Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Research Article

SYNTHESIS, *IN SILICO* MOLECULAR DOCKING STUDIES AND ANTIMICROBIAL ACTIVITY OF NORFLOXACIN SCHIFF BASES

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ABSTRACT

The molecular docking and antimicrobial activity studies of synthesized norfloxacin schiff bases were performed, in order to provide insights into the mechanism of action of potential antimicrobial drugs for resistant microorganisms. antimicrobial activity of compounds was investigated in vitro under aseptic conditions, using the disk diffusion method, against various gram positive and gram negative pathogenic microorganisms such as Pseudomonas aeruginosa (P.A.), Staphylococcus aureus (S. aureus), Helicobacter pylori (H. pylori), Escherichia coli (E. coli), Methicillin-resistant Staphylococcus aureus (MRSA) and some fungal strains such as, Aspergillus fumigatus, Pneumocystis carinii and Aspergillus niger. A series of these compounds were prepared and have been shown to inhibit pathogenic growth, judging from the area of the zone of inhibition. The area of zone of inhibition of compounds found from 6 mm^2 to 48 mm^2. Among the synthesized compounds; compound SV-22 showed good activity against E. coli; Compound SV-23 showed good activity against S.aureus. compounds SV-22, SV-23, SV-24, SV-25, SV-26, SV-27 and SV-28 exhibited promising antibacterial activity against all the selected bacterial strains at 300 µg/ml dose.

Keywords: *Norfloxacin, Schiff bases, Antimicrobial, Molecular docking*

INTRODUCTION

Quinolones are synthetic antibacterial compounds based on a 4- quinolone skeleton. Quinolones have been clinically successful and more used to treat bacterial infection. Fluoroquinolones target bacterial type-II topoisomerases, generally DNA gyrase in gram negative bacteria and DNA topoisomerase in gram positive bacteria. The synthesis and evaluation of over 10,000 quinolone derivatives resulted in thorough knowledge of the structure-activity relationship for many quinolone substituents [1].

The first analogue of this class, nalidixic acid, was synthesized in 1962 and used for the treatment of urinary tract infections. It is more active against Gram-positive than Gram-negative organisms. Fluoroquinolones are extremely useful for the treatment of a variety of infections, including urinary tract infections, soft tissue infections, respiratory infections, bone-joint infections, typhoid fever, sexual transmitted diseases, prostatitis, community acquired pneumonia, acute bronchitis and sinusitis [2].

Most of the quinolones currently on the market or underdevelopment have only moderate activity against many Gram-positive cocci, including Staphylococci and Streptococci [3]. Norfloxacin is a second generation fluoroquinolone used to treat various bacterial infections. It is more effective against Gram-negative organisms than Gram-positive ones. This moderate activity against some of the Gram-positive species limited its use in bacterial infections [4]. Molecular docking plays an important role in the rational design of drugs. In the field of molecular modelling,

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docking is a method which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. Molecular docking can be defined as an optimization problem, which would describe the ‘‘best-fit’’ orientation of a ligand that binds to a particular protein of interest [5,6]. Schiff bases, heterocyclic compounds such as oxadiazoles and mercaptotriazoles were reported to have a broad spectrum of antibacterial activity [7,8].

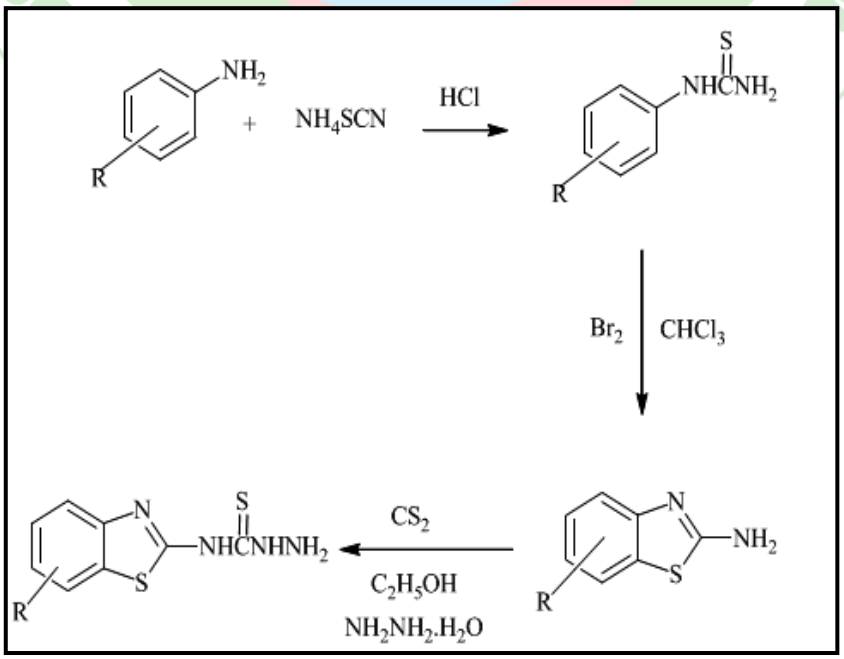
Different structural modifications in the quinoline nucleus have been made to increase antimicrobial activity and improve its performance. During 1980’s, it was discovered that a fluorine atom at position 6 and piperazine ring at position 7 greatly enhance the spectrum of activity of these antibiotics. In a structure activity relationship 4-oxo group is considered essential for antibacterial activity and therefore, modifications of this moiety has been not much explored. In the present study the modification of 4-oxo group has been explored to confirm whether this group is really essential or not. On the other hand 2- amino benzthiazole derivatives have shown promising antibacterial activities. Therefore, schiff bases of 2-amino benzthiazole with 4-oxo group of fluoroquinolones are expected to enhance antibacterial activity of fluoroquinolones [9,10].

Recently a relatively new approach to the rational design of antimicrobial agents has been introduced based on some new quinolone molecules. Ciprofloxacin, [1- cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(piperazinyl)-3-quinoline carboxylic acid], a typical second generation fluroquinolone, has been in clinical use for more than a decade and sold for $US 1.5 billion in 1996 [11].

In the present study, we introduced various Schiff bases, 1,3,4-oxadiazole- 5-thione and 4-amino-1,2,4-triazole-3-thione into the quinolone antibacterial norfloxacin at its C-6 position and to evaluate the effect of these groups on the antibacterial activity. Molecular docking study was then employed for the analysis with training set composed of 16 novel compounds whose inhibitory activities are unknown, in order to find out the molecular facilities responsible for biological activities. Then antibacterial screening was done to determine their MIC values.

Therefore, schiff bases of 2-amino benzthiazole with 4-oxo group of fluoroquinolones are expected to enhance antibacterial activity of fluoroquinolones. These compounds were prepared as per Scheme 1.

Step 1:-



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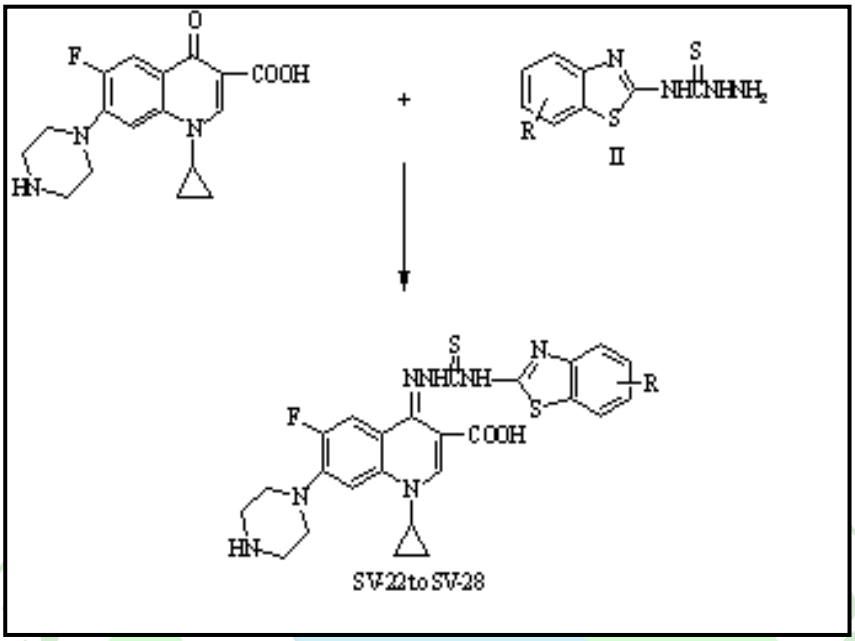
Step 2:-



Scheme 1: Synthesis of Schiff base of norfloxacin

MATERIALS AND METHODS

Chemistry-general aspects

The compounds described in this article were synthesized by the multi-step reaction protocol described in the Scheme 1. Melting points were taken in glass capillary tubes on a Veego VMP-1 Apparatus and are uncorrected. All the new compounds were characterized by spectroscopic data (^{1}HNMR, MS and IR). The spectral data of the new compounds reported in this study correlate with the proposed structures. The ^{1}H-NMR were recorded on Bruker DRX-300 (300 MHz FT-NMR) using DMSO as solvent and TMS as an internal standard. The IR spectra of compounds were recorded on Shimadzu FT-IR spectrometer using KBr pellet technique and are expressed in cm^{-1}. ESI-MS spectra were recorded on a Mariner System 5304 mass spectrometer.

General Procedure for Synthesis of Schiff bases

Compound I: Benzothiazole-2-yl amine

Compound [I] was synthesized by heating aniline (0.3 moles) and concentrated hydrochloric acid (25ml). 0.4 mole of saturated solution of ammonium thiocynate in water (30gm in 60ml water) was added slowly in above solution. The reaction mixture was boiled until the solution got turbid. The solution was poured in ice water. The precipitate was filtered and recrystallized from ethanol to give phenylthiourea. Phenylthiourea (0.1 mole) in glacial acetic acid (75ml) was brominated by using bromine solution in glacial acetic acid (5%) till the orange yellow color appeared. The slurry was poured in cold water and make alkaline with 50% aq. Ammonia solution. The precipitate was filtered and washed with water, dried and recrystallize by using ethanol. The melting point was found to be 156°C.

Compound II: N-(benzothiazol-2-yl)hydrazine carbothioamide

0.01mole of product I was dissolved in ethanol using potassium hydroxide as base. An equi-molar amount of CS_2 and hydrazine hydrate were then separately added drop wise to the solution of product I with stirring at 0-5°C temperature. A light yellow solid was precipitated at the end of the reaction. The product obtained was filtered and recrystallized with ethanol.

Schiff base of norfloxacin with N-(benzothiazol-2-yl)hydrazine carbothioamide

Equimolar quantities (approx. 0.01mole) of Compound II and Norfloxacin were separately

dissolved in a minimum amount of ethanol and then they were mixed together followed by addition of 5 ml glacial acetic acid. The solution was refluxed for 10 hrs. Then cooled to room temperature and poured into ice cold water .The solid product was collected through filtration and then were air dried. The product was re-dissolved in ethanol for re-crystallization and filtered to give a product. The physicochemical properties of the Schiff bases are described in Table 1. The spectral characteristics are given in Table 2.

In-silico drug docking

Binding affinities of the synthesized compounds into topoisomerase-II The molecular docking studies showed a good correlation between their MIC and auto dock binding free energy. Almost all the compounds used for docking showed best fit Root Mean Square Difference (RMSD) value of 0.000 with topoisomerase II (3ILW). Among the compounds tested for docking study, 3a showed high affinity with low energy of -7.4 kcal/mol with employed protein. Binding between 3ILW and compound 3a indicates very good inhibition with calculated rmsd. Compounds 3, 3a, 3b, 3c, 3d, 3e, 3f, 4, 4a, 4b, 4c, 5, 5a, 5b, 5c showed good inhibition with affinity range between -7.4 to -6.4 kcal/mol. Docking between 1 and 2 with 3ILW protein indicated weak inhibition with low energy value of -6.3 kcal/mol with calculated rmsd. The statistical analysis revealed that most of the compounds showed a significant linear regression coefficient (R^2 = 0.8–0.9)[12].

Antimicrobial studies

Two factors influence the Minimal Inhibitory Concentration (MIC) of fluoroquinolones; the rate of penetration into the bacterial cell and its inhibitory activity of DNA gyrase. Although, most of the studies proposed that a substituent at tenth position of the norfloxacin ring is related to the binding site with enzyme through electrostatic interactions, our aim here was to study the influence the structural change of the carboxylic group of the quinolone ring. The results of antibacterial activity of norfloxacin derivatives against a panel of Gram positive and Gram negative bacteria are represented in Table 1 in comparison with that of the reference drug norfloxacin. The compounds were screened for antimicrobial activity against three Gram-positive bacterial strains (*Staphylococcus aureus, Staphylococcus epidermidis,* and *Bacillus subtilis*) and three Gram-negative bacterial strains (*Escherichia coli, Shigella* and *Pseudomonas aeruginosa*) and one fungal strain (*Candida albicans*) by twofold serial dilution method. DMSO was used as control, showed no zone of inhibition. The compounds exhibited good antibacterial effect towards gram positive species when compared to the standard norfloxacin. At the same time, the analogues were retaining antibacterial activity towards gram negative species when compared to standard norfloxacin. Among the synthesized compounds tested for antimicrobial activity compounds 3a–3f, 4a–4c, 5a–5c have good antibacterial activity against *S. aureus* and 3a, 3b, 3f showed good MIC value of 0.125 lg/ml. The modification of carboxylic acid group into Schiff bases leads to increase the antibacterial activity against gram positive species. The presence of N=C moiety may be the reason for this in compounds 3a–f. Introduction of heterocyclic compounds into the carboxylic acid group also increase the antibacterial activity particularly against the gram positive species. The other titled compounds also had antimicrobial activity at a concentration of 0.25 lg/ml and showed good activity against *S. aureus*. The synthesized compounds 3b, 3f, and 4c showed good antimicrobial activity at a concentration of 0.25 lg/ml against *S. epidermidis* and *B. subtilis* when compared to the standard. The other titled compounds showed antimicrobial activity at a concentration of 0.5 lg/ml and had good activity against *S. epidermidis* when compared to standard. The synthesized compounds showed moderate antibacterial activity against gram negative organisms[13,15] (Tables 2, 3).

RESULTS AND DISCUSSION

In-silico molecular docking

The 3D structure of Topoisomerase II chain A (3ILWA) was extracted from protein data bank at the NCBI (National Centre for biotechnology information, http:// www.ncbi.nib.hlm.gov). 3ILWA is a crystal structure of the DNA Gyrase. The synthesized compounds which are

analogues of norfloxacin were taken for prediction of 3D structure and energy was minimized for flexible docking using Argus lab (Argus Lab 4.0.1, Mark A. Thompson, Planaria Software LLC, Seatle, WA, http://www.arguslab.com). The structures of these synthesized compounds and enzyme are shown in Fig. 1. In the docking study receptor was treated as a rigid body and a grid potential was used to evaluate the scoring function. Here 3D structure of protein Topoisomerase chain A was used as receptor and all the synthesized compounds were used as ligands. In Autodock vina 4.0 (Trott and Olson 2010), nonpolar hydrogen atoms were removed from the receptor file and their partial charges were added to the corresponding carbon atoms. The grid calculation were set up, 4.9 3 -20.8 3 64.6 A° grid originating at 40, 40, 40 with resolution of 0.375 A° , respectively, was generated around the compound.

Antibacterial screening

The *in vitro* antibacterial activity of Schiff bases of norfloxacin was investigated against gram positive organisms (*Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus)* and gram negative organisms *(Helicobacter pylori, Escherichia coli* and *Pseudomonas aeruginosa).* All analogues, showed comparable antibacterial activity at the dose 300 µg/ml against all the tested strains. Results indicate that compounds SV-22 showed maximum activity against *E. coli* (zone of inhibition=34 mm^2 and MIC=40 µg/ml at the dose of 300 µg/ml) in comparison to other strains used by us. Compounds SV-23, SV-24 and SV-28 showed maximum activity against *S. aureus* (zone of inhibition=37 mm^2, 28 mm^2 and 31 mm^2 respectively, MIC=57 µg/ml, 80 µg/ml and 80 µg/ml respectively at the dose of 300 µg/ml) in comparison to other strains. Compound SV-22 and SV-25 showed maximum activity against *S. aureus* (for both the compounds, zone of inhibition=26 mm^2 and MIC=88 µg/ml at the dose of 300 µg/ml) in comparison to other strains.

Antifungal screening: Norfloxacin is an antibacterial drug and inactive against fungi, in order to evaluate the result of addition of different functional groups to its basic structure, the antifungal activity of its derivatives was carried out against; *A. fumigatus*, *P. carinii* and *A. niger* and results are summarized in Tables 4. It was found from the result that compound SV-28 has got enhanced activity against all the antifungal strains used. The compound SV-27 also showed moderate activity against *A. fumigatus*.

Table 1: Physicochemical properties of the Schiff bases (SV-22 to SV-28)

SN	Code	Mol. Formula	Mol. Weight	Melting Point	% Yield	Solubility	Elemental Analysis (%) Calculated/Found		
							C	H	N
1.	SV-22	$C_{24}H_{24}FN_7O_2S_2$	525.14	247°C	5 6%	Ethanol	54.84 54.74	4.60 4.56	18.65 18.64
2.	SV-23	$C_{25}H_{26}FN_7O_2S_2$	539.15	256°C	41%	Ethanol	55.64 55.61	4.86 4.82	18.17 18.20
3.	SV-24	$C_{26}H_{28}FN_7O_2S_2$	553.17	217°C	46%	Ethanol	56.40 56.30	5.10 5.07	17.71 17.65
4.	SV-25	$C_{25}H_{26}FN_7O_2S_2$	539.15	267°C	42%	Ethanol	55.64 55.54	4.86 4.82	18.17 18.12
5.	SV-26	$C_{26}H_{28}FN_7O_2S_2$	553.17	217°C	46%	Ethanol	56.40 56.30	5.10 5.07	17.71 17.65

6.	SV-27	$C_{26}H_{28}FN_7O_2S_2$	553.17	217°C	46%	Ethanol	56.40 56.30	5.10 5.07	17.71 17.65
7.	SV-28	$C_{26}H_{28}FN_7O_2S_2$	553.17	217°C	46%	Ethanol	56.40 56.30	5.10 5.07	17.71 17.65

Table 2: Spectral data of the Schiff bases (SV-22 to SV-28)

S. No.	Compound Name	Code	IR
1.	4-(2-(benzothiazol-2-ylcarbamothioyl)hydrazono)-1-ethyl-6-fluoro-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-22	C=O 1618, COOH 1709 $\nu_{C=O}$ in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178cm^{-1}; Ar.C-Hstr,1621/ 1535/1460cm^{-1}; Ar. C=C ring str. 3305cm^{-1}; C-H methyl str. 3429cm^{-1}; N-H str. 1305cm^{-1}; sec N-H str.1113cm^{-1}; C=S 1210 cm^{-1}; C-F str. 1277 cm^{-1}; C-N (piperazine) 1027 cm^{-1};
2.	1-ethyl-6-fluoro-4-(2-(4-methylbenzothiazol-2-ylcarbamothioyl)hydrazono)-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-23	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr.1113.3cm^{-1}:Ar–N str.
3.	1-ethyl-6-fluoro-4-(2-(4-ethylbenzothiazol-2-ylcarbamothioyl)hydrazono)-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-24	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr.1113.3cm^{-1}:Ar–N str.
4.	1-ethyl-6-fluoro-4-(2-(5-methylbenzothiazol-2-ylcarbamothioyl)hydrazono)-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-25	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr. 1113.3cm^{-1}:Ar–N str.
5.	(E)-4-(2-(4,5-dimethylbenzo[d]thiazol-2-ylcarbamothioyl)hydrazono)-1-ethyl-6-fluoro-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-26	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr.1113.3cm^{-1}:Ar–N str.
6.	(E)-4-(2-(5,6-dimethylbenzo[d]thiazol-2-ylcarbamothioyl)hydrazono)-1-ethyl-6-fluoro-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-27	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr.1113.3cm^{-1}:Ar–N str.
7.	(E)-4-(2-(4,7-dimethylbenzo[d]thiazol-2-ylcarbamothioyl)hydrazono)-1-ethyl-6-fluoro-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid	SV-28	IR C=O 1618, COOH 1709 (C=O) in COOH, NH 3600-3200, C=C (Ar nucleus) 1544/1500, C=N 3178.0cm^{-1};Ar.C-Hstr, 1621.8,1535.1, 1460.6cm^{-1}; Ar. C=C ring str.3305.1cm^{-1} C-H methyl str. 3429.9cm^{-1} :N-H str. 1305.4cm^{-1}sec N-Hstr.1113.3cm^{-1}:Ar–N str.

Table 3: Antibacterial activity of the Schiff bases (SV-22 to SV-28)

S. N.	Compound Code	Conc. (µg/ml)	P. aeruginosa		H. pylori		E. coli		S. aureus		M.R.S.aureus	
			ZOI	MIC (µg/ml)	ZOI	MIC (µg/ml)	ZOI	MIC (µg/ml)	ZOI	MIC (µg/ml)	ZOI	MIC (µg/ml)
1.	SV-22	300	22	100	8	300	34	40	26	88	19	114
		100	8		0		14		9		7	
		30	0		0		6		0		0	
2.	SV-23	300	24	100	10	240	23	88	37	57	22	100
		100	8		0		9		14		8	
		30	0		0		0		0		0	
3.	SV-24	300	18	133	12	200	16	133	28	80	24	100
		100	6		0		6		10		8	
		30	0		0		0		0		0	
4.	SV-25	300	19	114	8	300	21	100	26	88	16	133
		100	7		0		8		9		6	
		30	0		0		0		0		0	
5.	SV-26	300	18	133	14	133	27	80	22	100	18	133
		100	6		6		10		8		6	
		30	0		0		0		0		0	
6.	SV-27	300	12	200	10	240	18	133	19	133	12	200
		100	0		0		6		6		0	
		30	0		0		0		0		0	
7.	SV-28	300	14	133	8	300	28	80	31	80	16	133
		100	6		0		10		10		6	
		30	0		0		0		0		0	
8.	Norfloxacin (Control)			0.12		1.04		0.07		0.12		0.19

Table 4: Antifungal activity the Schiff bases (SV-22 to SV-28)

Compound Code	*A. niger*	*P. carinii*	*A. fumigatus*
SV-22	0	10	0
SV-23	16	0	0
SV-24	0	0	0
SV-25	14	12	8
SV-26	8	0	0
SV-27	0	0	8
SV-28	8	0	0

A. niger= Aspergillus niger, P. carinii= Pneumocystis carinii, A. fumigates=Aspergillus fumigatus

Table 5: Toxicology Analysis

Ligad name	*ADMET_ BBB*	*ADMET BBB_ Level*	*ADMET_ Absorption _ Level*	*ADMET_ Solubility*	*ADMET_ Solubility_ Level*	*ADMET_ hepatotoxicity*	*ADMET_ hepatotoxicity _ Probability*	*ADMET_ CYP2D6*	*ADMET_ CYP2D6_ Probability*	*ADMET_ PPB_ Level*	*TOPKAT_ Ames_ Prediction*	*TOPKAT_ Ames_ Probability*	*TOPKAT_ Ames_ Score*
SV22	**-1.146**	**3**	**0**	**-5.432**	**2**	**0**	**0.384**	**0**	**0.455**	**0**	**Non-Mutagen**	**0.328014**	**-11.22**
SV23	**-0.996**	**3**	**0**	**-5.872**	**2**	**1**	**0.562**	**0**	**0.475**	**0**	**Non-Mutagen**	**0.430116**	**-9.07**
SV24	**-0.855**	**3**	**0**	**-6.128**	**1**	**1**	**0.609**	**0**	**0.386**	**0**	**Non-Mutagen**	**0.309318**	**-11.62**
SV25	**-0.996**	**3**	**0**	**-5.854**	**2**	**1**	**0.523**	**1**	**0.504**	**0**	**Non-Mutagen**	**0.445284**	**-8.74**
SV26	**-0.846**	**3**	**0**	**-6.292**	**1**	**1**	**0.536**	**0**	**0.386**	**0**	**Non-Mutagen**	**0.45572**	**-8.52**
SV27	**-0.846**	**3**	**0**	**-6.273**	**1**	**0**	**0.397**	**0**	**0.425**	**0**	**Non-Mutagen**	**0.470411**	**-8.20**
SV28	**-0.846**	**3**	**0**	**-6.31**	**1**	**1**	**0.649**	**0**	**0.316**	**0**	**Non-Mutagen**	**0.474438**	**-8.11**

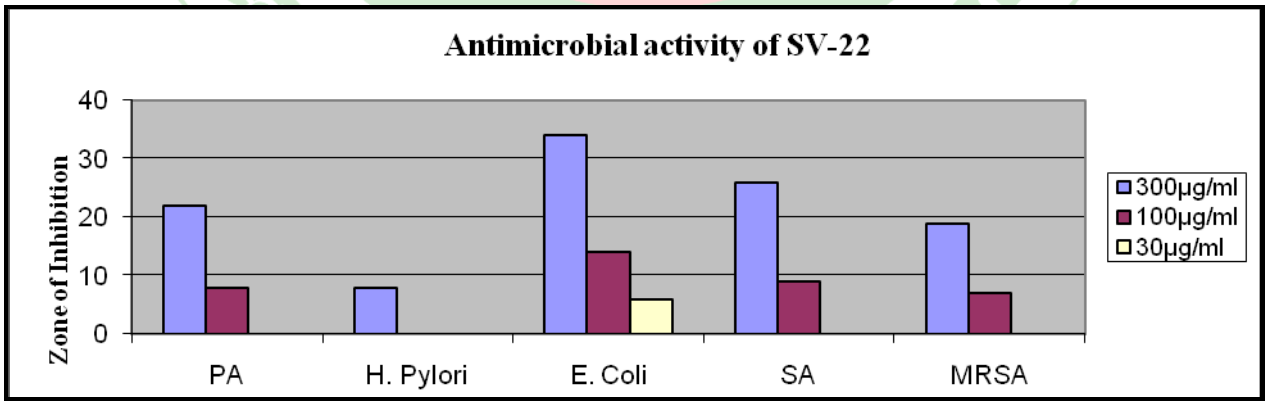


Figure 1: Zone of Inhibition of the Schiff bases SV-22 at Different Concentrations

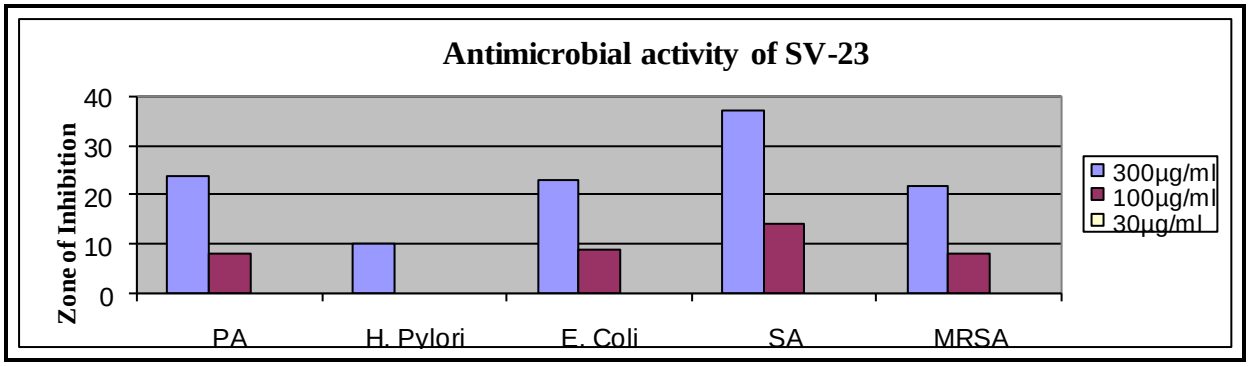


Figure 2: Zone of Inhibition of the Schiff bases SV-23 at Different Concentrations

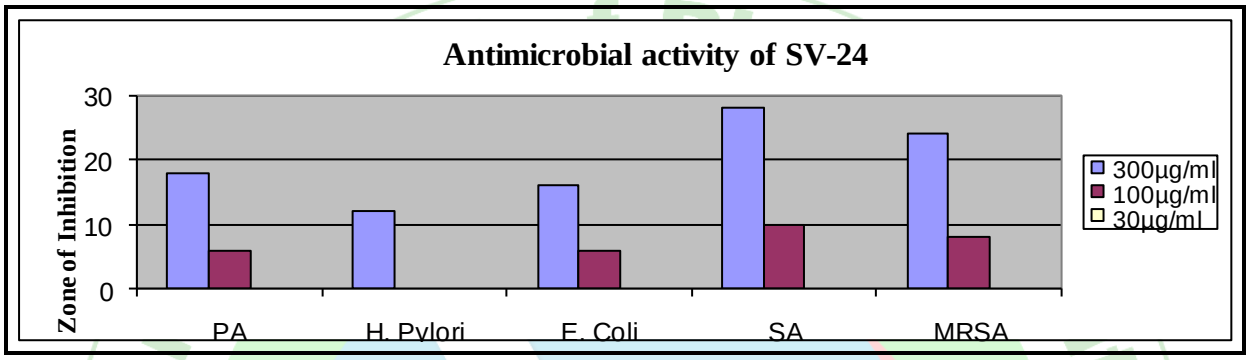


Figure 3: Zone of Inhibition of the Schiff bases SV-24 at Different Concentrations

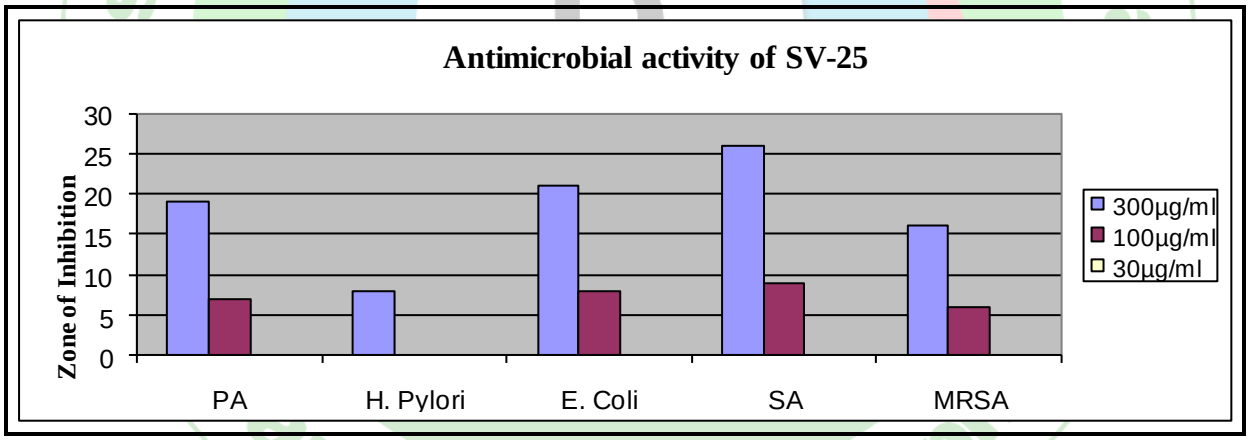


Figure 4: Zone of Inhibition of the Schiff bases (SV-25 at Different Concentrations

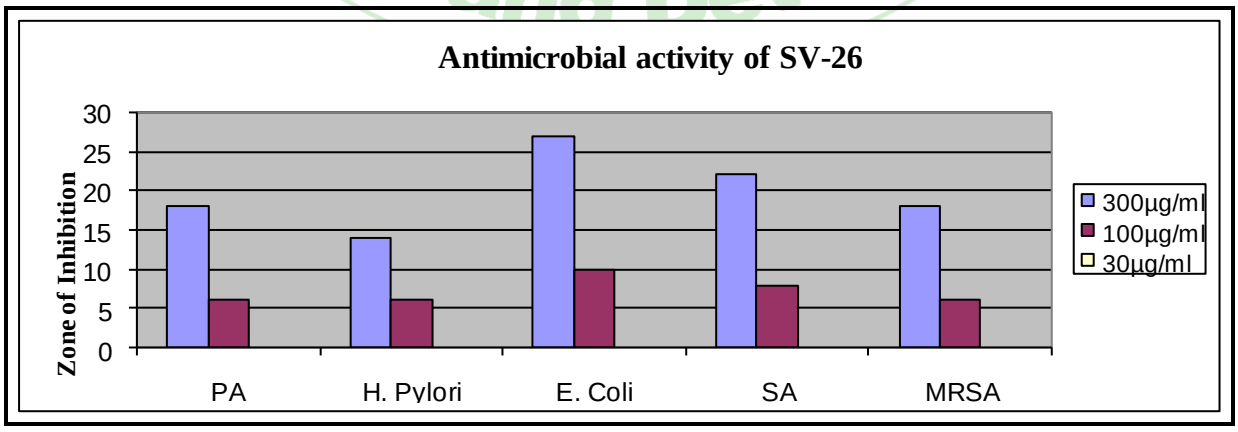


Figure 5: Zone of Inhibition of the Schiff bases SV-26 at Different Concentrations

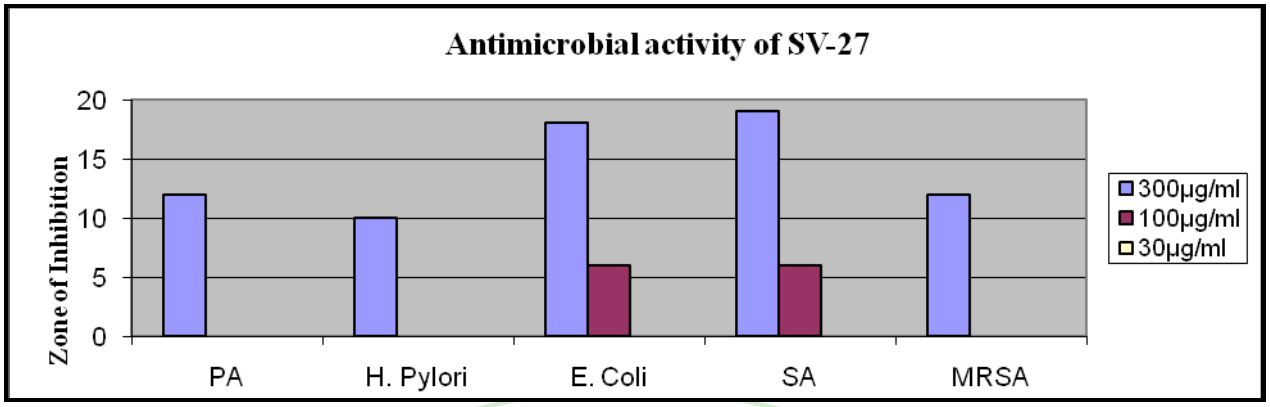


Figure 6: Zone of Inhibition of the Schiff bases SV-27 at Different Concentrations

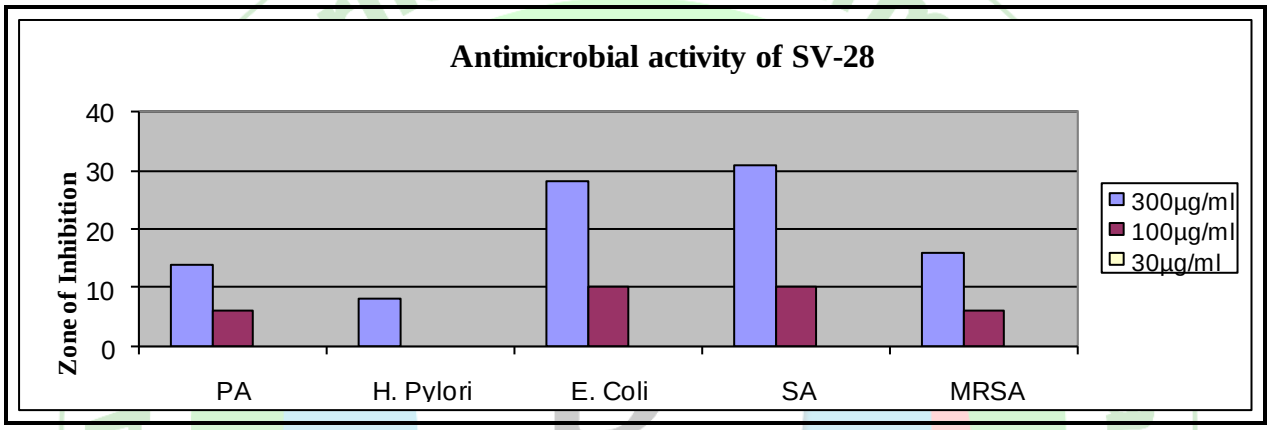


Figure 7: Zone of Inhibition of the Schiff bases SV-28 at Different Concentrations

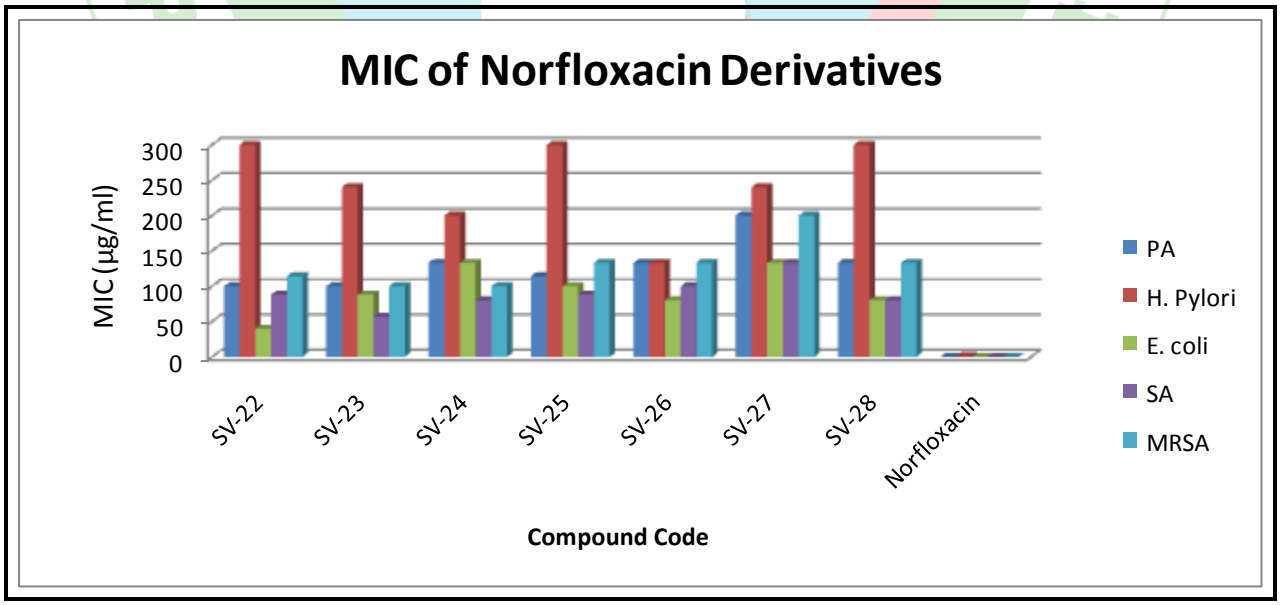


Figure 8: Minimum Inhibitory Concentration (MIC) the Schiff bases (SV-22 to SV-28)

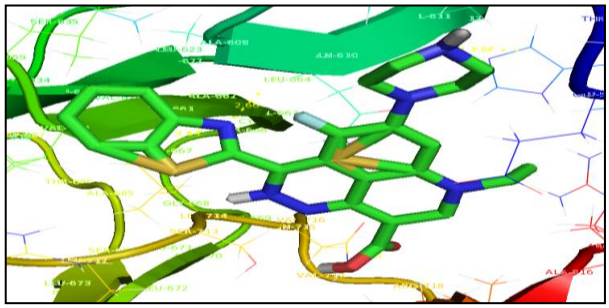


Fig 9: Best affinity mode of synthesized compounds SV-22

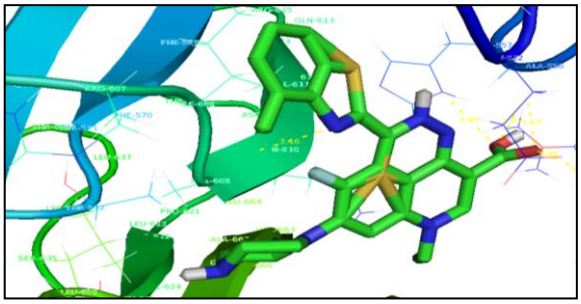


Fig. 10: Best affinity mode of synthesized compounds SV-23

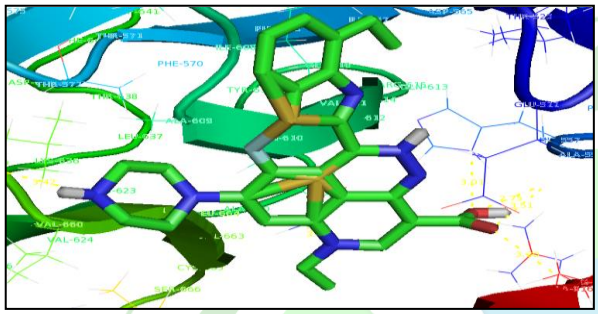


Fig11: Best affinity mode of synthesized compounds SV-24

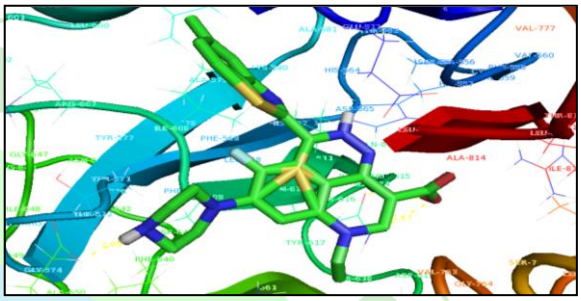


Fig. 12: Best affinity mode of synthesized compounds SV-25

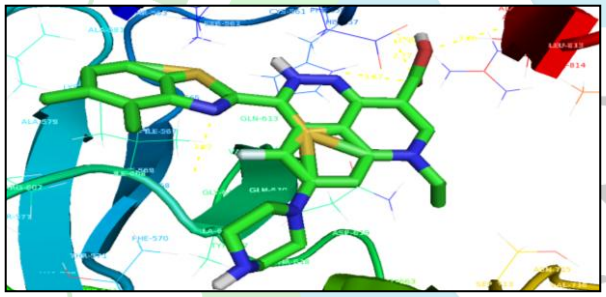


Fig13: Best affinity mode of synthesized compounds SV-26

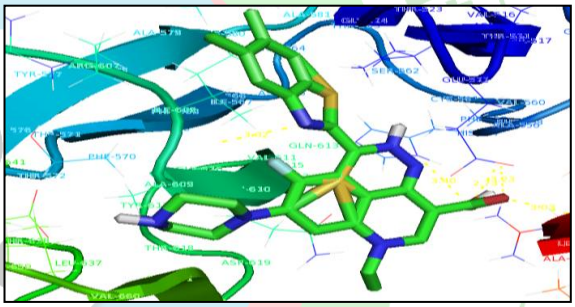


Fig. 14: Best affinity mode of synthesized compounds SV-27

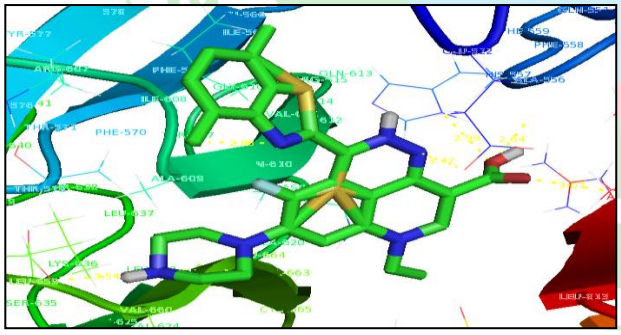


Fig15: Best affinity mode of synthesized compounds SV-28

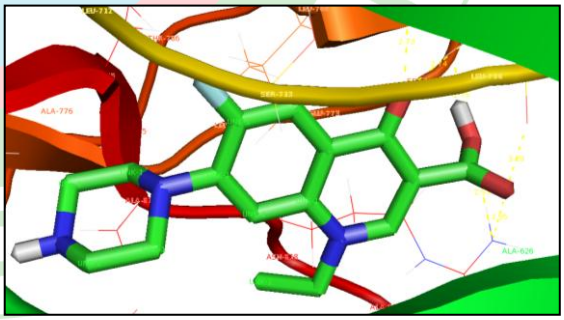


Fig16: **Norfloxacin (Reference Drug)**

SUMMARY

Antimicribial activity was performed on all synthesized compounds. From all the synthesized compounds, compound Compound SV-22 showed good activity against *E. coli;* Compound SV-23 showed good activity against *S.aureus.* Compounds SV-22, SV-23, SV-24, SV-25, SV-26, SV-27 and SV-28 exhibited promising antibacterial activity against all the selected bacterial strains at 300 µg/ml dose.

Compound SV-28 has got enhanced activity against all the antifungal strains used. The compound SV-27 also showed moderate activity against *A. fumigatus*.

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