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Quinoline-bearing 1,6-dihydropyrimidine azo dye derivatives: Synthesis, antimicrobial activity, molecular docking, ADMET, and dye fastness studies

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A series of novel Quinoline-Pyrimidine hybrids **(3a-p)** has been synthesized to address the issue of microbial resistance and provide new dye molecules for the textile industry. The compounds with naphthol group substitutions, such as compound **3c** against *S. aureus*, *E. coli* and *C. albicans*, and compound **3b** against *C. albicans*, showed excellent antimicrobial activity. In docking studies, compound **3b** and **3c** had shown the highest docking score against both Topoisomerase IV and CYP51 enzymes ranging from 8.31 to 8.55 compared to reference drugs. Additionally, *in-silico* pharmacokinetic and toxicity prediction data indicated that compound **3b** had the highest drug score (0.73), with compound **3c** close behind at 0.72. Furthermore, upon evaluating the dyeing performance and colour fastness of cotton and silk, we noticed that phenol derivatives with hydroxyl and nitro-substituted compounds (**3a**, **3n**, **3o**, and **3p**) exhibited outstanding fastness properties on fabrics.

Keywords: Quinoline-Pyrimidine, Azo dye, Antimicrobial, Molecular Docking, ADMET

Introduction

The rise of microbial resistance requires the development of new antimicrobial agents that are more effective than those currently available on the market. One approach to address this issue is to create hybrid molecules by combining two or more bioactive heterocyclic moieties into a single molecular framework, which can potentially enhance their activity [1-7]. Additionally, it appears that modifying the structural form of the existing antimicrobial drug trimethoprim, which contains a pyrimidine motif in its core structure, could lead to an increase in biological activity. Fig. 1 illustrates the design concept for this approach. Trimethoprim, a highly effective drug used to treat general bacterial infections[8], can be modified by replacing the hydrogen on the pyrimidine ring with a substituted quinoline, which itself possesses potent biological properties[9]. The side chain's aromatic moiety was substituted by the ester group, and the adjacent amino group was replaced by methoxy to decrease steric hindrance and increase functionality. An azo group was introduced, followed by various phenol derivatives through modification of the amino group. Compounds containing azo groups have a wide range of medicinal applications[10]. Quinoline-pyrimidine fused heterocyclic compounds were designed because they are associated with crucial bio-activities such as antimicrobial, antitubercular, anticancer, and antimalarial activities[11-14]. Azo dyes have a default application as dyes themselves, comprising more than 50% of all commercial dyes or colorants[15]. Azo dyes find applications in textiles, papers, leather, additives, foodstuff, cosmetics, holographic data storage materials, xerography laser materials, laser printing, materials for organic solar cells, chemo-sensors, harmonic nonlinear optical materials, and optical switching devices[16-17]. Numerous azo dyes and their derivatives are utilized as intermediates in the dye industry[18]. Quinoline and Pyrimidine N-heterocycles were introduced to the azo moiety, as the literature survey suggests that the introduction of heterocycles into the structure of azo dye could enhance dyeing properties due to the chromophoric strength and hydrophobic nature of the heterocyclic ring. This advantage leads to better dispersibility, dyeability, and intrinsic conjugation in the structure, resulting in excellent properties. The article details the results of the research on the

synthesis of these compounds and discusses their several properties.

Experimental Section

Spectral data of synthesized compounds

All chemicals used were of AnalaR grade. ^{1}H-NMR (500 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on Bruker ultra-shield spectrometer usingDMSO-d_6 and $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Coupling constants (J) were indicated in hertz (Hz), and abbreviations such as s (singlet), d (doublet), t (triplet), and m (multiplet) were used. The Infrared spectra (ν, cm^{-1}) of all the compounds were recorded on a Perkin-Elmer FTIR spectrophotometer using KBr. Mass spectra were obtained on SHIMADZU GC-2010+ ultra LCMS spectrometer. Elemental analyses were performed on an ECS 4010 Elemental Combustion System (Costech Instruments) and the results were within the accepted range (±0.40) of the calculated values. The melting points were determined on an electro thermal melting point apparatus (Model 9100, Electrothermal Engineering Ltd.) and were reported uncorrected. The completion of reaction and purity of compounds were checked on aluminum coated TLC plates 60 F245 (E. Merck) using Methanol: Chloroform (0.5:9.5 V/V) as mobile phase and visualized under ultraviolet (UV) light or in an iodine chamber.

Preparation of 2-chloroquinoline-3-carbaldehyde (1)

2-Chloroquinoline-3-carbaldehyde was synthesized by known literature method and spectral data is included in Supplementary Information[19].

Preparation of ethyl 2-amino-4-(2-chloroquinolin-3-yl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (2)

A mixture of 2-chloroquinoline-3-carbaldehyde **(1)** (0.01 mol), ethyl 3-oxobutanoate (0.01 mol) and guanidine (0.03 mol) in ethanol (25 mL) containing conc. HCl (0.01 mol) were refluxed for 4 h. The completion of reaction was monitored by TLC. The reaction mixture was poured into ice water. The separated products were filtered out, washed thoroughly with water, dried and recrystallized from ethanol to afford the desired compound. Light brown solid, yield 81%, m.p. 176-177 °C. IRν_{max} cm^{-1}: 3275 (2° N-H), 3089, 2986 (CH), 2779 (C-H), 1606 (C=N), 1416 (C=C), 1224 (C-N), 1003 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 7.34-7.98 (m, 5H,Ar-H), 4.24 (q, J=6.0 Hz, 2H, CH_2,), 4.19 (m, 1H, CH), 1.89 (s, 2H, NH_2), 1.64 (d, 1H, NH), 1.50 (t, J=6.0 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 168.3 (C=O), 160.2 (C-NH_2), 152.9, 150.2 (C–Cl), 133.5132.4, 130.1, 126.1, 125.7, 94.0, 61.5, 51.5 (C–CH_3), 19.7, 14.7. MS (m/z): 344.1(M^+). Anal. Calcd for $C_{17}H_{17}ClN_4O_2$: C 59.2, H 4.97, N 16.25; Found C 59.33, H 4.88, N 16.29%.

General procedure for preparation ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxyphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3a-p)

A solution of ethyl 2-amino-4-(2-chloroquinolin-3-yl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate **(2)** (0.01 mol) was prepared in minimum amount of HCl (2 mL). A cold solution of sodium nitrite below 5°C was then added to it with continuous stirred. A solution of phenol derivative (0.01 mol) was prepared by dissolving in sodium hydroxide solution then cooled to 0°C. The cold diazonium salt was

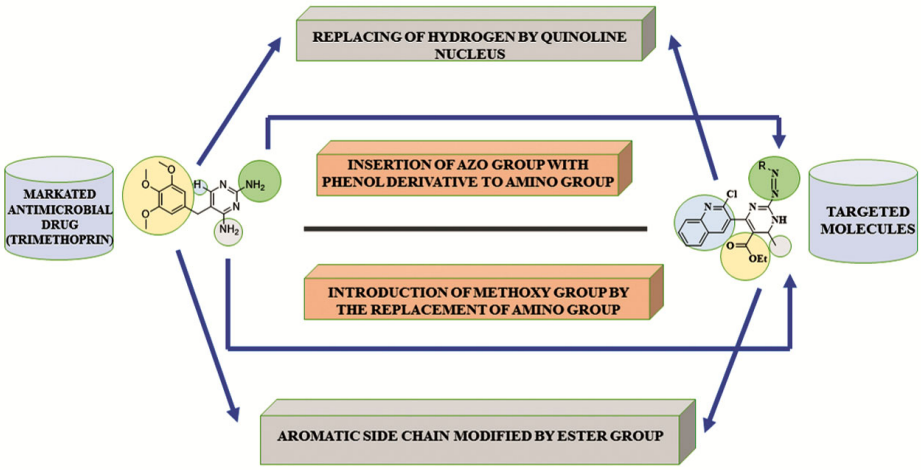


Fig. 1 — Concept designing of hybrid antimicrobial based on marketed drug

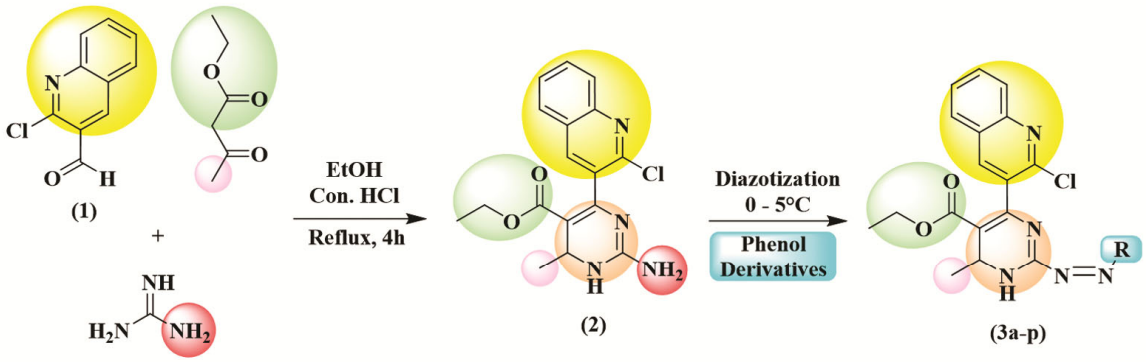
added to solution of phenol derivative in sodium hydroxide kept at 0°C. The solid dye was filtered out, dried and recrystallized from ethanol (Scheme 1). All experimental and spectral data are provided in Supplementary Information.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxyphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3a): Light yellow solid, yield 79%, m.p. 174-176°C.IRν_{max} cm^{-1}: 3375 (2° N-H), 3255 (OH), 2689 (C-H), 1625 (C=N), 1408 (C=C), 1223 (C-N), 1012 (C-O), 745 (Ar-Cl). ^{1}H NMR (500 MHz, DMSO-d_6, δppm): 6.93-8.04 (m, 9H, Ar-H), 5.01 (s, 1H, OH), 4.26 (q,J=6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 1.64 (d, 1H, NH), 1.53 (d,J = 6.0 Hz, 3H, CH_3), 1.39 (t, J=6.0 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 168.3 (C=O), 158.3 (C-OH), 152.9, 150.2 (C–Cl), 149.2, 139.9, 136.6, 132.4, 130.1, 126.1, 125.7, 121.1, 117.1, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 450.13(M^+). Anal. Calcd for $C_{23}H_{20}ClN_5O_3$: C 61.40, H 4.48, N 15.57; Found C 61.53, H 4.56, N 15.46%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((1-hydroxynaphthalen-2-yl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3b): Light brown solid, yield 76%, m.p. 188-190°C. IRν_{max} cm^{-1}: 3225 (2° N-H), 3180 (OH), 2689 (C-H), 1609 (C=N), 1417 (C=C), 1208 (C-N), 1021 (C-O), 743 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 7.32-8.00 (m, 11H, Ar-H), 7.03 (s, 1H, OH), 4.24 (q,J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 1.50 (d, J = 6.10 Hz, 3H, CH_3), 1.39 (t, J = 6.0 Hz, 3H, CH_3), 1.17 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3 168.3 (C=O), 152.9, 151.3 (C-OH), 150.2 (C-Cl), 136.6, 132.4, 130.1, 128.7, 126.1, 125.7, 122.3, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 499.14 (M^+). Anal. Calcd for $C_{27}H_{22}ClN_5O_3$: C 64.87, H 4.44, N 14.01; Found C 64.75, H 4.54, N 14.11%.

Ethyl4-(2-chloroquinolin-3-yl)-2-((2-hydroxynaphthalen-1-yl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3c): Light brown solid, yield 79%, m.p. 185-187°C. IR$\nu_{max}$$cm^{-1}$: 3250 (2° N-H), 3205 (OH), 2656 (C-H), 1603 (C=N), 1407 (C=C), 1257 (C-N), 1011 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 7.31-8.07 (m, 11H, Ar-H), 4.24 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 1.80 (s, 1H, OH), 1.67 (d, 1H, NH), 1.50 (d, J = 6.0 Hz, 3H, CH_3), 1.32 (t, J = 6.0 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 168.3 (C=O), 156.1 (C-OH), 152.9, 150.2 (C-Cl), 149.2, 136.6, 132.4, 130.1, 126.1, 120.1, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 499.14 (M^+). Anal. Calcd for $C_{27}H_{22}ClN_5O_3$: C 64.87, H 4.44, N 14.01; Found C 64.76, H 4.56, N 14.13%.

Eethyl-4-(2-chloroquinolin-3-yl)-2-((2,6-dihydroxyphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3d): Light yellow solid, yield 72%, m.p. 180-182°C. IR$\nu_{max}$$cm^{-1}$: 3290 (2° N-H), 3235 (OH), 2750 (C-H), 1620 (C=N), 1417 (C=C), 1218 (C-N), 1015 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.47-7.69 (m, 8H, Ar-H), 4.25 (q, , J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 4.17 (m, 2H, OH), 1.50 (d, J = 6.10 Hz, 3H, CH_3), 1.38 (t, J = 6.0 Hz, 3H, CH_3), 1.09 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 158.7 (C-OH), 158.7 (C-OH), 152.9, 150.2 (C-Cl), 136.6, 132.4, 131.7, 130.1, 126.1,



Where **R**= **3a** - C_6H_5O (Phenol); **3b** - $C_{10}H_7O$ (1-Naphthol); **3c** - $C_{10}H_7O$ (2-Naphthol); **3d** - $C_6H_5O_2$ (Resorcinol); **3e** - C_7H_7O (o-Cresol); **3f** - $C_7H_7O_2$; **3g** - $C_7H_5O_2$; **3h** - $C_7H_5O_3$; **3i** - $C_8H_8O_2N$; **3j** - C_7H_7O (p-cresol); **3k** - $C_6H_5O_3$ (Pyrogallol); **3l** - $C_{13}H_9O_3$; **3m** - C_7H_7O (m-Cresol); **3n** - $C_6H_5O_2$ (Catechol); **3o** - $C_6H_4NO_3$ (p-Nitrophenol); **3p** - $C_6H_4NO_3$ (o-Nitrophenol)

Scheme 1 — Synthetic route for the preparation of compounds **3a-p**

109.1, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 465.12 (M^+). Anal. Calcd for $C_{23}H_{20}ClN_5O_4$: C 59.30, H 4.33, N 15.03; Found C 59.39, H 4.24, N 15.12%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-3-methylphenyl)diazenyl)-6-methyl-1,6-dihydro pyrimidine-5-carboxylate (3e): Light brown solid, yield 78%, m.p. 172-174°C. IR$v_{max}cm^{-1}$: 3380 (2° N-H), 3145 (OH), 2609 (C-H), 1615 (C=N), 1402 (C=C), 1250 (C-N), 1008 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.94-7.66 (m, 8H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.24 (s, 1H, OH), 4.19 (m, 1H, CH), 2.32 (s, 3H, CH_3), 1.50 (d, J = 6.0 Hz, 3H, CH_3), 1.38 (t, J = 6.0 Hz, 3H, CH_3), 1.10 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 152.9, 150.8 (C-OH), 150.2 (C-Cl), 138.2, 136.6, 133.9, 132.4, 130.1, 126.1, 110.7, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 463.14 (M^+). Anal. Calcd for $C_{24}H_{22}ClN_5O_3$: C 62.14, H 4.78, N 15.10; Found C 62.18, H 4.67, N 15.22%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2,6-dihydroxy-4-methylphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3f): Gray white solid, yield 73%, m.p. 176-178°C. IR$v_{max}cm^{-1}$: 3305 (2° N-H), 3255 (OH), 3170 (OH), 2780 (C-H), 1609 (C=N), 1412 (C=C), 1210 (C-N), 1011 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.40-7.66 (m, 7H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 4.18 (m, 2H, OH), 2.35 (s, 3H, CH_3), 1.49 (d, J = 6.10 Hz, 3H, CH_3), 1.38 (t, J=6.0 Hz, 3H, CH_3), 1.01 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 157.8 (C-OH), 152.9, 150.2 (C-Cl), 145.3, 136.6, 132.4, 131.7, 130.1, 126.1, 110.7, 97.7, 61.5, 52.8 (C-CH_3), 21.8, 19.7, 14.7. MS (m/z): 479.14 (M^+). Anal. Calcd for $C_{24}H_{22}ClN_5O_4$: C 60.06, H 4.62, N 14.59; Found C 60.15, H 4.53, N 14.68%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((3-formyl-2-hydroxyphenyl)diazenyl)-6-methyl-1,6-dihydro-pyrimidine-5-carboxylate (3g): Light yellow solid, yield 83%, m.p. 180-182°C. IR$v_{max}cm^{-1}$: 3350 (2° N-H), 3102 (OH), 2715 (C-H), 1720 (CO), 1609 (C=N), 1412 (C=C), 1210 (C-N), 1011 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 10.11 (s, 1H, CHO), 10.04 (s, 1H, OH), 7.20-8.04 (m, 8H, Ar-H), 4.25 (q, J = 5.90 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 1.69 (d, 1H, NH), 1.53 (d, J = 6 Hz, 3H, CH_3), 1.39 (t, J = 5.90 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 192.3 (CHO), 168.3 (C=O), 160.6 (C-OH), 152.9, 150.2 (C-Cl), 149.2, 136.6, 136.1, 132.4, 131.7, 130.0, 126.1, 121.4, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 477.12 (M^+). Anal. Calcd for $C_{24}H_{20}ClN_5O_4$: C 60.32, H 4.22, N 14.65; Found C 60.38, H 4.13 N 14.68%.

3-((4-(2-chloroquinolin-3-yl)-5-(ethoxycarbonyl)-6-methyl-1,6-dihydropyrimidin-2-yl)diazenyl)-2-hydroxybenzoic acid (3h): Light Brown solid, yield 69%, m.p. 198-200°C. IR$v_{max}cm^{-1}$: 3242 (2° N-H), 3240 (OH), 2645 (C-H), 1780 (C=O), 1618 (C=N), 1390 (C=C), 1225 (C-N), 1018 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 10.11 (s, 1H, COOH), 6.83-8.11 (m, 8H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 3.77 (s, 1H, OH), 1.49 (d, J = 6.10 Hz, 3H, CH_3), 1.38 (t, J = 6.0 Hz, 3H, CH_3), 1.02 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 171.51 (COOH), 170.26, 168.3 (C=O), 155.74 (C-OH), 152.9, 150.2 (C-Cl), 140.2, 136.6, 132.4, 131.1, 130.0, 126.1, 120.2, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 493.12 (M^+). Anal. Calcd for $C_{24}H_{20}ClN_5O_5$: C 58.36, H 4.08, N 14.18; Found C 58.24, H 4.18, N 14.26%.

Ethyl-2-((5-acetamido-2-hydroxyphenyl)-diazenyl)-4-(2-chloroquinolin-3-yl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3i): Brown solid, yield 75%, m.p. 206-208°C. IR$v_{max}cm^{-1}$: 3280 (2° N-H), 3145 (OH), 2735 (C-H), 1820 (CO), 1602 (C=N), 1340 (C=C), 1245 (C-N), 1016 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 8.97 (s, 1H, OH), 7.02-7.99 (m, 8H, Ar-H), 6.27 (s, 1H, NH), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 2.22 (s, 3H, CH_3), 1.50 (d, J = 6.10 Hz, 3H, CH_3), 1.37 (t, J = 6.0 Hz, 3H, CH_3), 1.18 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.4 (CONH), 170.3, 168.3 (C=O), 155.74 (C-OH), 152.9, 150.2 (C-Cl), 140.2, 136.6, 132.4, 131.1, 130.0, 126.1, 120.2, 97.7, 61.5, 52.8 (C-CH_3), 23.8 (CH_3-CO), 19.7, 14.7. MS (m/z): 506.15 (M^+). Anal. Calcd for $C_{25}H_{23}ClN_6O_4$: C 59.23, H 4.57, N 16.58; Found C 59.17, H 4.63, N 16.50%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-5-methylphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3j): Light brown solid, yield 78%, m.p. 176-178°C. IR$v_{max}cm^{-1}$: 3230 (2° N-H), 3180 (OH), 2685 (C-H), 1826 (CO), 1625 (C=N), 1356 (C=C), 1236 (C-N), 1046 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.86-7.99 (m, 8H, Ar-H), 4.41 (s, 1H, OH), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 2.32 (s, 3H, CH_3), 1.49 (d, J = 6.10 Hz, 3H, CH_3), 1.37 (t, J = 6.0 Hz, 3H, CH_3), 1.09 (d, 1H, NH); ^{13}C-NMR (100

MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 152.9, 152.3 (C-OH), 150.2 (C-Cl), 139.8, 136.6, 132.4, 131.1, 130.0, 126.1, 124.6, 97.7, 61.5, 52.8 (C-CH_3), 21.2 (C-CH_3), 19.7, 14.7. MS (m/z): 463.14 (M^+). Anal. Calcd for $C_{24}H_{22}ClN_5O_3$: C 62.14, H 4.78, N 15.10; Found C 62.22, H 4.66, N 15.23%.

Ethyl-4-(2-chloroquinolin-3-yl)-6-methyl-2-((2,3,4-trihydroxyphenyl)diazenyl)-1,6-dihydropyrimidine-5-carboxylate (3k): Brown solid, yield 78%, m.p. 190-192 °C. IR$v_{max}$$cm^{-1}$: 3250 (OH), 3186 (2° N-H), 2785 (C-H), 1865 (CO), 1601 (C=N), 1310 (C=C), 1202 (C-N), 1015 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 8.88 (s, 1H, OH), 6.34-7.66 (m, 7H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 3.16 (s, 1H, OH), 2.46 (s, 1H, OH), 1.49 (d, J = 6.10 Hz, 3H, CH_3), 1.39 (t, J = 6.0 Hz, 3H, CH_3), 1.02 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 152.9, 152.3 (C-OH), 150.2 (C-Cl), 140.4 (C-OH), 136.6, 133.1 (C-OH), 132.4, 131.1, 130.0, 126.1, 125.6, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 481.12 (M^+). Anal. Calcd for $C_{23}H_{20}ClN_5O_5$: C 57.33, H 4.18, N 14.53; Found C 57.45, H 4.07, N 14.64%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-3-(phenoxycarbonyl)phenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3l): Yellow solid, yield 66%, m.p. 194-196°C. IR$v_{max}$$cm^{-1}$: 3075 (OH), 2915 (2° N-H), 2765 (C-H), 1836 (CO), 1605 (C=N), 1313 (C=C), 1256 (C-N), 1021 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 7.07-7.96 (m, 7H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 3.67 (s, 1H, OH), 1.50 (d, J = 6.10 Hz, 3H, CH_3), 1.37 (t, J = 6.0 Hz, 3H, CH_3), 1.22 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 169.7, 168.3 (C=O), 158.6 (C-OH), 152.9, 150.2 (C-Cl), 140.7, 136.6, 132.4, 131.1, 130.0, 126.1, 125.6, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 579.15 (M^+). Anal. Calcd for $C_{30}H_{24}ClN_5O_5$: C 63.22, H 4.24, N 12.29; Found C 63.33, H 4.16, N 12.41%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-4-methylphenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3m): Brown solid, yield 82%, m.p. 176-178°C. IR$v_{max}$$cm^{-1}$: 3125 (OH), 2975 (2° N-H), 2705 (C-H), 1820 (CO), 1619 (C=N), 1346 (C=C), 1237 (C-N), 1005 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.83-7.99 (m, 8H, Ar-H), 4.59 (s, 1H, OH), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 2.35 (s, 3H, CH_3), 1.49 (d, J = 6.10 Hz, 3H, CH_3), 1.37 (t, J = 6.0 Hz, 3H, CH_3), 1.10 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 153.2 (C-OH), 152.9, 150.2 (C-Cl), 142.8, 136.6, 132.4, 131.1, 130.0, 126.1, 123.1, 97.7, 61.5, 52.8 (C-CH_3), 21.2 (C-CH_3), 19.7, 14.7. MS (m/z): 463.14 (M^+). Anal. Calcd for $C_{24}H_{22}ClN_5O_3$: C 62.14, H 4.78, N 15.10; Found C 62.27, H 4.63, N 15.23%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2,3-dihydroxy-phenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3n): Light brown solid, yield 77%, m.p. 182-184°C. IR$v_{max}$$cm^{-1}$: 3188 (OH), 2977 (2° N-H), 2715 (C-H), 1829 (CO), 1625 (C=N), 1356 (C=C), 1228 (C-N), 1016 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.75-8.01 (m, 8H, Ar-H), 4.25 (q, J = 6.0 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 3.79 (s, 1H, OH), 1.49 (d, J = 6.1 Hz, 3H, CH_3), 1.39 (t, J = 6.0 Hz, 3H, CH_3), 1.01 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 152.9, 150.2 (C-Cl), 146.6 (C-OH), 145.8, 136.6, 132.4, 131.7, 130.1, 126.1, 110.7, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 465.12 (M^+). Anal. Calcd for $C_{23}H_{20}ClN_5O_4$: C 59.30, H 4.33, N 15.03; Found C 59.42, H 4.25, N 15.11%

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-5-nitrophenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3o): Light brown solid, yield 70%, m.p. 204-206°C. IR$v_{max}$$cm^{-1}$: 3295 (OH), 2967 (2° N-H), 2659 (C-H), 1856 (CO), 1617 (C=N), 1339 (C=C), 1237 (C-N), 1009 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 6.20-8.69 (m, 8H, Ar-H), 5.51 (s, 1H, OH), 4.26 (q,J = 5.90 Hz, 2H, CH_2), 4.19 (m, 1H, CH), 1.67 (d, 1H, NH), 1.49 (d, J = 6.0 Hz, 3H, CH_3), 1.36 (t, J = 5.90 Hz, 3H, CH_3); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 163.1 (C-OH), 152.9, 150.2 (C-Cl), 143.2, 139.7 (NO_2), 136.6, 132.4, 131.7, 130.1, 126.1, 116.6, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 494.11 (M^+). Anal. Calcd for $C_{23}H_{19}ClN_6O_5$: C 55.82, H 3.87, N 16.98; Found C 55.97, H 3.95, N 16.85%.

Ethyl-4-(2-chloroquinolin-3-yl)-2-((2-hydroxy-3-nitrophenyl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate (3p): Brown solid, yield 68%, m.p. 186-188°C. IR$v_{max}$$cm^{-1}$: 3285 (OH), 2947 (2° N-H), 2689 (C-H), 1866 (CO), 1616 (C=N), 1319 (C=C), 1217 (C-N), 1026 (C-O), 745 (Ar-Cl). ^{1}H NMR(500 MHz, DMSO-d_6, δppm): 7.26-8.14 (m, 8H, Ar-H), 5.43 (s, 1H, OH), 4.23 (q, J = 5.90 Hz, 2H,

CH_2), 4.19 (m, 1H, CH), 1.49 (d, J = 6.0 Hz, 3H, CH_3), 1.36 (t, J = 5.90 Hz, 3H, CH_3), 0.96 (d, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δppm): 170.3, 168.3 (C=O), 152.9, 150.2 (C-Cl), 147.0 (C-OH), 142.1, 136.6, 134.4 (NO_2), 132.4, 131.7, 130.1, 126.1, 120.7, 97.7, 61.5, 52.8 (C-CH_3), 19.7, 14.7. MS (m/z): 494.11 (M^+). Anal. Calcd for $C_{23}H_{19}ClN_6O_5$: C 55.82, H 3.87, N 16.98; Found C 55.96, H 3.95, N 16.84%.

Biological Assay

The antimicrobial activity was assessed using the agar well diffusion method with Mueller-Hinton agar and sterilized potato dextrose agar media[20]. The synthesized compounds were tested for antimicrobial activity against several microorganisms: Gram-positive bacteria (Staphylococcus aureus [MTCC-96] and Bacillus subtilis [MTCC-441]), Gram-negative bacteria (Escherichia coli [MTCC-1687]), and fungi (Candida albicans [MTCC-227] and Aspergillus niger [MTCC-282]). All compounds were dissolved in chloroform and diluted to a final concentration of 50 µg/mL. Ampicillin (50 µg/mL), chloramphenicol (50 µg/mL), and fluconazole (50 µg/mL) were used as standard drugs under identical conditions. Chloroform was used as a control. The zone of inhibition was measured to determine the antimicrobial activity.

Computational methods

Docking study

To predict the probable mechanism of synthesized molecules for their antimicrobial activity, in silico docking study was carried out. Docking study was performed using SYBYL-X-2.1 software (Tripos Inc, St Louis, MO, USA)[21]. All the structures were drawn by sketch function of SYBYL-X-2.1 software. Hydrogen atoms were added to all the structures and Gasteiger–Hückel charges were assigned to each atom. Standard tripos force field was used to carry out energy minimization process with maximum iterations 5000 and energy change 0.5 kcal/(mol*A)[22, 23]. Further, all the compounds were evaluated using different enzymes of bacterial and fungi origin namely topoisomerase IV and CYP51. The three-dimensional crystal structures of these two enzymes were retrieved from RCSB protein data bank. The crystal structure of topoisomerase IV enzyme obtained from Escherichia coli K-12 complexed with a ligand (1AV) was used for docking study (PDB ID: 4HZ0, Chain A & B, resolution 2.20Å)[24]. For CYP51, crystal structure obtained from Candida albicans complexed with ligand (1YN) was considered for docking study (PDB ID: 5V5Z, Chain A, resolution 2.90Å)[25].After retrieval of crystal structures, proteins were preprocessed by deleting water molecules and bound ligand. Hydrogen atoms were added to proteins and atomic charges were given to the protein (AMBER7FF99) and bound ligand (Gasteiger–Hückel). Protein was minimized using Powell method with gradient termination with maximum iterations 5000 and energy change of 0.5 kcal/ (mol*A). Further, all the molecules were docked into the binding site of enzymes using Surflex-Dock module. Protomol (binding site) was generated by removing the bound ligand from the crystal structure of protein. Docking study was carried out using default Surflex-Dock parameters. Total score value was calculated for each compound and H-bond interactions were observed to check the binding affinity with protein. Maestro 11.2 software was used for the exact visualization of hydrophobic and pi-pi interactions of each compound[26].

***In-silico* pharmacokinetic and toxicity prediction**

In silico pharmacokinetic and toxicities predictions are crucial in drug design and discovery as many lead compounds become fail to become a drug candidate. This methodology is more dominant during lead optimization as it can offer direction about modification of structure which will improve physicochemical properties. ADMET properties comprise the evaluation of various factors which are relevant not only for the estimation of the drug pharmacologically active concentration at the therapeutic targets but also for adverse effect and evaluation of toxicity. In-silico pharmacokinetic properties and toxicities were predicted using OSIRIS property explorer which uses Chou and Jurs algorithm, based on computed atom contributions[27, 28].

Dyeing Assay

Dyeing on cotton fabric

The fabric was dyed with 2% dye (calculated based on the weight of the fabric) and 1% NaCl (used as a dispersing agent) at a liquor ratio of 20:1. The process began at 60°C and then the temperature was increased to 130°C for 30 min and maintained for 1 h. After cooling, the fabric was removed and treated with a solution of 2% sodium bisulfite, 2% NaOH, and 0.1% NaCl at 70°C for 30 min. Finally, the fabric was rinsed and dried at 60°C.

Dyeing on silk fabric

The fabric was dyed using 2% dye (calculated based on the weight of the fabric) and 1% Na_2CO_3 as a dispersing agent. It was kept at a liquor ratio of 20:1. The process began at 60°C, and the temperature was then raised to 130°C for 30 min and maintained for 1 hr. After cooling, the fabric was removed and treated with a solution of 2% urea, 2% NaOH, and 0.1% NaCl at 70°C for 30 min. Finally, the fabric was rinsed and dried at 60°C[(Ref.29)].

Fastness Properties

Rubbing fastness

The dyed cotton fabric was positioned on the base of the crockmeter so that it lay flat on the abrasive cloth, with its long dimension aligned with the direction of rubbing. A piece of white testing cloth was then allowed to slide back and forth on the fabric being tested, making 10 complete turns of the crank for a total of 20 times. The staining on the white testing cloth was then evaluated based on a grayscale.

Colour fastness

A piece of dyed cotton fabric was sandwiched between two pieces of undyed cotton fabric, all of the same length, and then washed at 50°C for 30 min. After the soaping treatment, the specimen was removed and rinsed twice in cold water, followed by rinsing in cold running tap water. It was then squeezed and air-dried at a temperature not exceeding 60°C. The staining on the undyed adjacent fabric was evaluated using the gray scale. Original photographs of each dye on cotton and silk were provided in the Supplementary Information.

Results and Discussion

Chemistry

The synthetic route for preparing compounds ethyl-4-(2-chloroquinolin-3-yl)-2-((2-aryl)diazenyl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate **(3a-p)** is outlined in Scheme 1. The synthesis to obtain ethyl 2-amino-4-(2-chloroquinolin-3-yl)-6-methyl-1,6-dihydropyrimidine-5-carboxylate **(2)** involved a classical Biginelli synthesis, which is a three-component one-pot condensation. A mixture of 2-chloroquinoline-3-carbaldehyde **(1)**, ethyl 3-oxobutanoate, and guanidine was mixed in ethanol using conc. HCl as a catalyst, and refluxed for 4 h to prepare a compound with a pyrimidine ring in its core structure and two methoxy groups at the terminal of the structure. The diazotization process was applied using various phenol derivatives to achieve target molecules **3a-p** having an -OH group at the β-position of the azo group. The structures of the synthesized derivatives were confirmed by ^{1}H NMR, ^{13}C-NMR, FTIR, and Mass spectroscopy.

Antimicrobial Screening Evaluation

The data presented in Table 1 indicates that the newly synthesized compounds showed varying degrees of activity against all the tested bacterial and fungal strains when compared to standard drugs. Compound **3c**, which contains 2-naphthol, demonstrated excellent activity against S. aureus, E. coli, and C. albicans. Compound **3b**, containing 1-naphthol, exhibited excellent activity against C. albicans and also showed very good activity against all other tested microbes. Compound **3f** (ZOI, 20 μg/mL, B. subtilis; 18 μg/mL, C. albicans) exhibited equipotent antimicrobial activity compared to standard drugs.The other synthesized compounds showed mild to good activity against the tested bacterial and fungal strains.

Molecular Docking Studies and Interaction Analysis

To investigate the molecular mechanism of compounds **3a-p**, docking studies were conducted. The study involved multiple bacterial and fungal targets including Dehydrosqualene synthase, Topoisomerase IV, Glucosamine-6-phosphate synthase, DNA gyrase, CYP51, Squalene epoxidase, and Alpha-beta tubulin. The results showed that compounds **3a-p** exhibited promising activity against only two targets: Topoisomerase IV and CYP51, as indicated in Table 2. The docking results for the compounds against Dehydrosqualene synthase, Glucosamine-6-phosphate synthase, DNA gyrase, Squalene epoxidase, and Alpha-beta Tubulin can be found in the Supplementary Information (Table S1).

Docking results of compounds against Topoisomerase IV (PDB ID: 4HZ0)

The study used the crystal structure of the protein with PDB ID 4HZ0 at a resolution of 2.20 Å. Ampicillin and Chloramphenicol were used as standard drugs to compare the docking results of each compound. Compounds **3b** and **3c** showed total score values of 8.49 and 8.31, respectively. In Table 2, the total score values of Ampicillin and Chloramphenicol were found to be 6.91 and 7.38, respectively.

Table 1 — Antimicrobial screening data for zones of inhibition of compounds 3a-p

Compound	Conc (µg/mL)in Chloroform	Zone of inhibition in mm*				
		Bacterial strains			Fungal strains	
		S. aureus	*E. coli*	*B. subtilus*	*A. niger*	*C. albicans*
3a	50	9	11	12	10	8
3b	50	20	23	22	19	26
3c	50	28	26	22	12	30
3d	50	15	12	10	14	16
3e	50	8	10	12	10	8
3f	50	18	19	20	10	18
3g	50	16	10	9	8	8
3h	50	8	7	12	8	9
3i	50	7	11	12	10	9
3j	50	20	14	8	7	7
3k	50	10	10	12	10	16
3l	50	12	10	10	12	16
3m	50	10	10	12	8	10
3n	50	8	8	8	7	7
3o	50	21	15	16	12	18
3p	50	20	18	17	12	16
Ampicillin	50	26	25	25	-	-
Chloramphenicol	50	20	21	24	-	-
Fluconazole	50	-	-	-	26	25
Control (Chloroform)	50	5	5	5	5	5

*Diameter of well (bore size) - 5 mm

Table 2 — Docking result of synthesized compounds 3a-p

Compound	Total Score*	
	Topoisomerase IV (PDB ID: 4HZ0)	CYP51 (PDB ID: 5V5Z)
3a	6.29	5.36
3b	8.49	8.37
3c	8.31	8.55
3d	5.84	4.49
3e	6.26	5.95
3f	6.52	4.95
3g	7.82	7.57
3h	5.81	6.71
3i	6.73	6.33
3j	6.07	6.11
3k	5.98	6.22
3l	6.79	7.92
3m	7.51	5.65
3n	7.83	6.95
3o	7.15	5.72
3p	6.98	6.02
Ampicillin	6.91	5.79
Chloramphenicol	7.38	5.12
Fluconazole	---	7.01

*Total score is expressed in -log10 (K_d) units to represent binding affinities

The '-NH_2' functionality of Ampicillin showed H-bonding interactions with amino acids Asp69 and Thr163, as shown in Fig. 2a. The docking results of a representative compound **3b** are shown in Fig. 2b. The naphthalene ring present in compound **3b** formed a pi-cation interaction with the amino acid Arg72. Additionally, the hydroxyl group of the naphthalene ring interacted with the amino acid Gly73 via H-bonding. The carbonyl oxygen atom also participated in a H-bonding interaction with the amino acid Asn42.

Docking results of compounds against CYP51 (PDB ID: 5V5Z)

The crystal structure of CYP51 with PDB ID 5V5Z (resolution of 2.90 Å) was utilized for the docking study. Compounds 3b and 3c demonstrated promising results against the CYP51 enzyme, with total score values of 8.37 and 8.55, respectively (refer to Table 2). The total score value of the standard drug fluconazole was 7.01. The binding interactions of fluconazole with CYP51 are depicted in Fig. 3a The triazole ring of fluconazole interacts with the amino acid His377 through pi-pi stacking interaction. The phenyl ring is also involved in pi-pi stacking

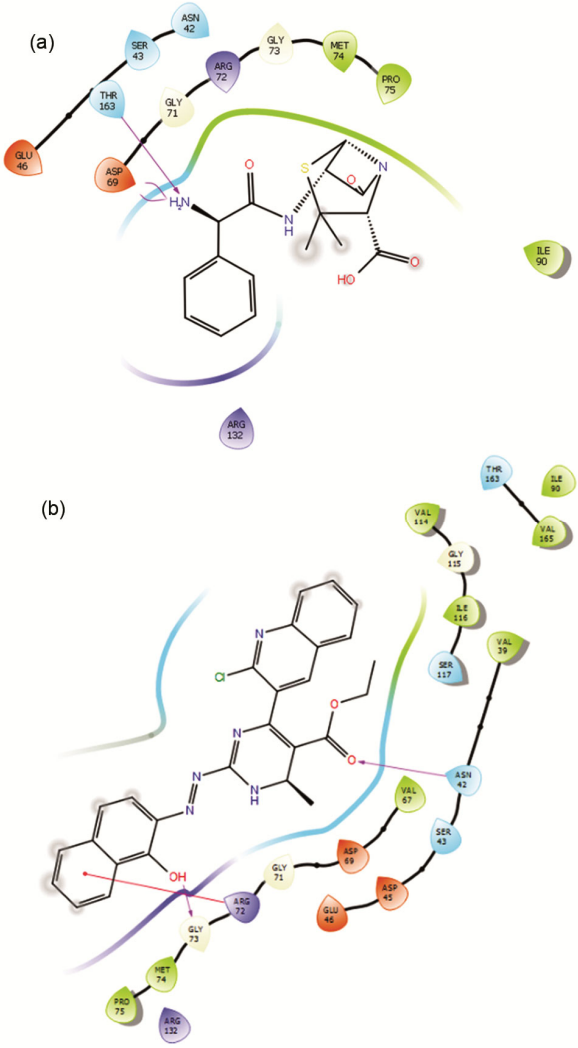


Fig. 2 — Docking results of topoisomerase IV binding with (a) Ampicillin and (b) Compound 3b (H-bonding is represented by pink line and red line indicates pi-cation interaction)

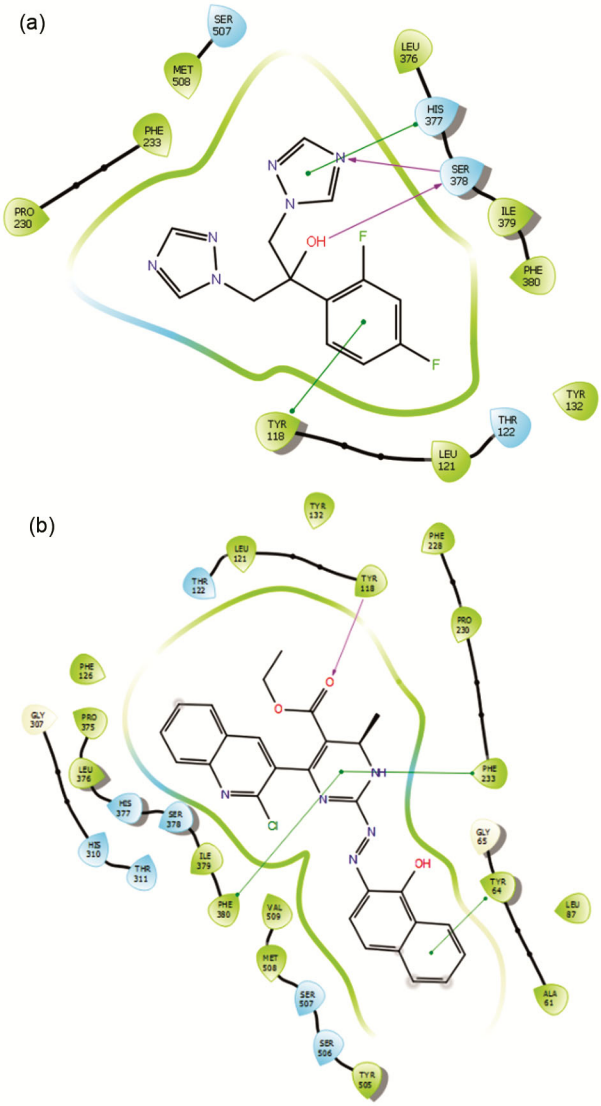


Fig. 3 — Docking results of CYP51 binding with A) Fluconazole B) Compound 3b(H-bonding is indicated by pink line and green line indicates pi-pi stacking interaction)Covalent docking

interaction with Tyr118. Fluconazole forms an H-bonding interaction with the amino acid Ser378 (see Fig 2a). The docking interactions of a representative compound 3b are illustrated in Fig. 2b. The pyrimidine ring of compound 3b engages in pi-pi stacking interactions with amino acids Phe233 and Phe380. The naphthalene ring also participates in pi-pi stacking interaction with the amino acid Tyr64. Additionally, the carbonyl oxygen atom forms an H-bonding interaction with the amino acid Tyr118, as shown in Fig. 3b.

Toxicities prediction and pharmacokinetic parameters

In Table 3, it is evident that none of the compounds exhibit the predicted toxicities, including mutagenicity, tumorigenicity, irritating impact, and reproductive toxicity. Furthermore, the projected drug scores indicate that all compounds have favorable drug scores, suggesting that the developed compounds may be safe, effective, and bioavailable. Notably, compound **3b** has the highest drug score (0.73) among the others. Additionally, compound **3c** also correlated with 0.72 drug score in this study.

Dyeing ability assessment

The dyed cotton and silk fabrics displayed vibrant colors and good depth. Compounds **3o** and **3p** showed excellent color and rubbing fastness on cotton

Table 3 — Toxicities prediction and Pharmacokinetic parameters of designed compounds 3a-p

Compound	Mutagenicity	Tumorigenicity	Irritant	Reproductive effective	cLog P	Solubility	Drug score
3a	NO	NO	NO	NO	3.5	-4.89	0.46
3b	NO	NO	NO	NO	4.3	-4.70	0.73
3c	NO	NO	NO	NO	3.8	-4.19	0.72
3d	NO	NO	NO	NO	3.7	-5.87	0.49
3e	NO	NO	NO	NO	4.1	-2.90	0.37
3f	NO	NO	NO	NO	3.5	-4.08	0.60
3g	NO	NO	NO	MR	4.1	-4.18	0.55
3h	NO	NO	NO	NO	3.7	-3.48	0.59
3i	NO	NO	NO	NO	2.8	-4.31	0.57
3j	NO	NO	NO	NO	4.4	-5.29	0.67
3k	NO	NO	NO	NO	2.8	-3.96	0.36
3l	NO	NO	NO	NO	2.9	-5.19	0.30
3m	NO	NO	NO	NO	3.2	-4.75	0.51
3n	NO	NO	NO	NO	4.5	-4.43	0.59
3o	NO	NO	NO	NO	3.6	-5.65	0.61
3p	NO	NO	NO	NO	2.9	-4.87	0.38

NO = No toxicity

fabrics. Compounds **3a**, **3b**, **3d**, **3k**, **3m**, and **3n** also exhibited excellent rubbing fastness properties as cotton dyes. Compounds **3e** and **3h** showed excellent color and rubbing fastness on silk fabric. Compounds **3c**, **3l**, **3m**, and **3n** demonstrated excellent color fastness. Additionally, **3a**, **3b**, **3e**, **3h**, **3i**, and **3o** showed excellent rubbing properties as silk dyes. Thus, compounds **3a**, **3n**, **3o**, and **3p** were the promising dye candidates for selected fabrics. All other newly synthesized heterocyclic azo dyes resulted in moderate to very good colour and rubbing fastness on the dyed fabrics. Scanned pictures of these fabrics can be found in Table 4.

Table 4 — Fastness property data for compounds 3a-p

Compound	Cotton		Silk	
	Colour fastness	Rubbing fastness	Colour fastness	Rubbing fastness
3a	4.5	5	4.5	5
3b	4	5	4.5	5
3c	3	4.5	5	4.5
3d	4.5	5	4	3.5
3e	4	4.5	5	5
3f	4	4.5	3.5	4
3g	4	3.5	4	3.5
3h	2.5	3	5	5
3i	3	3.5	4	5
3j	4.5	4.5	4.5	4
3k	4.5	5	4.5	3.5
3l	2	4.5	5	4.5
3m	4.5	5	5	3
3n	4.5	5	5	4.5
3o	5	5	4.5	5
3p	5	5	4.5	4.5
Standard Gray Scale Numbers			5 = Excellent, 4 = Very Good, 3 = Good, 2 = Fair, 1 = Poor	

Structural activity relationship study

The antimicrobial activity of the synthesized compounds is influenced by the various substituents (-R) attached to the azo group as shown in Fig. 4. Compounds **3b** (1-naphthol) and **3c** (2-naphthol) containing fused rings with a hydroxy group showed a significant increase in antimicrobial activity. Compounds **3d**, **3f**, **3k**, and **3l** with EDGs at *ortho*, *meta*, and *para* positions and at least one hydroxy group at *ortho* positions, displayed remarkable enhancement of antimicrobial activity. On the other hand, compounds **3o** and **3p**, with electron-withdrawing groups (EWGs) at the *meta* position ($-NO_2$) with respect to attachment and along with a single hydroxy group, showed a moderate increase in activity. However, compounds **3e**, **3g**, **3h**, **3i**, and **3j** with -CHO, -COOH, $-CH_3$, $NHCOCH_3$functional groups at the *meta* position, exhibited decreased activity. In conclusion, the presence of fused rings and EDGs at specific positions (*ortho*, *meta* and *para*) along with hydroxyl groups led to an increase in antimicrobial activity.

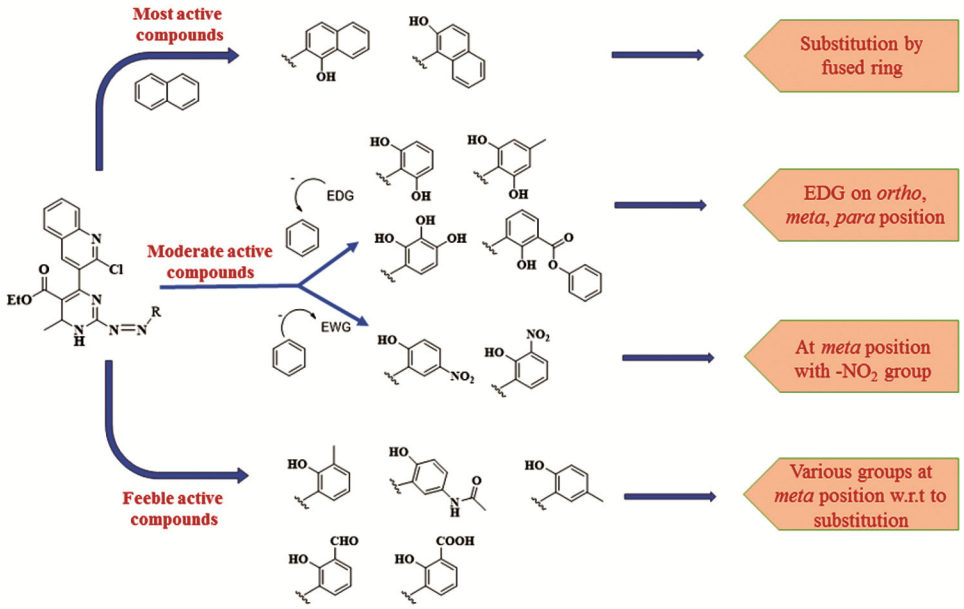


Fig. 4 — Structural Activity Relationship of the targeted molecules effecting antimicrobial activity

Conclusion

The aim of the current research was to design and develop more potent novel compounds with antimicrobial and dyeing applications. Compound **3c** (ZOI, 28 µg/mL, *S. aureus*; 26 µg/mL, *E. coli*; 30µg/mL, *C. albicans*) and **3b** (ZOI, 26 µg/mL, *C. albicans*) showed excellent antimicrobial activity. In addition, compound **3b** (8.49; Topoisomerase IV and 8.37; CYP51) had the highest dock scores and the highest drug score (0.73), while compound **3c** (8.31; Topoisomerase IV and 8.55; CYP51) showed significant dock scores with equivalent high drug score (0.72). None of the synthesized compounds were found to be toxic in the *in-silico* toxicity prediction study. Based on these results, it was concluded that the naphthol-substituted compounds **3b** and **3c** could be lead compounds for further structural optimization and development as potential candidates for antimicrobial drug discovery. Furthermore, the results of dyeability testing indicated that substituted compounds **3a**, **3n**, **3o** and **3p** were the most promising cotton and silk fabric dyes, displaying excellent hues on fabrics with evenness in depth, as well as admirable fastness properties referencing grayscale. These compounds could be promising fabric dyes for the textile industry.

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Supplementary Information

Supplementary information is available on the website http://nopr.niscpr.res.in/handle/123456789.

Conflict of interest

The authors declare no conflict of interest.

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