



Synthesis, Insilico and Antibacterial Activity Studies of Substituted Dihydro-1, 2-Oxazole Benzopyran-2-One Hybrids

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Authors' contributions

This work was carried out in collaboration among all authors. Authors AK and PK designed the study, performed the statistical analysis, and wrote the protocol. Author PN helped in antimicrobial study. Author SMR managed the literature searches. Author AD helped in drafting the final manuscript. All authors read and approved the final manuscript.

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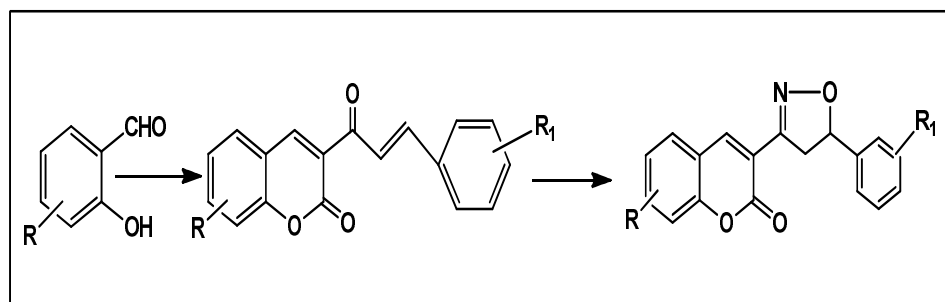
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ABSTRACT

A series of substituted dihydro-1, 2-oxazole benzopyran-2-one (SR1-SR6) were synthesized through the intermediate substituted benzopyran-2-one chalcones and were characterized using spectral analysis. Compounds were docked with receptor DNA Gyrase B (PDB code: 5L3J) to know its interaction and binding energy; ranges -3.38 to -2.15 kcal/mol. Further these compounds were tested for antibacterial activity using tube dilution method and MIC values were observed; ranges 3.12 to 25 µg/ml. Compound 3-(5-(m-tolyl)-4,5-dihydroisoxazol-3-yl)-2H-chromen-2-one (SR3) showed the best interaction with binding energy -3.38 kcal/mol and antimicrobial activity having MIC 3.12 µg/ml.

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GRAPHICAL ABSTRACT

Keywords: Benzopyran-2-one; chalcones; DNA Gyrase B; antibacterial activity.

1. INTRODUCTION

Microbial infection from recent past has become a challenging problem for health care provider and scientists [1] Finding a new antimicrobial agents and antimicrobial targets is in great demand to obviate the threat caused by these life-threatening infections [2]. Since the resistance towards pathogenic bacteria is growing for present molecule. Therefore, it has become compulsory need for the scientist to develop the antimicrobial molecule which can treats various infection worsen the of quality life of the patient and eventually leads to normal life.

Oxazole is a significant class of the aromatic heterocyclic family. Due presence of heteroatom nitrogen and oxygen in the ring makes a privileged molecule. Many substituted oxazole precursor shows various biological activities such as brain-derived neurotropic factor inducers [3], analgesic [4], trypanocidal [5], anti-mitotic with pro-apoptotic [6], antifungal [7], anti-inflammatory [8], anti-depressant [9], anti-microbial [10], anti-diabetic [11] and antiobesity agents. Besides this, oxazole derivatives show antiproliferative activity for many cancer cells, especially human prostate cancer and human epidermoid carcinoma [12-13]. It has been even used as antimicrobial agent by preventing the bacterial protein synthesis. One the very frequently used molecule contains oxazole ring is linezolid; which is used in treatment of multidrug resistance infection. Apart from these cycloserine and furazolidone also contain oxazole ring and used as antimicrobial agent by preventing a bacterial cell wall synthesis and damaging bacterial DNA respectively. [14-15]

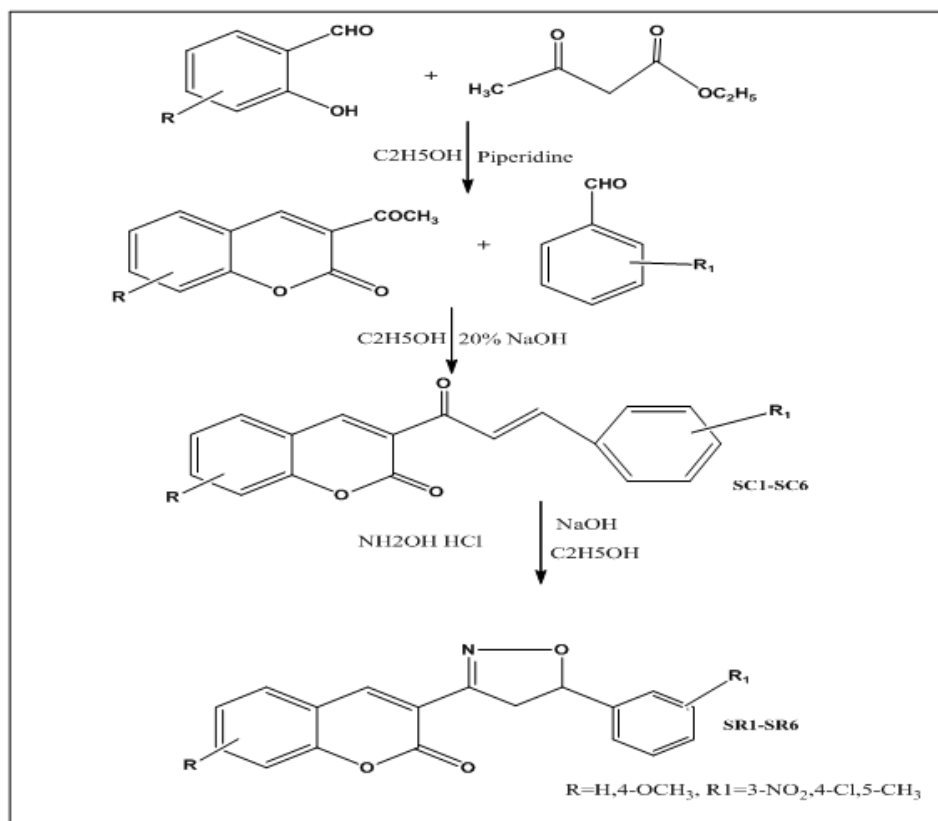
At the same time benzopyran derivatives have versatile biological properties such as anti-inflammatory [16-17], antioxidant [18], vasorelaxant [19], cytotoxic [20], anti-HIV [21], antitubercular [22] and antimicrobial [23]. Presently antimicrobial molecule containing benzopyran ring is novobiocin acts by targeting Bacterial DNA gyrase and topoisomerase IV and control the topological state of DNA during replication and acts as antimicrobial agent [24-26].

Therefore we plan to synthesize oxazole benzopyran-2-one hybrids and choose DNA gyrase receptor to dock with the synthesized compound and evaluate its binding pattern with the receptor.

2. MATERIALS AND METHODS

DNA gyrase by molecular docking studies and evaluate its anti-bacterial activity by tube dilution method. Melting points were determined by open capillary and are uncorrected. The IR spectra (in ATR technique) were recorded in Tensor 27 spectrophotometer, Bruker optic (Germany). ¹H NMR spectra were recorded (CDCl₃) on Bruker spectrometer (400Mz) using TMS as an internal standard. Chemical shift values are given in δ scales. The mass spectra were recorded using a Jeol-D-300 Mass spectrometer (70eV), Shimadzu (Japan) by FAB. Elemental analyses were performed using Vairo Elemental Model, C, H, N analyzer. The completion of the reaction was checked by thin layer chromatography (TLC) on silica gel-G coated plates by using suitable solvent system and observed in UV light. Commercial grade solvents and reagents obtained from Sigma-Aldrich with purity ≥ 98% were used.

Scheme



2.1 General Procedure for the Synthesis of Substituted Dihydro-1, 2-Oxazole Benzopyran-2-One Hybrids

2.1.1 Step 1: synthesis of benzopyran-2-one

A mixture of substituted salicylaldehyde (0.05 mol) and ethyl acetoacetate was added to 250ml conical flask. It was then condensed by adding sufficient piperidine drop wise with stirring in ice cold condition. The reaction mixture was then kept overnight in refrigerator. The solid lumps were broken in cold ethanol. The resulting yellow colored solid mass was then filtered and washed with cold ethanol to remove the excess piperidine. It was then recrystallized from ethanol to give white needle shaped crystals.

2.1.2 Step 2: Synthesis of substituted benzopyran-2-one Chalcone (SC1-SC6)

A mixture of substituted 3-acetyl coumarin (0.01 mol) and different substituted benzaldehyde (0.01 mol) in 20 ml absolute ethanol was stirred together at room temperature for 24 hours in the

presence of 20% sodium hydroxide. The completion of the reaction was monitored by TLC. The reaction mixture was then poured into crushed ice and acidified with 2N hydrochloric acid with stirring. The product obtained was filtered, washed with water and recrystallized from ethanol.

2.1.3 Step 3: Substituted 3 Dihydro-1, 2-Oxazole Benzopyran-2-one (SR1-SR6)

A mixture of chalcones (0.01 mol), hydroxyl amine (0.01 mol) was dissolved in 10 ml of ethanolic NaOH and stirred for 5-6 hrs with a magnetic stirrer. The completion of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was poured into crushed ice. The precipitated solid was filtered, washed with cold water and recrystallized from ethanol [27].

2.2 Molecular Docking Study

Molecular docking study was performed to know the interactions between ligand (synthesized

compounds) and receptor. All computational analysis was carried out on Schrodinger 2018-3 suite device Maestro 11.7.012, (ligprep, glide XP docking, grid generation). This software package programmed on DELL Inc.27" workstation machine running on Intel Core i7-7700 CPU@ 3.60 GHz x8, processor with 8GB RAM and 1000 GB hard disk with Linux –X6_64 as the operating system. For docking calculation, the protein Protein data bank PDB (code: 5L3J) was downloaded from protein data bank and refined using protein preparation wizard. Docking score were calculated using maestro (Schrodinger) software. The binding affinity was assessed in terms of binding free energies (S-score, kcal/mol) [28]. All synthesized compounds were docked in the groove of binding site present in DNA Gyrase B 5L3J.

2.3 Evaluation of Antibacterial Activity

2.3.1 Determination of minimum inhibitory concentration by tube dilution method

2.3.1.1 Control tests

Negative control

In this no growth is expected. It confirms that the medium is sterile.

Positive control

In this the growth of the inoculated organism is expected. This indicates that (a) the nutrient of medium supports the growth of organism that has been inoculated. (b) Inoculation of live organisms.

Procedure

Double concentration of the nutrient broth was prepared. Distribute each 2.5 ml into 9 test tubes and label them A1 to A9. Distribute 2.5 ml in two test tubes and label them as positive control and negative control. Prepare drug stock solution of 2000 µg/ml by dissolving the drug in water. From this stock solution the following dilutions were prepared; 2.5 ml of the stock solution diluted to 25 ml with water to give 200 µg/ml. Serial dilution of the same was performed to give 100 µg/ml, 50 µg/ml, 25 µg/ml, 12.5 µg/ml and 6.25 µg/ml respectively. Add 2.5 ml each double concentration nutrient broth to 2.5 ml of the above dilutions so that the concentration further gets halved. i.e., 100 µg/ml, 50 µg/ml, 25 µg/ml, 12.5 µg/ml, 6.25 µg/ml 3.12 µg/ml and 1.56µg/ml respectively. Add 2.5 ml of water to positive control and negative control tube and mix well.

Mix all the tubes well close with non-absorbent cotton plugs and sterilize by autoclaving 15 lbs./sq. in (121° C) for 15 min. Cool the tubes to room temperature and inoculate all the tubes with one loopful of the test organism *E.coli*, except in the negative control tube. Incubate all the tube at 37°C for 48 hrs and observe the turbidity [29].

3. RESULTS AND DISCUSSION

In the present study the oxazole benzopyran-2-one hybrid derivatives were synthesized by infusing benzopyran ring and oxazole ring and were studied for molecular docking study and antibacterial activity.

In the process of synthesis, the starting material substituted salicylaldehyde and ethyl acetoacetate were reacted as the mentioned procedure and lead to formation of intermediates as substituted benzopyran-2-one chalcone. (SC1-SC6). These intermediates were characterized using N.M.R, I.R and Mass spectroscopy. The observed peak value and chemical shift value of IR and N.M.R were 1760 cm^{-1} , 1480 cm^{-1} , 6.89 (1H, d, J = 16.5 Hz), which shows the presence C=O, C=C functional group and eneone proton thus confirm the formation of intermediates. These intermediates were further reacted with hydroxyl amine as the procedure leads to the formation of final compounds substituted 3 dihydro-1,2-oxazole benzopyran-2-one (SR1-SR6). The conformation of these compounds was done based on the spectral studies. The peak value 1256 cm^{-1} (C-O-N str) and 1610 cm^{-1} (C=N str) and chemical shift value 6.19 (1H, dd, j = 7.9, 6.8 Hz) O-C-H of isoxazol confirm the formation of final compounds. The physiochemical parameter these intermediates and final compounds are reported in Table 1 and 2.

Final compounds interaction pattern with DNA Gyrase B (PDB code: 5L3J) were studied and was compared with standard drug ciprofloxacin. Compound SR3 shows the best interaction pattern with best binding energy -3.38 kcal/mol. This form hydrogen bond, hydrophobic interaction, charged negatives and polar interaction with respective amino acids VAL -19, ALA-18, VAL-19, ILE-23, LEU-126,16, 98, PRO-23, ARG-20,22 LYS-21 and THR-165. Apart from the SR3 the compound shows hydrogen bond is SR1&SR6-forms one hydrogen bonds. The other interaction patterns and dockings core for all other compounds are shown in the Table 3, 4 and Figs 1, 2, 3.

SR1-SR6 was evaluated for antibacterial activity by using tube dilution method and a result is mentioned in Table 5 and figure 4. 3-(5-(m-tolyl)-4, 5-dihydroisoxazol-3-yl)-2H-chromen-2-one (SR3) have shown the best antibacterial activity having MIC value 3.12 µg/ml. The effect of the substitution in the phenyl ring region as R1 and substitution in the-acetyl-2H-chromen-2-one region as R. Substituted 3 Dihydro-1,2-oxazole Benzopyran-2-one were considered to summarize the structural activity relationship, when the R1 substituent is electron pumping group like methyl it increases antibacterial activity; at the same time electron withdrawing group like nitro and chloro decreases. Similarly, when the R hydrogen was replaced with methoxy group there was decrease in the antibacterial activity.

3.1 Spectral Data

3.1.1 3-acetyl-7-methoxy-2H-chromen-2-one

It was obtained as yellow crystals (EtOH).mp 143-145°C; UV (EtOH) λ_{\max} (log ϵ) 294 (4.26) nm; R_f = 0.52 (n-hexane: ethyl acetate, 8:2) IR ν_{\max} 3000(C-H aromatic), 1510 (C=Cstr), 1670(C=O str), 1220(C-O-C str) cm^{-1} ; $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 2.34 (3H, s), 3.80 (3H, s), 5.30 (1H, d), 5.53 (1H, d), 6.42-6.46 (2H, dd), 6.42 (dd), 7.71 (1H, s), 8.08 (1H, dd).MS: m/z = 219(M^+); *Anal.* Calcd for $\text{C}_{18}\text{H}_{11}\text{NO}_5$: C, 66.05; H, 4.62; O 29.33; Found: C, 66.09; H, 4.57; O, 29.32.

3.1.2 3-(3-(4-nitrophenyl) acryloyl)-2H-chromen-2-one (SC1)

It was obtained as yellow crystals (EtOH).mp 167-169°C; UV (EtOH) λ_{\max} (log ϵ) 282 (4.21) nm; R_f = 0.47 (n-hexane: ethyl acetate, 8:2) IR ν_{\max} 3010(C-H aromatic), 1490 (C=Cstr), 1710(C=O str), 1250(C-O-C str) 1040(Ar C-NO₂str) cm^{-1} ; $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 6.63 (1H, s), 6.89 (1H, d), 7.35-7.50 (4H, 7.43 (ddd), 7.47 (ddd), 7.39 (ddd), 7.50 (1H, ddd), 7.72 (1H, ddd), 7.93-8.07 (3H, 8.04 (ddd), 7.97 (d)).MS: m/z = 321(M^+); *Anal.* Calcd for $\text{C}_{18}\text{H}_{11}\text{NO}_5$: C, 67.29; H, 3.45; N, 4.36; Found: C, 67.26; H, 3.42; N, 4.31.

3.1.3 3-(3-(m-tolyl) acryloyl)-2H-chromen-2-one (SC3)

It was obtained as yellow crystals (EtOH). mp 174-176°C; UV (EtOH) λ_{\max} (log ϵ) 286 (4.24) nm; R_f = 0.39 (n-hexane: ethyl acetate, 8:2) IR

ν_{\max} 3010(C-H aromatic), 1480 (C=C str), 1710(C=O str), 1250(C-O-C str); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 2.42 (3H, s), 6.67 (1H, s), 6.79 (1H, d), 7.18 (1H, ddd), 7.30 (1H, ddd), 7.36-7.53 (4H, 7.43 (ddd), 7.45 (ddd), 7.50 (ddd), 7.40 (ddd), 7.49 (1H, ddd), 7.67-7.83 (2H, 7.72 (ddd), 7.79 (d)).MS: m/z = 291(M^+); *Anal.* Calcd for $\text{C}_{19}\text{H}_{14}\text{O}_3$: C, 78.61; H, 4.86; O, 16.53; Found: C, 78.58; H, 4.87; O, 16.56.

3.1.45-methoxy-3-(3-(4-nitrophenyl) acryloyl)-2H-chromen-2-one (SC4)

This compound was obtained as yellow crystals (EtOH); mp 188-190°C; UV (EtOH) λ_{\max} (log ϵ) 296 (4.26) nm; R_f = 0.51 (n-hexane: ethyl acetate, 7:3) IR ν_{\max} 3010(C-H aromatic), 1480 (C=C str), 1710(C=O str), 1380 (C-H aliphatic bending), 1250(C-O-C str); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 3.82 (3H, s), 6.49 (1H, s), 6.58 (1H, dd), 6.96 (1H, d), 7.27 (1H, dd), 7.35-7.50 (3H, 7.39 (dd), 7.46 (ddd), 7.94 (1H, d), 8.04 (2H, ddd).MS: m/z = 351 (M^+); *Anal.* Calcd for $\text{C}_{19}\text{H}_{13}\text{NO}_6$: C, 64.96; H, 3.73; N, 3.99; Found: C, 64.93; H, 3.77; N, 4.01.

3.1.5 3-(5-(4-nitrophenyl)-4,5-dihydroisoxazol-3-yl)-2H-chromen-2-one (SR1)

It was obtained as yellowish green crystals (EtOH); mp 196-198°C; UV (EtOH) λ_{\max} (log ϵ) 296 (4.26) nm; R_f = 0.62 (n-hexane: ethyl acetate, 6:4) IR ν_{\max} 3130(C-H aromatic), 1530 (C=C str), 1720(C=O str), 1380 (C-H aliphatic bending), 1250(C-O-C str), 1256 (C-O-N str) and 1610 (C=N str) $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 3.05-3.22 (2H, 3.11 (dd), 3.17 (dd), 6.28 (1H, dd), 7.34 (1H, ddd, J = 7.7, 7.5, 1.1 Hz), 7.42 (1H, ddd), 7.62-7.73 (3H, 7.66 (ddd), 7.69 (ddd), 7.98-8.07 (4H, 8.02 (ddd), 8.04 (ddd), 8.02 (s)).MS: m/z = 336.07 (M^+); *Anal.* Calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_5$: C, 64.29; H, 3.60; N, 8.33; Found: C, 64.27; H, 3.64; N, 8.31.

3.1.6 3-(5-(m-tolyl)-4,5-dihydroisoxazol-3-yl)-2H-chromen-2-one (SR3)

It was obtained as yellow solid (EtOH); mp 173-175°C; UV (EtOH) λ_{\max} (log ϵ) 304 (4.26) nm; R_f = 0.67 (n-hexane: ethyl acetate, 6:4) IR ν_{\max} 3140(C-H aromatic), 1540 (C=C str), 1720(C=O str), 1380 (C-H aliphatic bending), 1250(C-O-C str), 1256 (C-O-N str) and 1610 (C=N str) $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 2.25 (3H, s), 3.03 (1H, dd), 3.20 (1H, dd), 6.19 (1H, dd), 7.14-7.23 (4H, 7.17 (ddd), 7.20 (ddd), 7.34 (1H, ddd), 7.42 (1H, ddd), 7.69 (1H, ddd), 8.01-

Table 1. Physicochemical data of substituted benzopyran-2-one Chalcones (SC1-SC6)

Com. Code	R	R1	Mol. Formula	Mol.Wt	Physical State	M.P ^o C	%Yield
SC1	H	NO ₂	C ₁₈ H ₁₁ NO ₅	321	yellow crystals	167-169	66
SC2	H	Cl	C ₁₈ H ₁₁ ClO ₃	311	yellow crystals	181-183	62
SC3	H	CH ₃	C ₁₉ H ₁₄ O ₃	291	yellow crystals	174-176	68
SC4	4-OCH ₃	NO ₂	C ₁₉ H ₁₃ NO ₆	351	yellow crystals	188-190	72
SC5	4-OCH ₃	Cl	C ₁₉ H ₁₃ ClO ₄	341	yellow crystals	202-204	74
SC6	4-OCH ₃	CH ₃	C ₂₀ H ₁₆ O ₄	320	yellow crystals	190-192	75

Table 2. Physicochemical data of 3 dihydro-1,2-oxazole benzopyran-2-one (SR1-SR6)

Com. Code	R	R1	Mol. Formula	Mol.Wt	Physical State	M.P ^o C	%Yield
SR1	H	NO ₂	C ₁₈ H ₁₂ N ₂ O ₅	336	yellowish green crystals	196-198	74
SR2	H	Cl	C ₁₈ H ₁₂ ClNO ₃	325	yellow crystals	202-204	70
SR3	H	CH ₃	C ₁₉ H ₁₅ NO ₃	305	yellow crystals	173-175	75
SR4	4-OCH ₃	NO ₂	C ₁₉ H ₁₄ N ₂ O ₆	366	yellow crystals	216-218	70
SR5	4-OCH ₃	Cl	C ₁₉ H ₁₄ ClNO ₄	355	yellow crystals	205-207	72
SR6	4-OCH ₃	CH ₃	C ₂₀ H ₁₇ NO ₄	336	yellow crystals	220-222	78

Table 3. Data of docking score of SR1-SR6

SR1	SR2	SR3	SR4	SR5	SR6	Ciprofloxacin
-2.82	-2.99	-3.38	-2.15	-2.60	-2.47	-4.94

Table 4. List of major interaction between amino acid and receptors5L3J

Comp. Code	Hydrogen bond	Hydrophobic bond	Charged negatives	Polar interaction
SR1	ASP-73	ALA-47, VAL-71,97,120 ILE 78,PRO-79	ASP-73,GLU-50	HID55,THR-165,ASN-46
SR 2	-	ALA-47,53,VAL43,120, 147,ILE-78,PRO-79	ARG-76,136	THR165,ASN-46
SR 3	VAL -19	ALA-18,VAL-19,ILE-23 ,LEU 126, 16, 98, PRO-23	ARG-20,22 LYS-21	THR-165
SR 4	-	ALA-47,VAL 43, 71, 120, 167,ILE-74,98,PRO-79	ASP-49,73 GLU-50	THR165,ASN-46
SR 5	-	ALA-47,VAL-43, 71, 120,167,ILE-78,94,MET-95,166	ASP-49,73GLU-50	THR165,ASN-46
SR 6	ARG-136	ALA-53,ILE-70,PRO-79	ASP-49,GLU-50	THR165,ASN-46,HID-55
Ciprofloxacin	VAL-71	ALA-47,VAL-43, 71, 120, 167,ILE-74,94,PRO-79	ASP-73,GLU-50	ASN-46,HID-55,GLU-72

Table 5. Antimicrobial activity 3 Dihydro-1,2-Oxazole Benzopyran-2-one Derivatives (SR1-SR6)

Comd Code	100µg/ml	50 µg/ml	25 µg/ml	12.5 µg/ml	6.25 µg/ml	3.12 µg/ml	1.56 µg/ml
SR1	-	-	-	-	-	+	+
SR2	-	-	-	-	-	+	+
SR3	-	-	-	-	-	-	+
SR4	-	-	-	+	+	+	+
SR5	-	-	-	-	+	+	+
SR6	-	-	-	-	+	+	+
Ciprofloxacin	-	-	-	-	-	-	-

+: Growth, -: No growth; Negative control: No growth observed, Positive control: growth observed

Compound	SR1	SR2	SR3	SR4	SR5	SR6	SR7
MIC (µg/ml)	6.25	6.25	3.12	25	12.5	12.5	1.56

5L3J - minimized - SR2

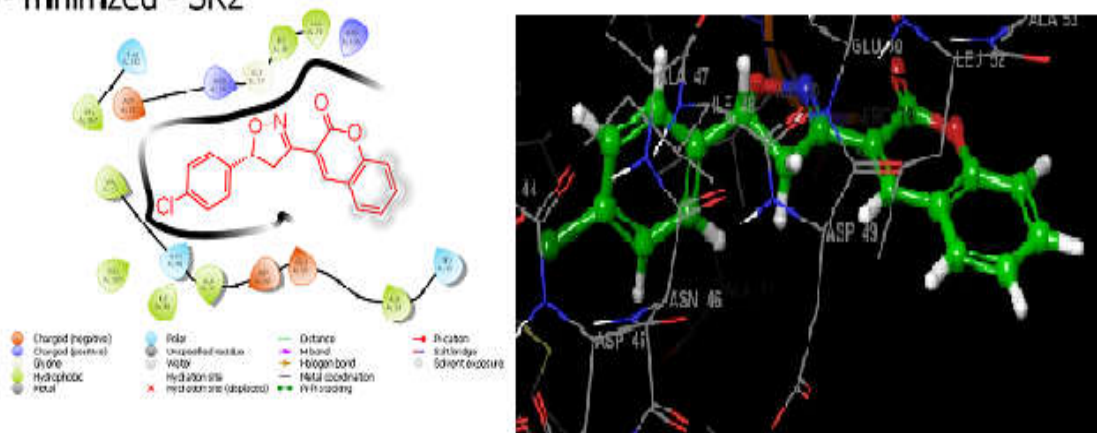


Fig. 1. 2-D and 3-D Ligand interaction compound SR2 with 5L3J receptor

5L3J - minimized - SR3

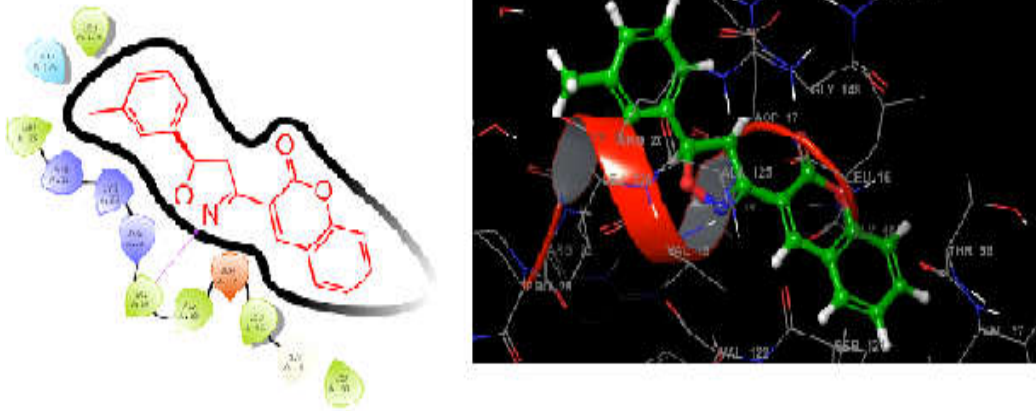


Fig. 2. 2-D and 3-D Ligand interaction compound SR3 with 5L3J receptor

5L3J - minimized - CIPROX

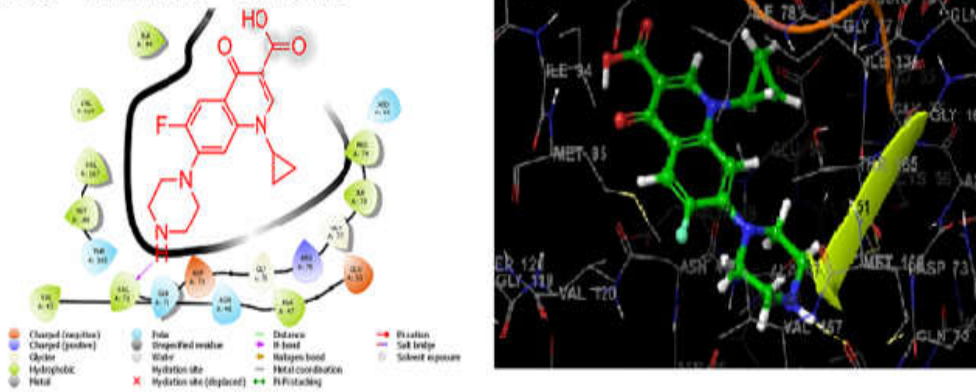


Fig. 3. 2-D and 3-D Ligand interaction compound ciprofloxacin with 5L3J receptor

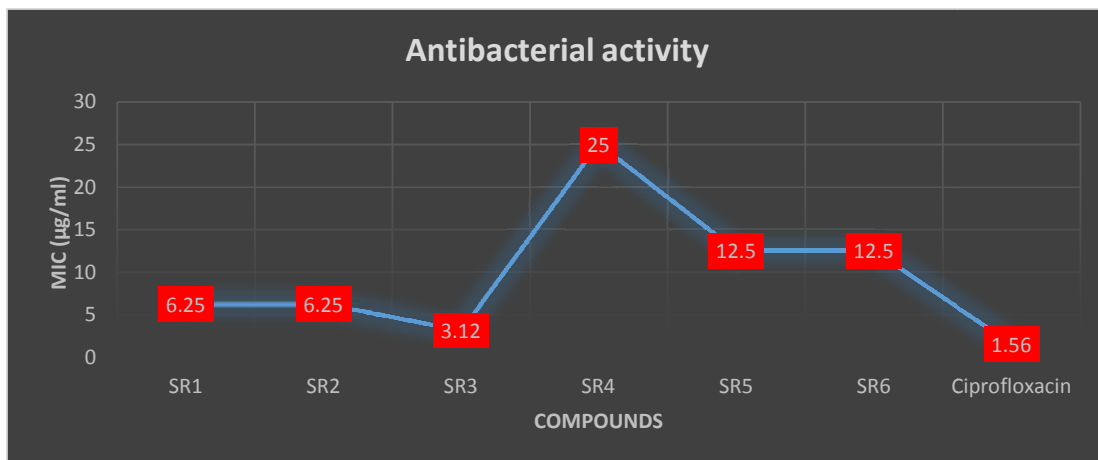


Fig. 4. MIC value of compounds SR1-SR6 by tube dilution method

8.07 (2H, 8.02 (s), 8.04 (ddd).MS: m/z = 305.07 (M⁺); *Anal.* Calcd for C₁₉H₁₅NO₃: C, 74.74; H, 4.95; N, 4.59; Found: C, 74.77; H, 4.98; N, 4.60.

3.1.7 3-(5-(4-chlorophenyl)-4,5-dihydroisoxazol-3-yl)-5-methoxy-2H-chromen-2-one (SR5)

It was obtained greenish yellow crystals (EtOH).It was obtained as orange solid; mp205—207°C; UV (EtOH) λ_{max} (log ε) 315 (4.28) nm;R_f= 0.57 (n-hexane: ethyl acetate, 5:5)IR ν_{max}3130(C-H aromatic), 1530 (C=C str), 1720(C=O str),1380 (C-H aliphatic bending), 1260(C-O-C str),810(C-Cl str),1256 (C-O-N str) and 1615(C=N str) ¹HNMR (CDCl₃, 400 MHz): δ 2.96 (1H, dd), 3.12 (1H, dd.), 3.89 (3H, s), 6.07 (1H, dd), 6.52 (1H, dd), 6.70 (1H, dd.), 7.51 (1H, t.), 7.66 (2H, ddd), 7.92 (1H, s), 8.02 (2H, ddd).MS: m/z = 355.07 (M⁺); *Anal.* Calcd for C₁₉H₁₄ClNO₄: C, 64.14; H, 3.97; N, 3.94; Found: C, 64.11; H, 3.99; N, 3.95.

4. CONCLUSIONS

Six substituted 3- dihydro-1,2-oxazole benzopyran-2-one derivatives were studied for three parameters; its synthesis, interaction with DNA gyrase B, and its antibacterial property. In this regards, synthesis of compounds SR1-SR6 had good yield in the range of 70-78 percent and compound SR6 had maximum yield of 78 percent, similarly these compounds interacted well with DNA gyrase B and also showed score in the range of -3.38 to -2.15 kcal/mol; compound SR3 had maximum score of -3.38 kcal/mol. As antibacterial agents the MIC value of compounds was ranges as 3.12 to 25 µg/ml and compound SR3 proved to be as best antibacterial agent with MIC Value 3.12 µg/ml.

Therefore it can be concluded that substituted oxazole benzopyran-2-one can be good antimicrobial agent against the various different bacteria microorganisms and can be further tested.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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