbonate. The crude product was recrystallized from acetone to afford the corresponding compound in 72% yield.

Synthesis of 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-R_7-substituted-quinoline-3-carboxylic acid (step-4): The product from step-3, 7-chloro-1-ethyl-6-fluoro-1,4-dihydro-4-oxo-quinolone-3-carboxylic acid (0.01 mol), was taken in pyridine (10 mL) with triethylamine (3 mL), followed by the addition of the appropriate heterocyclic amine, namely piperazine or imidazole (0.05 mol), in a double-necked round-bottom flask. The reaction mixture was subjected to microwave irradiation at 455 W for 6 min. After completion, the mixture was cooled to room temperature, poured onto crushed ice and neutralized with dilute HCl. The precipitated solid was filtered, washed, and dried to obtain the desired product.

Synthesis of 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-R_7 substituted quinoline-3-carbohydrazide (step-5): A mixture of the step-4 intermediate, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-R_7-substituted quinoline-3-carboxylic acid (20.0 g, 55.0 mmol) and 85% hydrazine hydrate (20.0 g, 340.0 mmol) was heated under reflux for 24 h. After completion of the reaction, the formed precipitate was collected by filtration and purified by recrystallization from 95% ethanol (100 mL). The desired product was obtained in 67% yield.

Synthesis of 1-ethyl-6-fluoro-3-(5-mercapto-1,3,4-oxadiazol-2-yl)-R_7 substituted quinoline-4(1*H*)-one (step-6): A mixture of the step-5 intermediate, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-R_7-substituted quinoline-3-carbohydrazide (10 g, 27.0 mmol) and carbon disulfide (3.1 g, 30.0 mmol) in 95% ethanol (150 mL) was refluxed for 10 h. After completion, the precipitated product was filtered and washed with anhydrous ethanol to afford the crude hydrazide carbodithioic acid derivative. The product was obtained in 72% yield.

Synthesis of 1-ethyl-6-fluoro-3-(4-amino-5-mercapto-*s*-triazole-3-yl)-R_7 substituted quinoline–4(1*H*)-one (step-7): The step-6 intermediate, 1-ethyl-6-fluoro-3-(5-mercapto-1,3,4-oxadiazol-2-yl)-R_7-substituted quinoline-4(1*H*)-one, was treated with a mixture of 85% hydrazine hydrate (20.0 g, 340.0 mmol) and 40% NaOH (3.0 g, 30.0 mmol), followed by refluxing for 12 h. After solvent removal, water (200 mL) and activated charcoal (0.5 g) were added and the suspension was further refluxed for 1 h. The charcoal was removed by filtration and the filtrate was adjusted to pH 8.0 using conc. HCl. The precipitated product was collected and recrystallized from DMF-ethanol to obtain the yellow solid in 72% yield.

Synthesis of title compounds (D_{13}-D_{24}): The mixture of product step-7 (1-ethyl-6-fluoro-3-(4-amino–5-mercapto–*s*-triazole-3-yl)-R_7 substituted quinoline-4(1*H*)-one) (1.0 g, 2.3 mmol) and various substituted aromatic aldehydes such as 4-nitro benzaldehyde (2.5 mmol), 4-bromo benzaldehyde (2.5 mmol), 4-fluoro benzaldehyde (2.5 mmol), 4-chloro benzaldehyde (2.5 mmol), 4-hydroxy benzaldehyde (2.5 mmol), 4-methyl benzaldehyde (2.5 mmol) in glacial acetic acid (15 mL) was added and the mixture heated under reflux for 24 h

(**Scheme-I**). After removal of the solvent under reduced pressure, the residue was dissolved in DMF-ethanol and the resulting Schiff base precipitate of compound **D13-D24** were collected.

1-Ethyl-6-fluoro-3-(5-mercapto-4-((4-nitrobenzylidene)-amino)-4*H*-1,2,4-triazole-3-yl)-7-(piperazin-1-yl)quinolin-4(1*H*)-one (D13): Yield: 78.4%; IR (ATR, ν_{max}, cm^{-1}): 3399 (NH_2), 3080 (C–H, arom.), 2926 (C–H, aliph.), 1709 (C=O, quinolone carbonyl), 1628 (C=N, azomethine/triazole) + (C=C, arom.), 1505 (NO_2, asymm.), 1346 (NO_2, sym.), 1197 (C–F), 1250-1100 (C–N, piperazine), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.5 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 7.0-8.5 (m, aromatic protons), 8.45 (s, 1H, CH=N). MS-ESI: *m/z* 522.16 (M+1). Elemental analysis of $C_{24}H_{23}FN_8O_3S$: calcd. (found) %: C, 55.16 (55.38); H, 4.44 (4.28); F, 3.64 (3.86); N, 21.44 (21.12); O, 9.18 (9.46); S, 6.14 (5.92).

3-(4-((4-Bromobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-1-ethyl-6-fluoro-7-(piperazin-1-yl)quinolin-4(1H)-one (D14): Yield: 82.1%; IR (ATR, ν_{max}, cm^{-1}): 3419 (NH_2), 3048 (C–H, arom.), 2941 (C–H, aliph.), 1713 (C=O, quinolone carbonyl), 1626 (C=N, azomethine/ triazole) + (C=C, arom.), 1250-1100 (C–N, piperazine), 1300-1000 (C–F), 1220-1050 (C–S), 493 (C–Br); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.5 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 7.0-8.5 (m, aromatic protons), 8.50 (s, 1H, CH=N). MS-ESI: *m/z* 555.09 (M+1). Elemental analysis of $C_{24}H_{23}BrFN_7OS$: calcd. (found) %: C, 51.80 (52.08); H, 4.17 (3.95); Br, 14.36 (14.62); F, 3.41 (3.19); N, 17.62 (17.30); O, 2.88 (3.12); S, 5.76 (5.52).

1-Ethyl-6-fluoro-3-(4-((4-fluorobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-7-(piperazin-1-yl)quinolin-4(1*H*)-one (D15): Yield: 78.6%; IR (ATR, ν_{max}, cm^{-1}): 3436 (NH_2), 3067 (C–H, arom.), 2960-2920 (C–H, aliph.), 1692 (C=O, quinolone carbonyl), 1616 (C=N, azomethine/ triazole) + (C=C, arom.), 1250-1100 (C–N, piperazine), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5–3.5 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 7.0-8.5 (m, aromatic protons), 8.40 (s, 1H, CH=N). MS-ESI: *m/z* 495.17 (M+1); Elemental analysis of $C_{24}H_{23}F_2N_7OS$: calcd. (found) %: C, 58.17 (58.42); H, 4.68 (4.46); F, 7.67 (7.93); N, 19.79 (19.48); O, 3.23 (3.45); S, 6.47 (6.23).

3-(4-((4-Chlorobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-1-ethyl-6-fluoro-7-(piperazin-1-yl)-quinolin-4(1*H*)-one (D16): Yield: 81.3%; IR (ATR, ν_{max}, cm^{-1}): 3360 (NH_2), 3059 (C–H, arom.), 2923 (C–H, aliph.), 1690 (C=O, quinolone carbonyl), 1620-1600 (C=N, azomethine/ triazole) + (C=C, arom.), 1250-1100 (C–N, piperazine), 1400-1000 (C–F), 1220-1050 (C–S), 606 (C–Cl); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.5 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 7.0-8.5 (m, aromatic protons), 8.45 (s, 1H, CH=N). MS-ESI: *m/z* 511.14 (M+1). Elemental analysis of: $C_{24}H_{23}ClFN_7OS$: calcd. (found) %: C, 56.30 (56.58); H, 4.53 (4.31); Cl, 6.92 (7.18); F, 3.71 (3.47); N, 19.15 (18.83); O, 3.12 (3.36); S, 6.26 (6.02).

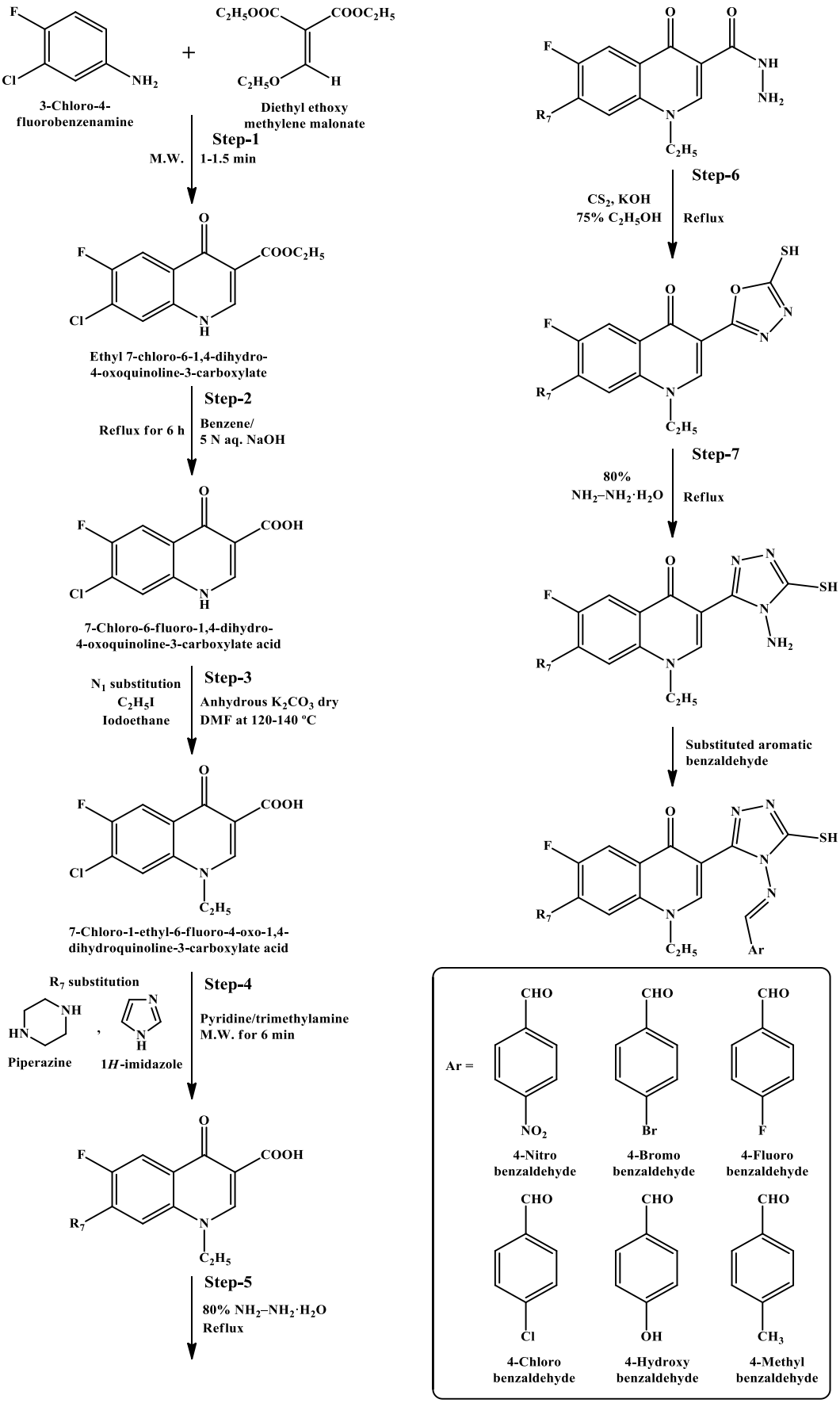
1-Ethyl-6-fluoro-3-(4-((4-hydroxybenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-7-(piperazin-1-yl)quinolin-4(1*H*)-one (D17): Yield: 69.5%; IR (ATR, ν_{max}, cm^{-1}): 3400-3278 (NH_2), 3249 (O–H, phenolic, br.), 3020 (C–H, arom.), 2938 (C–H, aliph.), 1690 (C=O, quino-lone carbonyl), 1620-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, piperazine), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.5 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 7.0–8.5 (m, aromatic protons), 8.40 (s, 1H, CH=N), 10.9 (s, 1H, OH). MS-ESI: *m/z* 493.17 (M+1). Elemental analysis of $C_{24}H_{24}FN_7O_2S$: calcd. (found) %: C, 58.40 (58.66); H, 4.90 (4.68); F, 3.85 (4.07); N, 19.87 (19.55); O, 6.48 (6.74); S, 6.50 (6.26).

1-Ethyl-6-fluoro-3-(5-mercapto-4-((4-methylbenzylidene)amino)-4*H*-1,2,4-triazole-3-yl)-7-(piperazin-1-yl)quinolin-4(1*H*)-one (D18): Yield: 74.2%; IR (ATR, ν_{max}, cm^{-1}): 3488 (NH_2), 3160 (C–H, arom.), 2906 (C–H, aliph.), 1680 (C=O, quinolone carbonyl), 1620-1600 (C=N, azo-methine/triazole) + (C=C, arom.), 1100–1250 (C–N, pipera-zine), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, CH_3–CH_2–), 4.10 (q, 2H, CH_3–CH_2–), 2.60–3.50 (m, 8H, piperazine CH_2), 3.00 (s, 1H, SH), 2.30 (s, 3H, Ar–CH_3), 6.50–8.20 (m, aromatic protons), 8.35 (s, 1H, CH=N); MS-ESI: *m/z* 491.19 (M+1). Elemental analysis of $C_{25}H_{26}FN_7OS$: calcd. (found) %: C, 61.08 (61.36); H, 5.33 (5.11); F, 3.86 (4.10); N, 19.95 (19.63); O, 3.25 (3.49); S, 6.52 (6.28).

1-Ethyl-6-fluoro-7-(1*H*-imidazol-1-yl)-3-(5-mercapto-4-((4-nitrobenzylidene)amino)-4*H*-1,2,4-triazole-3-yl)quinolin-4(1*H*)-one (D19): Yield: 84.5%; IR (ATR, ν_{max}, cm^{-1}): 3407 (NH_2), 3102 (C–H, arom.), 2957 (C–H, aliph.), 1685 (C=O, quinolone carbonyl), 1620-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1520 (NO_2, asymm.), 1322 (NO_2, symmetric), 1250-1100 (C–N, imidazole), 1000–1400 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5–3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 6.8-8.4 (m, aromatic protons), 8.50 (s, 1H, CH=N). MS-ESI: *m/z* 504.11 (M+1). Elemental analysis of $C_{23}H_{17}FN_8O_3S$: calcd. (found) %: C, 54.76 (55.02); H, 3.40 (3.18); F, 3.77 (4.01); N, 22.21 (21.89); O, 9.51 (9.77); S, 6.35 (6.11).

3-(4-((4-Bromobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-1-ethyl-6-fluoro-7-(1*H*-imidazol-1-yl)-quinolin-4(1*H*)-one (D20): Yield: 79.2%; IR (ATR, ν_{max}, cm^{-1}): 3428 ((NH_2), 3060 (C–H, arom.), 2960 (C–H, aliph.), 1720 (C=O, quinolone carbonyl), 1635-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, imidazole), 1400-1000 (C–F), 1220-1050 (C–S), 488 (C–Br); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5–3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 6.8–8.4 (m, aromatic protons), 8.45 (s, 1H, CH=N) MS-ESI: *m/z* 537.04 (M+1). Elemental analysis of $C_{23}H_{17}BrFN_7OS$: calcd. (found) %: C, 51.31 (51.58); H, 3.18 (2.96); Br, 14.84 (15.10); F, 3.53 (3.29); N, 18.21 (17.89); O, 2.97 (3.21); S, 5.95 (5.71).

1-Ethyl-6-fluoro-3-(4-((4-fluorobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-7-(1*H*-imidazol-1-yl)-quinolin-4(1*H*)-one (D21): Yield: 73.6%; IR (ATR,



Scheme-I: Synthesis of (**D13-D24**) derivatives of norfloxacin

ν_{max}, cm^{-1}): 3445 (NH_2), 3058 (C–H, arom.), 2960-2920 (C–H, aliph.), 1705 (C=O, quinolone carbonyl), 1640-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, imidazole), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 6.8-8.4 (m, aromatic protons), 8.40 (s, 1H, CH=N); MS-ESI: *m/z* 477.12 (M+1). Elemental analysis of $C_{23}H_{17}F_2N_7OS$: calcd. (found) %: C, 57.85 (58.12); H, 3.59 (3.37); F, 7.96 (8.20); N, 20.53 (20.21); O, 3.35 (3.59); S, 6.71 (6.47).

3-(4-((4-Chlorobenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-1-ethyl-6-fluoro-7-(1*H*-imidazol-1-yl)-quinolin-4(1*H*)-one (D$_{22}$): Yield: 80.7%; IR (ATR, ν_{max}, cm^{-1}): 3372 (NH_2), 3128 (C–H, arom.), 2960-2920 (C–H, aliph.), 1692 (C=O, quinolone carbonyl), 1620-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, imidazole), 1000–1400 (C–F), 1050–1220 (C–S), 630 (C–Cl). ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 6.8-8.4 (m, aromatic protons), 8.45 (s, 1H, CH=N). MS-ESI: *m/z* 493.09 (M+1). Elemental analysis of $C_{23}H_{17}ClFN_7OS$: calcd. (found) %: C, 55.93 (56.20); H, 3.47 (3.25); Cl, 7.18 (7.44); F, 3.85 (3.61); N, 19.85 (19.53); O, 3.24 (3.48); S, 6.49 (6.25).

1-Ethyl-6-fluoro-3-(4-((4-hydroxybenzylidene)amino)-5-mercapto-4*H*-1,2,4-triazole-3-yl)-7-(1*H*-imidazol-1-yl)-quinolin-4(1*H*)-one (D$_{23}$): Yield: 67.4%; IR (ATR, ν_{max}, cm^{-1}): 3400-3295 (NH_2), 3268 (O–H, phenolic, br.), 3128 (C–H, arom.), 2932 (C–H, aliph.), 1738 (C=O, quinolone carbonyl), 1620-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, imidazole), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 6.8-8.4 (m, aromatic protons), 8.40 (s, 1H, CH=N), 10.9 (s, 1H, OH). MS-ESI: *m/z* 475.12 (M+1). Elemental analysis of $C_{23}H_{18}FN_7O_2S$: calcd. (found) %: C, 58.10 (58.38); H, 3.82 (3.60); F, 4.00 (4.24); N, 20.62 (20.30); O, 6.73 (6.99); S, 6.74 (6.50).

1-Ethyl-6-fluoro-7-(1*H*-imidazol-1-yl)-3-(5-mercapto-4-((4-methylbenzylidene)amino)-4*H*-1,2,4-triazole-3-yl)-quinolin-4(1*H*)-one (D$_{24}$): Yield: 75.9%; IR (ATR, ν_{max}, cm^{-1}): 3460 (NH_2), 3180 (C–H, arom.), 2914 (C–H, aliph.), 1698 (C=O, quinolone carbonyl), 1620-1600 (C=N, azomethine/triazole) + (C=C, arom.), 1250-1100 (C–N, imidazole), 1400-1000 (C–F), 1220-1050 (C–S); ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm): 1.20 (t, 3H, $J \approx 7$ Hz, CH_3), 4.10 (q, 2H, $J \approx 7$ Hz, CH_2), 2.5-3.2 (m, imidazole protons), 3.00 (s, 1H, SH), 2.30 (s, 3H, Ar–CH_3), 6.8-8.4 (m, aromatic protons), 8.35 (s, 1H, CH=N); MS-ESI: *m/z* 473.14 (M+1). Elemental analysis of $C_{24}H_{20}FN_7OS$: calcd. (found) %: C, 60.88 (61.16); H, 4.47 (4.04); F, 4.01 (4.25); N, 20.71 (20.39); O, 3.38 (3.62); S, 6.77 (7.04).

Antimicrobial activity: All synthesized title compounds (**D$_{13}$-D$_{24}$**) were evaluated for their antimicrobial potential. The antibacterial activity was assessed against Gram-positive strains, *Staphylococcus aureus* ATCC 6438P and *Staphylococcus epidermidis* ATCC 155 as well as Gram-negative strains, *Escherichia coli* ATCC 25922 and *Klebsiella pneumoniae* ATCC 29665, using nutrient agar medium. The antifungal activity was examined against *Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC 46645 on Sabouraud dextrose agar. Preliminary screening was carried out by the paper disc diffusion technique, while minimum inhibitory concentration (MIC) values were determined using the agar streak dilution method.

Paper disc diffusion technique: The sterilized medium (autoclaved at 120 ºC for 30 min) was cooled to 40-50 ºC and inoculated with microbial suspension (1 mL/100 mL medium) containing approximately 10^5 CFU/mL, adjusted to the McFarland barium sulphate standard. The inoculated medium was poured into Petri dishes to obtain a uniform depth of 3-4 mm. Sterile paper discs impregnated with test compounds (100 µg/mL in DMF) were placed on the solidified agar surface. The plates were allowed to pre-diffuse at room temperature for 1 h, followed by incubation at 37 ºC for 24 h for antibacterial studies and 48 h for antifungal studies [30]. All assays were conducted in triplicate for each compound and micro-organism. Zones of inhibition were measured using a digital caliper and the results were expressed as mean ± standard deviation (SD, n = 3). Norfloxacin (100 µg/disc) and ketoconazole (100 µg/disc) were employed as standard drugs for antibacterial and antifungal evaluation, respectively.

Minimum inhibitory concentration (MIC): The MIC of the synthesized compounds (**D$_{13}$-D$_{24}$**) was determined by the agar streak dilution method [31]. A stock solution of each test compound (100 µg/mL) was prepared in DMF and appropriate graded concentrations were incorporated into molten sterile agar medium, using nutrient agar for antibacterial studies and Sabouraud dextrose agar for antifungal studies. The prepared medium (40-50 ºC) was poured into Petri dishes to a uniform depth of 3-4 mm and allowed to solidify. The microbial suspensions containing approximately 10^5 CFU/mL were then streaked onto the agar plates containing serial dilutions of the test compounds and incubated at 37 ºC for 24 h for bacteria and 48 h for fungi. The MIC value was defined as the lowest concentration of the compound that completely inhibited visible microbial growth. All determinations were carried out in triplicate for each compound and test organism. The reported MIC values represent the most reproducible results, with variation between replicates limited to one dilution step.

Molecular docking studies: Molecular docking studies of synthesised title compounds **D$_{13}$-D$_{24}$** with well-established structures of *S. aureus* and *E. coli* were performed using Auto Dock vina 1.12 version and chimera 1.12 version [32]. The binding pocket of the active site of DNA gyrase (PDB: 5IWM) for Gram-positive bacteria such as *S. aureus*, topo-isomerase-IV (PDB:3FV5) for Gram-negative bacteria such as *E. coli* and lanosterol-14-alpha demethylase (PDB:5ESE) for fungal-like *Saccharomyces cerevisiae*. The docking method includes the following steps. First, the ligand molecule was constructed, in the second step, the required protein was downloaded from PDB and the macromolecule was prepared and validated by X-ray crystallography. The third step is to identify binding affinity based on the extent to which the ligand binds to the protein of the molecule.

RESULTS AND DISCUSSION

The introduction of the 1,2,4-triazole ring and arylidene Schiff base at the C-3 position of the norfloxacin core was guided by structure–activity relationships of triazole-based antimicrobial agents. 1,2,4-Triazole scaffold is a nitrogen rich heterocycle that enhances antimicrobial activity by providing additional hydrogen bond donors and acceptors, as well as π-electron density for interactions with bacterial enzymes such as DNA gyrase and topoisomerase IV. In the synthesised series **D_{13}-D_{24}**, the triazole-mercapto unit and the *para*-substituted benzylidene moiety increase conjugation, lipophilicity and molecular polarizability, which may improve membrane permeability and strengthen hydrophobic and π–π interactions within the enzyme binding pocket, as supported by docking results. The enhanced antibacterial activity observed for nitro- and halogen-substituted derivatives (*e.g.* **D_{13}**, **D_{19}-D_{22}**) is consistent with the role of electron-withdrawing substituents in improving binding affinity and biological activity. Moreover, Schiff base moieties can form strong hydrogen bonds and act as ligands for biological targets, thereby enhancing antimicrobial activities.

The IR spectra of **D_{13}-D_{24}** are consistent with the proposed structures. Each derivative displays a broad N–H/NH_2 stretching band in the 3490-3270 cm^{-1} region and aromatic C–H stretches at 3080-3020 cm^{-1}, together with aliphatic C–H bands at 2960-2850 cm^{-1} arising from the ethyl and other alkyl substituents. The quinolone-4-one carbonyl appears as a strong band at 1720-1680 cm^{-1}, in the typical region for conjugated amide/carbonyl systems. The azomethine C=N and triazole ring C=N functionalities give medium-to-strong absorptions around 1640-1600 cm^{-1}, overlapping with aromatic C=C stretching vibrations, as reported for related Schiff bases and triazole derivatives [33]. For nitro-substituted compounds (**D_{13}**, **D_{19}**), the characteristic asymmetric and symmetric NO_2 bands are observed near 1550-1500 cm^{-1} and 1350-1320 cm^{-1}, respectively. The C–F stretching bands of the fluoroquinolone core appear in the 1400-1000 cm^{-1} region, while C–N stretches of piperazine or imidazole moieties are observed mainly between 1020 and 1300 cm^{-1}. The C–S/thiocarbonyl region shows bands in the 1225-1025 cm^{-1} region, consistent with thiocarbonyl and C–S stretching in conjugated systems [34]. In the halo-aryl deri-vatives, C–Cl and C–Br stretching bands are clearly observed in the 800-600 cm^{-1} and 600-500 cm^{-1} region, respectively, which further support the formation of the targeted quinoline-triazole Schiff base derivatives.

The ^{1}H NMR spectra of compounds **D_{13}-D_{24}** are also in agreement with the proposed structures. In all derivatives, the N-ethyl group of the quinolone nucleus appears as a triplet at δ ≈ 1.0-1.4 ppm (3H, CH_3, J ≈ 7 Hz) and a quartet or multiplet at δ ≈ 3.8-4.5 ppm (2H, CH_2, J ≈ 7 Hz), consistent with an ethyl fragment attached to nitrogen. The piperazinyl or imidazolyl methylene protons resonate as multiplets in the δ 2.5-3.8 ppm region with the expected total integration for each heterocycle. Aromatic protons of the quinolone core and benzylidene phenyl ring(s) appear as multiplets and doublets between δ 7.0 and 8.5 ppm with *para*-substituted phenyl rings showing the characteristic AA′ BB′ pattern (two doublets, 2H each). In all Schiff base derivatives, a diagnostic azomethine proton (-CH=N-) is observed as a singlet in the δ 8.8-9.3 ppm region. In hydroxyl-substituted derivatives (**D_{17}**, **D_{23}**), a downfield broad singlet at δ ≈ 10-11 ppm is attributed to the phenolic -OH, while in all compounds the thiol (SH) signal appears as a singlet.

Antibacterial activity: All the synthesised title compounds exhibited mild to moderate activity against both Gram-positive (*S. aureus* and *S. epidermidis*) and Gram-negative (*E. coli* and *K. pneumonia*) bacteria. Compounds **D_{13}**, **D_{19}**, **D_{20}**, **D_{22}** and **D_{21}** were found to possess significant antibacterial activity against Gram-positive organisms compared to the standard drug (norfloxacin) and had MIC values in the range of 0.8-3.9 μg/mL. Compounds **D_{13}**, **D_{14}**, **D_{15}**, **D_{16}** and **D_{17}** were found to possess significant antibacterial activity against Gram-negative organisms compared to the standard drug (norfloxacin) and had MIC values in the range of 0.7-4.8 μg/mL (Table-1). Compound **D_{20}** exhibited mild antibacterial activity compared to standard norfloxacin (0.6 μg/mL) with MIC value in the range of 0.7 μg/mL. This mild antibacterial activity may be due to the addition of a new bromobenzylidene group at third position of the triazole ring. Compound **D_{13}** exhibited mild Gram-negative antibacterial compared to standard norfloxacin (0.07 μg/mL) with MIC values in the range of (0.7 μg/mL). This mild antibacterial activity may be due to the addition of a nitrobenzylidene group at 3rd position of the triazole ring.

Antifungal activity: All the synthesised title compounds **D_{13}-D_{24}** were tested against two fungal organisms (*A. niger* and *A. fumigatus*) based on the zone of inhibition and MIC values. All compounds exhibited good activity and the results are expressed as mean ± SD (n = 3) (Table-1). Compounds **D_{13}**, **D_{18}**, **D_{14}**, **D_{15}** and **D_{19}** showed comparatively higher antifungal activity against *A. niger* compared to the standard ketaconazole. Compounds **D_{13}**, **D_{18}** and **D_{14}** were found to possess significant antifungal activity against *A. fumigatus* compared to the standard drug ketoconazole. The synthesised compounds exhibited MIC values in the range of 10.9-16.2 μg/mL. Compound **D_{13}** exhibited mild antifungal activity with MIC values of 10.9 μg/mL and 11.5 μg/mL compared to standard ketoconazole 10.8 μg/mL and 11.4 μg/mL. This mild antifungal activity may be due to the addition of a newly derived nitrobenzylidene group at 3rd position of the triazole ring.

Docking study: Molecular docking studies were carried out to evaluate the synthesized compounds (**D_{13}-D_{24}**) and identify structural features influencing antibacterial activity. The docking results indicated stronger predicted binding affinities for several derivatives than the standard drug norfloxacin, suggesting their potential as promising antibacterial candidates. Among all docked compounds **D_{19}**, **D_{20}** and **D_{22}** show good binding affinity and interaction with topoisomerase-II DNA gyrase enzyme (5IWM) compared to the standard drug norfloxacin.

Compound **D_{20}** has a higher docking score (-9.1 kcal/mol) against the bacterial *S. aureus* than standard drug norfloxacin (-7.5 kcal/mol) as shown in Fig. 1a. The enhanced docking score may be attributed to the introduction of the bromobenzylidene

TABLE-1
ANTIMICROBIAL ACTIVITY OF SYNTHESISED COMPOUNDS **D_{13}-D_{24}** (100 µg/disc)

Compounds	*In vitro* activity - Zone of inhibition, mm (MIC, µg/mL)					
	Gram-positive bacteria		Gram-negative bacteria		Fungi	
	S. aureus	*S. epidermidis*	*E. coli*	*K. pneumoniae*	*A. niger*	*A. fumigatus*
D_{13}	30.0 ± 0.66 (0.9)	30.0 ± 0.73 (1.0)	36.0 ± 0.58 (0.7)	37.0 ± 0.66 (0.8)	29.0 ± 0.93 (10.9)	33.0 ± 1.02 (11.5)
D_{14}	26.0 ± 0.81 (2.9)	25.0 ± 0.92 (3.9)	33.0 ± 0.61 (0.8)	34.0 ± 0.71 (3.9)	27.0 ± 1.06 (11.1)	31.0 ± 0.96 (11.0)
D_{15}	26.0 ± 0.70 (1.3)	26.0 ± 0.85 (2.6)	35.0 ± 0.53 (0.7)	36.0 ± 0.62 (3.4)	27.0 ± 1.12 (11.2)	30.0 ± 1.08 (11.2)
D_{16}	23.0 ± 0.94 (2.8)	23.0 ± 1.08 (3.4)	34.0 ± 0.62 (0.8)	36.0 ± 0.49 (4.2)	18.0 ± 1.23 (13.6)	20.0 ± 1.32 (15.2)
D_{17}	28.0 ± 0.77 (1.8)	29.0 ± 0.63 (1.6)	32.0 ± 0.77 (0.9)	33.0 ± 0.86 (3.4)	26.0 ± 1.17 (14.1)	23.0 ± 1.23 (16.2)
D_{18}	25.0 ± 0.87 (1.4)	21.0 ± 0.93 (2.9)	18.0 ± 0.87 (1.4)	21.0 ± 1.14 (2.8)	28.0 ± 0.96 (11.0)	32.0 ± 1.07 (11.1)
D_{19}	31.0 ± 0.68 (0.8)	31.0 ± 0.76 (0.9)	21.0 ± 1.05 (1.5)	19.0 ± 1.03 (2.6)	26.0 ± 1.09 (11.5)	30.0 ± 1.13 (11.3)
D_{20}	33.0 ± 0.58 (0.7)	32.0 ± 0.47 (0.5)	26.0 ± 1.02 (2.5)	25.0 ± 1.07 (4.8)	22.0 ± 1.21 (13.9)	20.0 ± 1.22 (14.6)
D_{21}	29.0 ± 0.71 (1.0)	29.0 ± 0.84 (1.2)	29.0 ± 0.92 (1.9)	24.0 ± 0.94 (3.9)	25.0 ± 1.20 (14.7)	26.0 ± 1.31 (15.1)
D_{22}	32.0 ± 0.69 (0.8)	31.0 ± 0.57 (0.7)	26.0 ± 1.13 (2.3)	25.0 ± 1.04 (4.5)	27.0 ± 1.15 (13.2)	29.0 ± 1.25 (14.3)
D_{23}	28.0 ± 0.97 (1.9)	27.0 ± 1.12 (2.6)	26.0 ± 0.98 (1.8)	26.0 ± 0.88 (3.5)	25.0 ± 0.97 (14.4)	25.0 ± 0.98 (15.6)
D_{24}	24.0 ± 0.88 (1.6)	22.0 ± 0.93 (1.8)	19.0 ± 0.61 (1.3)	21.0 ± 0.67 (3.6)	25.0 ± 0.88 (13.2)	25.0 ± 1.10 (14.9)
Norfloxacin	36.0 ± 0.44 (0.6)	35.0 ± 0.36 (0.13)	35.0 ± 0.26 (0.07)	36.0 ± 0.28 (0.06)	–	–
Ketoconazole	–	–	–	–	29.0 ± 0.81 (10.8)	33.0 ± 0.90 (11.4)
DMF	–	–	–	–	–	–

Zone of inhibition (mm) and MIC (µg/mL) values are given as mean ± SD (n = 3). Norfloxacin and ketoconazole served as standards, while DMF was used as control.

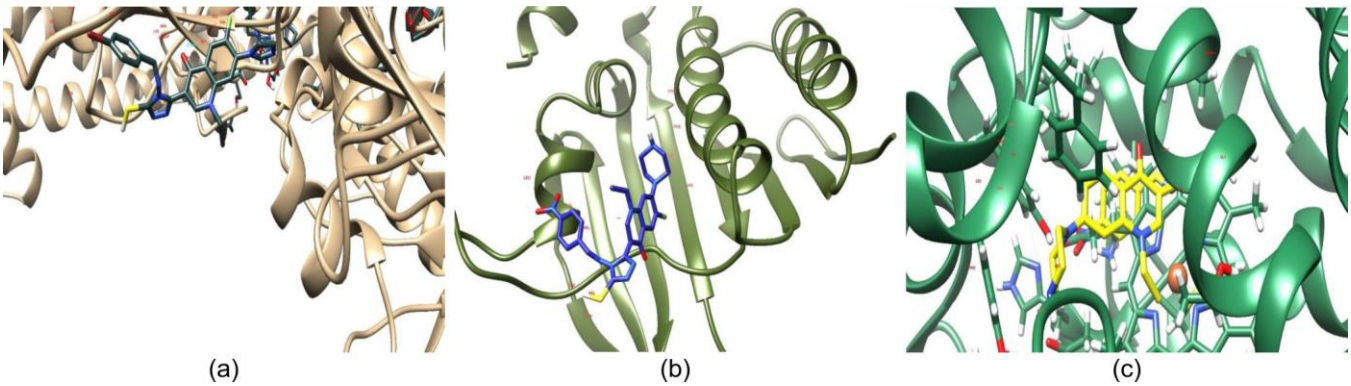


Fig. 1. Hydrogen-bond interactions of the synthesized compounds with selected microbial target enzymes: (a) compound **D_{20}** with topoisomerase II DNA gyrase of Gram-positive *S. aureus* (5IWM); (b) compound **D_{13}** with topoisomerase IV of Gram-negative *E. coli* (3FV5); and (c) compound **D_{13}** with lanosterol 14-α-demethylase of *S. cerevisiae* (5ESE)

substituent at the 3-position of the triazole ring in the norfloxacin scaffold. Docking scores of the remaining synthesized compounds are presented in Table-1.

In Gram-negative bacterial docking studies, compounds **D_{13}**, **D_{15}**, **D_{16}**, **D_{14}** and **D_{17}** exhibited favourable binding affinity and significant interactions with topoisomerase IV (3FV5) compared with norfloxacin. Among them, compound **D_{13}** showed the highest binding score (-7.7 kcal/mol) against *E. coli*, exceeding that of norfloxacin (-7.0 kcal/mol), as shown in Fig. 1b. The enhanced affinity may be associated with the presence of a nitrobenzylidene substituent at the 3-position of the triazole ring. The docking scores of the remaining compounds are listed in Table-1.

In fungal docking studies, compounds **D_{13}**, **D_{18}**, **D_{14}**, **D_{15}** and **D_{19}** showed favourable binding affinity and notable interactions with lanosterol 14-α-demethylase (PDB: 5ESE) compared with fluconazole. Compound **D_{13}** exhibited the highest docking score (-9.9 kcal/mol) against *S. cerevisiae*, surpassing fluconazole (-7.5 kcal/mol), as shown in Fig. 1c. The enhanced affinity may be attributed to the presence of a nitrobenzylidene substituent at the third position of the triazole ring. The docking scores of the remaining compounds are listed in Table-2.

Conclusion

In this work, 12 new Schiff base derivatives of norfloxacin with *s*-triazole moiety (**D_{13}-D_{24}**) were successfully synthesised and structurally characterized. All the compounds were evaluated through molecular docking against topoisomerase II (DNA gyrase), topoisomerase IV and lanosterol 14-α-demethylase to predict their antimicrobial potential. Docking analysis identified compounds **D_{19}**, **D_{20}** and **D_{22}** as promising candidates against Gram-positive bacteria, **D_{13}**, **D_{14}** **D_{15}**, **D_{16}**, and **D_{17}** against Gram-negative bacteria, and **D_{13}**, **D_{14}**, **D_{15}**, **D_{18}** and **D_{19}** against fungal pathogens. *In vitro* antimicrobial studies revealed moderate to significant activity among several derivatives. Compounds **D_{13}**, **D_{19}**, **D_{20}**, **D_{21}** and **D_{22}** showed notable activity against Gram-positive strains, while **D_{13}**, **D_{14}**, **D_{15}**, **D_{16}** and **D_{17}** were more effective against Gram-negative organisms. In antifungal screening, compounds **D_{13}**, **D_{14}**, **D_{15}**,

TABLE-2
DOCKING RESULT OF
SYNTHESISED COMPOUNDS (D_{13}-D_{24})

Compounds	Gram-positive bacteria (*S. aureus*)	Gram-negative bacteria (*E. coli*)	Fungi (*S. cerevisiae*)
D_{13}	-7.6	-7.7	-9.9
D_{14}	-8.1	-7.5	-9.5
D_{15}	-8.0	-7.6	-9.4
D_{16}	-8.1	-7.6	-9.1
D_{17}	-7.9	-7.5	-9.2
D_{18}	-7.4	-7.5	-9.6
D_{19}	-8.6	-6.6	-9.4
D_{20}	-9.1	-6.6	-9.2
D_{21}	-7.8	-6.8	-9.2
D_{22}	-9.0	-6.7	-9.3
D_{23}	-7.8	-7.3	-9.3
D_{24}	-8.0	-6.7	-9.4
Norfloxacin[a]	-7.5	-7.0	–
Fluconazole[b]	–	–	-7.5

[a]Norfloxacin: Standard antibacterial drug, [b]Fluconazole: Standard antifungal drug.

D_{18} and **D_{19}** demonstrated significant activity. The experimental findings in this study were in reasonable agreement with the docking results, particularly for *S. cerevisiae* and *S. aureus*.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

DECLARATION OF AI-ASSISTED TECHNOLOGIES

During the preparation of this manuscript, the authors used an AI-assisted tool(s) to improve the language. The authors reviewed and edited the content and take full responsibility for the published work.

REFERENCES

1. M.S. Refat, W.F. El-Hawary and M.A. Mohamed, *J. Mol. Struct.*, **1013**, 45 (2012); https://doi.org/10.1016/j.molstruc.2011.12.010
2. H.H.H. Mohammed, G.E.-D.A.A. Abuo-Rahma, S.H. Abbas and E.-S.M.N. Abdelhafez, *Curr. Med. Chem.*, **26**, 3132 (2019); https://doi.org/10.2174/0929867325666180214122944
3. A. Khanna, N. Kumar, R. Rana, J. Jyoti, A. Sharma, M. Muskan, H. Kaur and P.M.S. Bedi, *Bioorg. Chem.*, **153**, 107773 (2024); https://doi.org/10.1016/j.bioorg.2024.107773
4. D. Thompson, J. Xu, J. Ischia and D. Bolton, *BJUI Compass*, **5**, 5 (2024); https://doi.org/10.1002/bco2.286
5. S. Goenka, W. D. Wanswet, A. Sharma, P. Loomba, M. Jain and S. Tyagi, *Perspect. Med. Res.*, **13**, 208 (2025); https://doi.org/10.47799/pimr.1303.25.18
6. T.D.M. Pham, Z.M. Ziora and M.A.T. Blaskovich, *Med. Chem. Commun.*, **10**, 1719 (2019); https://doi.org/10.1039/C9MD00120D
7. C.F. Rodrigues and F. Silva, *Pathogens*, **14**, 525 (2025); https://doi.org/10.3390/pathogens14060525
8. I.-A. Lungu, O.-L. Moldovan, V. Biriş and A. Rusu, *Pharmaceutics*, **14**, 1749 (2022); https://doi.org/10.3390/pharmaceutics14081749
9. J. Fedorowicz and J. Sączewski, *Monatsh. Chem.*, **149**, 1199 (2018); https://doi.org/10.1007/s00706-018-2215-x
10. E.E. Effa, Z.S. Lassi, J.A. Critchley, P. Garner, D. Sinclair and P.L. Olliaro, *Cochrane Database Syst. Rev.*, **2011**, CD004530 (2011); https://doi.org/10.1002/14651858.CD004530.pub4
11. V. Huber-Spitzy, E. Arocker-Mettinger and I. Baumgartner, *Eur. J. Ophthalmol.*, **1**, 69 (1991); https://doi.org/10.1177/112067219100100203
12. B.A. Runyon, *Gastroenterology*, **91**, 1343 (1986); https://doi.org/10.1016/0016-5085(86)90185-X
13. J. Fernandez, M. Navasa, R. Planas, S. Montoliu, D. Monfort and G. Soriano, *Gastroenterology*, **133**, 818 (2007); https://doi.org/10.1053/j.gastro.2007.06.065
14. J.D. Grange, D. Roulot, G. Pelletier, E.A. Pariente, J. Denis and O. Ink, *J. Hepatol.*, **29**, 430 (1998); https://doi.org/10.1016/S0168-8278(98)80061-5
15. N.C. Chavez-Tapia, T. Barrientos-Gutierrez, F.I. Tellez-Avila, K. Soares-Weiser and M. Uribe, *Cochrane Database Syst. Rev.*, **2010**, CD002907 (2010); https://doi.org/10.1002/14651858.CD002907.pub2
16. R.R. Gurung, P. Maharjan and G.G. Chhetri, *Future Sci. OA*, **6**, FSO464 (2020); https://doi.org/10.2144/fsoa-2019-0122
17. P. Bharathy, P. V. Thanikachalam, S. Jayaprakash, P. Dowlath and P. Madhaiyan, *Biomed. Mater. Devices*, **4**, 625 (2026); https://doi.org/10.1007/s44174-024-00271-4
18. K. Vadakkan, K. Sathishkumar, S.K.U. Kuttiyachan, S.P.G. Govindankutty, A.N. Kumar and B.N. Devi, *Bioorg. Chem.*, **148**, 107465 (2024); https://doi.org/10.1016/j.bioorg.2024.107465
19. S. Mahesh, D.S. Carmelin and R. Muthusamy, *Cureus*, **16**, e56552 (2024); https://doi.org/10.7759/cureus.56552
20. O. Tenaillon, D. Skurnik, B. Picard and E. Denamur, *Nat. Rev. Microbiol.*, **8**, 207 (2010); https://doi.org/10.1038/nrmicro2298
21. M.A. Alhadlaq, O.I. Aljurayyad, A. Almansour, S.I. Al-Akeel, K.O. Alzahrani and S.A. Alsalman, *Gut Pathog.*, **16**, 57 (2024); https://doi.org/10.1186/s13099-024-00641-9
22. R.L. Vogt and L. Dippold, *Public Health Rep.*, **120**, 174 (2005); https://doi.org/10.1177/003335490512000211
23. M. Sebaiy, A. Abdullah, S. El-Shanawany, S. El-Adl, L. Abdel-Aziz and H. Hashem, *Asian J. Res. Chem.*, **4**, 1688 (2011).
24. K. Drlica and X. Zhao, *Microbiol. Mol. Biol. Rev.*, **61**, 377 (1997); https://doi.org/10.1128/MMBR.61.3.377-392.1997
25. K. Hemalatha, J. Selvin and K. Girija, *Asian J. Pharm. Res.*, **8**, 125 (2018); https://doi.org/10.5958/2231-5691.2018.00022.9
26. K. Rajakumari, K. Aravind, M. Balamugundhan, M. Jagadeesan, A. Somasundaram and P.B. Devi, *Eur. J. Med. Chem. Rep.*, **12**, 100233 (2024); https://doi.org/10.1016/j.ejmcr.2024.100233
27. S. Jayaraj and K. Hemalatha, *Futur. J. Pharm. Sci.*, **10**, (2024); https://doi.org/10.1186/s43094-024-00721-2
28. L.L. Shen and A.G. Pernet, *Proc. Natl. Acad. Sci. USA*, **82**, 307 (1985); https://doi.org/10.1073/pnas.82.2.307
29. K. Girija and D. Chacko, *Res. J. Pharm. Technol.*, **2**, 498 (2009).
30. S.H. Gillespie, Medical Microbiology Illustrated, Butterworth-Heinemann (1994).
31. P.M. Hawkey and D.A. Lewis, Medical Bacteriology: A Practical Approach, Oxford University Press, United Kingdom (1994).
32. K.H.S. Kumar and H. Parameshwar, *Res. J. Pharm. Technol.*, **11**, 3103 (2018); https://doi.org/10.5958/0974-360X.2018.00570.X
33. B. Kahveci, *Molecules*, **10**, 376 (2005); https://doi.org/10.3390/10020376
34. H.A. Elbadawy, A. Eldissouky, M.A. El-Apasery, D.S. Elsayed and E.A. Alaswad, *BMC Chem.*, **19**, 207 (2025); https://doi.org/10.1186/s13065-025-01571-6