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Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

SYNTHESIS, CHARACTERIZATION, MOLECULAR DOCKING STUDY OF GRAPHENE OXIDE CATALYZED NOVEL SCHIFF BASE AND THEIR ANTIMICROBIAL ACTIVITIES

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ABSTRACT

A straight forward and greener protocol has been disclosed for the synthesis of 2-(benzlidene)-1-(3-chloropyridin-2-yl) hydrazine derivatives via three component reaction of 3-chloro-2-hydrazinopyridine with substituted benzaldehyde and graphene oxide by using very convenient reaction conditions. The synthesized compounds have been characterized by FT-IR, ^{1}HNMR, ^{13}CNMR and LCMS. The molecular docking studies of synthesized compounds were conducted and found the possible information between synthesized compounds and DNA gyrase enzyme. Compounds (**3a-e**) have shown stronger inhibition of DNA gyrase compared to chlorobiocin. These compounds have shown reasonably good antibacterial and antifungal activities compared to the standard drugs Griseofulvin and Cefixime.

Keywords: Schiff bases, Aromatic aldehydes derivatives, Graphene Oxide, Toluene

1. INTRODUCTION

Schiff bases (SBs) are an important class of material science which ars widely used in various industrial and biomedical applications [1]. In addition, they have shown various biocidal activities such as anti-malarial, anti-bacterial, anti-fungal, anti-tuberculosis, insecticidal etc [2-7]. SB based complexes have also shown different biological activities like anti-cancer, anti-tumor, anti-alzieimer, anti-convulsant and many more [8-10]. SB based complexes have also been used in gas storage, dye sensitized solar cells and separation science due to its highly porous and larger surface area of metal organic framework [11-13]. SB is an aldehydes or ketone analogue containing nitrogen in which the C=O group is substituted by C=N-R group. It is typically prepared by nucleophlic addition followed by the condensation of an aldehydes or ketone with primary amine [14]. It is a building block which can be used as organomettalic reagents to give nucleophlic addition, cyclization and cycloaddition reactions [15]. SB-based complexes with varying metal oxidation states using green technology are important protocols for the design of environment friendly materials [16]. Use of catalyst in green technology has been identified as significant role in enhanced reaction selectivity, increased energy efficiency and lower byproduct formation [17]. Metal based catalysts such as copper, iron, zinc, manganese etc. are conventional catalyst for many organic reactions but the major disadvantages of this type of catalysts having intrinsic toxicity. Graphene oxide (GO) has been used as catalyst for many organic reactions due to their larger surface area, existence of different oxygen based functional groups like hydroxyl (OH), epoxy (-O-) and carboxylic acid (COOH) on its surface [18] with superb an excellent mechanical strength and electrical conductivity [19]. These functional groups on GO surface serves as anchoring sites for chemical functionalization and immobilization of inorganic complexes and nano particles [20].

In this paper, we have described the synthesis of SB, derived from 3-chloro-2-hydrazinopyridine and benzaldehyde and its chloro, methoxy, methyl and hydroxy substituted benzaldehyde in the presence of GO as a catalyst. These compounds were characterized by FT-IR, NMR and LC-MS.

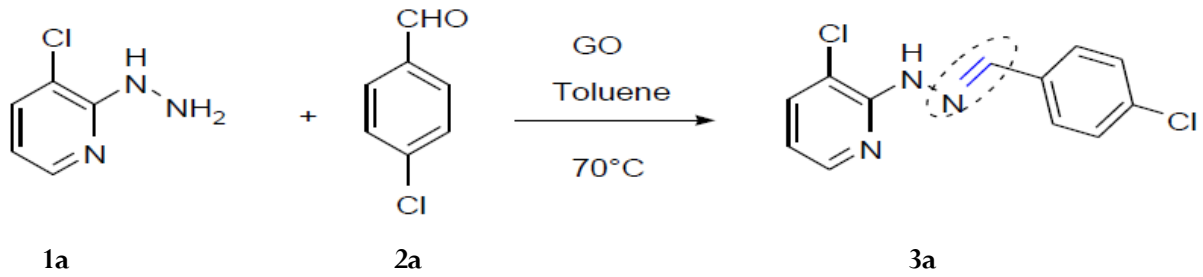
2. METERIAL AND METHODS

2.1. Chemistry and characterization

All the chemicals were purchased from Merck, India and were of analytical grade and double distilled water was used. GO was prepared from graphite powder using Hummer method [21]. FT-IR spectra were taken

on a Perkin Elmer spectrometer in KBr pellets and were reported in cm^{-1}. ^{1}H-NMR spectra were recorded on a JEOL (400 MHz) spectrometer, and chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Coupling constants (J) are reported in Hz. ^{13}C-NMR spectra were recorded on a JEOL (100MHz) spectrometer with complete proton decoupling and chemical shifts are reported in parts per million relative to the solvent resonance as the internal standard (DMSO-d_6).

Initially, 3-chloro-2-hydrazinopyridine (1a, 1.0 eq) condense with 4-chlorobenzaldehyde (**2a**, 1.05 eq) in presence of 10 times toluene as a solvent at 50°C and reaction time was 300 min to get **3a** compound with 60% yield (Table 1 -entry1). Further, all the reagents parameter were kept constant except reaction temperature 60°C, 80°C and 90°C and reaction time 180 min, 150 min and 150 min to get 3a compound with 62%, 70% and 71% yields respectively (Table 1, entry 2-4). In aforesaid entry 1-4 yield were less due to unreacted 3-chloro-2-hydrazinopyridine (**1a**). Further for more studies, we have used additionally 10% graphene oxide (GO) as a catalyst in reaction mixture for enhancimg the reaction conversion and yield. Reaction carried out at temperature 60°C, 70°C and 80°C and reaction time 120 min, 60 min and 60 min get 94 %, 96 % and 96 % yield respectively with complete consumption of **1a**. For screening of solvent, we have used ethanol instead of toluene in presence of GO catalyst (10 %) and reaction temperature was 70°C , 78°C, reaction time 120 min, 150 min to get **3a** compound in83-84 % yields respectively (Table 1 entry 8-9). Reaction without GO catalyst in ethanol solvent and reaction temperature 78°C was carried out to get 75 % yields (Table 1 entry 10). On the basis of aforesaid entry 1-10, we have finalized 3-Chloro-2-hydrazinopyridine (1a, 1.0 eq), substituted benzaldehyde (**2a** ,1.05 eq) and GO catalyst (10 %) in 10 times toluene and reaction temperature 60°C. All the parameters were as described in Scheme-1.



1a **2a** **3a**

Scheme 1: Optimization of 3a compound via catalyzed process using grapheme Oxide

Table 1: Schiff base optimization of 3a compound

Entry	Catalyst	Solvent	Reaction temp(°C)	Time(min)	Yield (%)
1	-	Toluene	50	300	60
2	-	Toluene	60	180	62
3	-	Toluene	80	150	70
4		Toluene	90	150	71
5	GO	Toluene	60	120	94
6	GO	Toluene	70	60	96
7	GO	Toluene	80	60	96
8	GO	Ethanol	70	120	83
9	GO	Ethanol	78	150	84
10	-	Ethanol	78	150	75

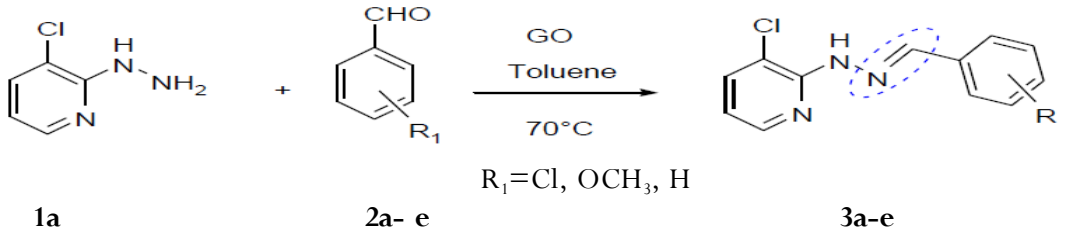
2.2. Novel Schiff base synthesis of 3a- e

Synthesis of 3a-e was performed by the reaction of 3-chloro-2-hydrazinopyridine (1a, 1.0 m-eq), substituted benzaldehyde (2a-e, 1.05 eq) and GO catalyst (10%) in 10 times toluene and reaction temperature 70°C. Completion of reaction conversion was checked by thin layer chromatography (TLC), reaction mass was filtered through hyflow bed powder and bed wash with

toluene and distilled out with 50% toluene under vacuum, filtered through paper and solid compound was washed with chilled Toluene and Hexane to get pure compounds (3a to 3e) product (Table-2 entry 1-5). All the parameters attained in Scheme-2 and the possible mechanism is depicted in Scheme 3.

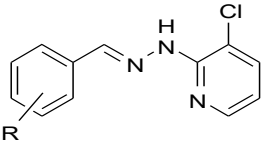
2.3. Reaction conditions

Synthesis of 3a-e by reaction of 1a (1.0 eq), 2a-e (1.05 eq), graphene Oxide (10 mol %), and in presence of 10 times toluene, reaction time 45-60 min in dried flask at 70°C was performed and 96%, 93%, 93%,95% and 94% yield, respectively, was obtained (Table 2 entry 1-5). Reaction parameters have been shown in Scheme-2.

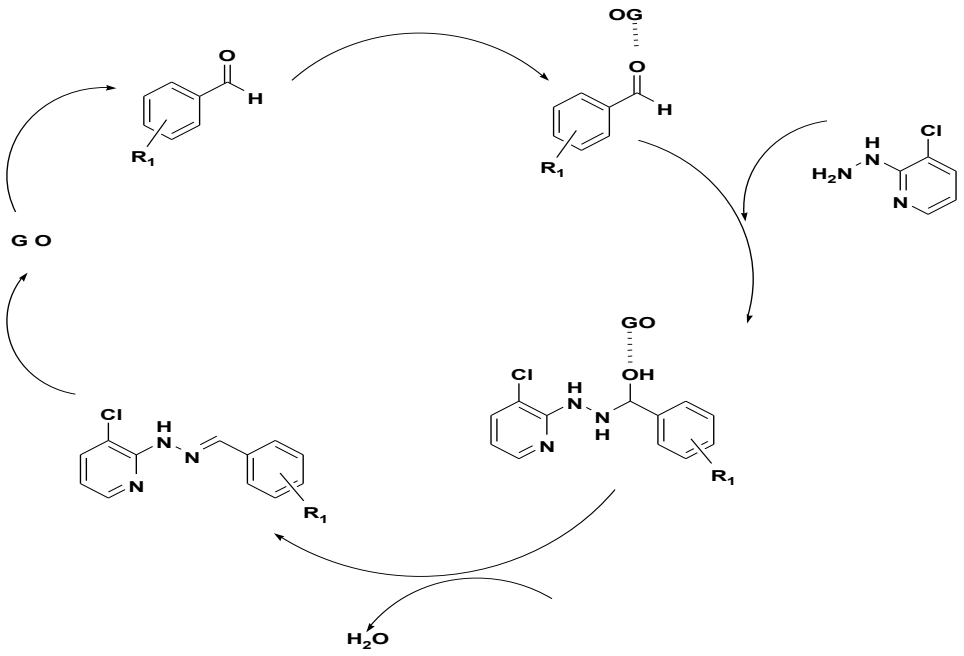


Scheme 2: Synthesis of novel Schiff base (3a-e)

Table 2: Synthesis of novel Schiff base from diverse substituted benzaldehyde *via* graphene oxide.



Entry	3-chloro-2-hydrazinopyridine	Substituted benzaldehyde(2a-e)	Product (3a-e)	Reaction temp.	Reaction time	Yield (%)
1	1a	4-chlorobenzaldehyde	3a R= 4-chloro	70°C	60 min	96
2	1a	2-chlorobenzaldehyde	3b R= 2-chloro	70°C	60 min	93
3	1a	4-hydroxybenzaldehyde	3c R=4-hydroxy	70°C	60 min	93
4	1a	3-methoxybenzaldehyde	3d R=3-methoxy	70°C	60 min	95
5	1a	benzaldehyde	3e R=H	70°C	60 min	94



Scheme 3: Possible path ways of Schiff base (3a-e)

2.4. Characterization of compounds

2.4.1. 2-(4-chlorobenzlidene)-1-(3-chloropyridin-2-yl)hydrazine (3a)

Lemon yellow solid, Yield: 96 %. M.P.: 170°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 8.38 (s,1H),8.19-8.18 (d, J=4.0 Hz,1H), 7.76-7.74 (dd, J=4.0 Hz, 1H), 7.70-7.67 (d, J=12 Hz,2H), 7.49-7.46 (m,2H),6.86-6.84 (m,1H),^{13} C NMR (100 MHz, DMSO-d_6): δ 150.50, 146.63, 141.46, 137.69, 134.27, 133.21, 128.81, 127.93, 116.14, 113.86 . IR (KBr) : N-H : 3011 cm^{-1}, imine –C=N: 1587 cm^{-1}, C-Cl : 706 cm^{-1}, para- di substituted benzene: 814 cm^{-1} , (E) trans: 954.8 cm^{-1}. MS (FAB; m/z): 267. M.F. $C_{12}H_9Cl_2N_3$, M. W: 266, HPLC Purity (Qualitative): 99.81%

Note: -NH group is disappearing in NMR after D_2O exchange.

2.4.2. 2-(2-chlorobenzlidene)-1-(3-chloropyridin-2-yl)hydrazine (3b)

Off white solid, Yield: 94 %. M.P.: 184°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 8.80 (s,1H), 8.20-8.19 (dd, J=4.0 Hz,1H), 8.04-8.02 (dd, J=8.0 Hz, 1H), 7.79-7.77 (dd, J=8.0 Hz,1H), 7.48-7.47 (m,1H),7.39-7.36 (m,2H), 6.88-6.85 (m,1H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 150.4, 146.44, 138.77, 137.86, 132.60, 132.28, 130.23, 129.78, 127.41, 126.45, 116.31, 114.07. IR (KBr): N-H : 3004cm^{-1} , imine - C=N: 1599 cm-1, C-Cl : 702 cm-1, ortho-disubstituted benzene: 754.94 cm^{-1} ,(E) Trans: 947cm-1. MS (FAB; m/z): 267. M.F. $C_{12}H_9Cl_2N_3$, M. W.: 266, HPLC Purity (Qualitative): 99.97%

Note: -NH group is disappearing in NMR after D_2O exchange.

2.4.3. 2-(2-hydroxybenzlidene)-1-(3-chloropyridin-2-yl) hydrazine (3c)

White solid, Yield: 93 %. M.P.: 150°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.91 (s, 1H), 10.85 (s,1H), 8.58 (s,1H),8.21-8.20 (dd, J=4.0 Hz,1H), 7.80-7.78 (dd, J=8.0 Hz, 1H), 7.38-7.36 (dd, J=4.0 Hz,1H), 7.26-7.22 (m,1H), 6.92-6.87 (m,3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.17, 149.99, 146.78, 144.69, 137.72, 130.12, 129.56, 129.10, 119, 116.35, 116.28, 113.71. IR (KBr): -OH: 3360 cm^{-1}, N-H: 3008 cm^{-1}, imine -C=N: 1611 cm-1, ortho-disubstituted benzene: 755 cm^{-1}, (E) trans: 956.95 cm^{-1}. MS (FAB; m/z): 248. M.F. $C_{12}H_{10}ClN_3O$, M. W.:247. HPLC Purity (Qualitative): 99.56%

Note: -NH and -OH group is disappearing in NMR after D_2O exchange.

2.4.4. 2-(3-methoxybenzlidene)-1-(3-chloropyridin-2-yl)hydrazine (3d)

Off white solid**,** Yield: 95 %. M.P.: 161°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s,1H), 8.37 (s,1H), 8.18-8.17 (dd, J=4.0 Hz,1H), 7.76-7.74 (dd, J=8.0 Hz,1H), 7.34-7.32 (m,1H), 7.24-7.22 (m,2H),6.95-6.94 (m,1H), 6.83-6.82 (m,1H), 3.79 (s,3H)^{13}C NMR (100 MHz, DMSO-d_6): δ 159.53, 150.58, 146.46, 142. 97, 137.68, 136.72, 129.82, 119.27, 115.90, 114.89, 113.88, 110.86, 55.14. IR (KBr): -OCH_3: 2850 cm^{-1}, N-H : 3015 cm^{-1}, imine-C=N: 1599 cm^{-1}, meta-substituted benzene: 785 cm^{-1} and 689 cm^{-1}, (E) trans: 978 cm^{-1}. MS (FAB; m/z): 262. M.F. $C_{13}H_{12}ClN_3O$, M. W.:261, HPLC Purity (Qualitative): 99.97%

Note: -NH group is disappearing in NMR after D_2O exchange.

2.4.5. 2-(benzlidene)-1-(3-chloropyridin-2-yl) hydrazin (3e)

Light yellow solid, **Yield**: 94 %. M.P.: 141°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s,1H), 8.37 (s,1H), 8.18-8.17 (dd, J=4.0 Hz,1H), 7.76-7.74 (dd= 8.0 Hz,1H), 7.34-7.32 (m,1H), 7.24-7.22 (m,2H), 6.95-6.94 (m,1H), 6.83-6.82 (m,1H),3.79 (s,3H) ^{13}C NMR(100MHz,DMSO-d_6): δ 159.53,150. 58,146.46, 142.97,137.68,136.72,129.82,119.27,115.90,114.89, 113.88,110.86,55.14. IR (KBr): N-H: 3271 $cm^{-1,}$ imine-C=N: 1670 cm^{-1}, mono-substituted benzene: 747.6 cm^{-1} and 690 cm^{-1},(E) trans: 952 cm^{-1}. MS (FAB; m/z): 232. M.F. $C_{12}H_{10}ClN_3$, M. W.:231. HPLC Purity (Qualitative): 97.90%

Note: -NH group is disappearing in NMR after D_2O exchange.

2.5. Molecular docking study

The Schiff base structural motif possesses extensive spectrum of biological activities. DNA gyrase play a vital role in selection of bacterial death. It has been come into sight that enormous Schiff bases derivatives have antibacterial property over inhibition of DNA gyrase. Based on these details we resolve to synthesize novel Schiff base derivatives in order to estimate their antibacterial effects [22].

2.5.1. Ligand preparation

The chemical structures of ligands were drawn by Chemdraw and minimized by MM2 force field and 3D

geometry optimization calculations for each ligand were performed.

2.5.2. Protein synthesis

The crystal structure of the DNA gyrase (PDB code 1KZN) with resolution 2.3Å was selected as the protein target downloaded from PDB (https://www.rcsb.org/).

Ligand and water molecules were removed distinction to protein file. The resulting crystallography structure was imported in Auto Dock [23].

2.5.3. Docking

Docking was performed with the routine process and default parameters of molecular docking Auto Dock 4.2 software and implemented pragmatic free energy function. Only polar hydrogens were added to the protein and all water molecules were removed from the protein file in Auto Dock Tools. The inhabitant ligand, chlorobiocin, was redocked to the binding spot. The grid box was centered with the coordinate sx = 18.258, y = 28.181, z = 36.291 for DNA gyrase (PDB code 1KZN). Grid box dimensions were 12 × 26 × 16 with a 1 Å grid points spacing. Grid maps were intended by Autogrid4. A lamarckian hereditary algorithm agenda with an adaptive whole technique investigate. Auto dock was used to calculate the different ligand conformers. At the end of docking experiment with 200 runs, a cluster analysis was performed. Conformations were clustered according to the root mean square deviation tolerance of 2.0 Å and were ranked according to the binding free energy. A variety of conformations of these ligands obtained from the docking process, the conformation with the most excellent scored pose and with the lowest binding energy was chosen for these ligands. Ligand plot software was worn to examine the hydrophobic and hydrogen bonding exchanges between the ligand and the enzyme [24].

2.6. Anti microbial screening

For antimicrobial study [25] four bacterial and two fungal strains were selected. Gram positive bacterial strains include *Staphylococcus aureus, Streptococcus Pyogenesand gram negative Escherichia Coli and Pseudomonas aeruginosaand.* Fungal strains *Candida albicans, Aspergillus clavatus* have been taken based on their clinical and pharmacological significance. Muller Hinton agar test was used for antimicrobial susceptibility test against bacteria. Bacterial strains were matured in Mueller-Hinton agar (MHA) plates (bacteria were mature in the nutrient puree at 37°C and kept up on nutrient agar slants at 4°C), PDA media can be used for the isolation and antimicrobial assay of fungi, at 28°C.

2.6.1. Zone of inhibition determination

Antifungal and anti-bacterial *in-vitro* activities were studied for synthesized samples. Activities of samples against bacterial and fungal pathogens were screened by the agar disk distribution technique (ADM) [26]. Schiff bases were dissolved in dimethylsulfoxide (DMSO), untainted by filtration using sintered funnel flask, and kept at 4°C. Intended for Kirby-Bauer test two Gram-positive, two Gram-negative, and two fungal strains were used as a standard antibiotic for the sake of comparison of the results with standard drugs cefixime and griseofulvin. The synthesized products have been screened for their *in-vitro* actions beside the gram positive *Staphylococcus aureus*. Schiff bases and standard drugs (5, 25 and 50 μg/ml) have been primed by using distilled H_2O nutrient agar tubes. Mueller-Hinton sterile agar plates were planted with indicator bacterial strains (10^8cfu) at 37°C for 3 hours. The Kirby-Bauer Test was studied for bacteria strain for 48 to 96 hours for selected fungal strains at 28°C after 18 to 24 hours of incubation at 37°C. This test is used to check the zone and size of inhibition and its values<8 mm were measured as not active.

3. RESULTS AND DISCUSSION

3.1. Molecular docking study

The type of molecular interactions, interacting atoms, proteins ligands and docking scores are shown in Table 3. The docking conformations of Schiff base derivatives in human DNA gyrase are given in Table -3 and 2D structure of the synthesized compounds (**3a-e**) and Chlorobiocin are given in Figs. 1-6. All the docking conformations of Schiff base (**3a-e**) showed highest docking scores *i.e.* -5.69, -5.93, -5.12, -5.37 and -5.33 respectively when compared to standard antibiotic drug chlorobiocin (-1.99), due to Schiff base interaction in addition to conventional hydrogen bonding with active pocket of DNA gyrase enzyme.

3.2. Pharmacology

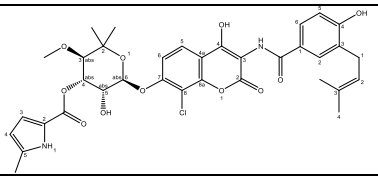
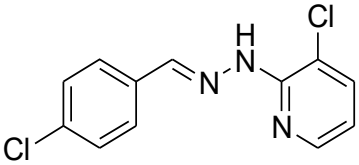
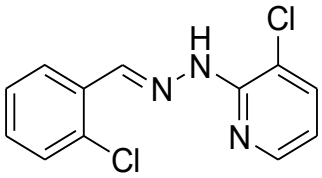
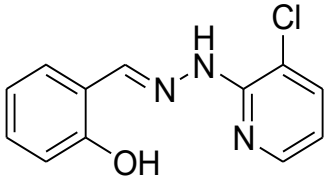
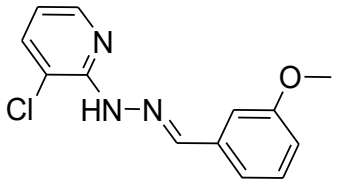
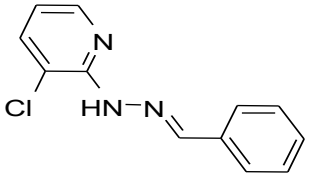
3.2.1. Antibacterial properties

All the synthesized compounds have shown a potent antibacterial activities against Gram positive and Gram negative bacteria. Among all tested compounds, compound **3b** showed an excellent antibacterial activities against *Staphylococcus aureus* whereas compound

3b against *Streptococcus pyogenes* and their zone of inhibition was 66%, and 86% respectively. Compound **3c** showed highest antibacterial activities against *Escherichia coli* with 79% of inhibition of growth. Compound **3d** showed more antibacterial activities against *Pseudomonas aeruginosa* and its zone of inhibition was found about 59% (Table 4).

The compounds 3a-e showed reasonably good anti-bacterial activities against *pathogenic bacteria* compared to standard drug (Cefixime). Zone of inhibition for cefixime against different pathogenic bacteria are tabulated in Table 5.

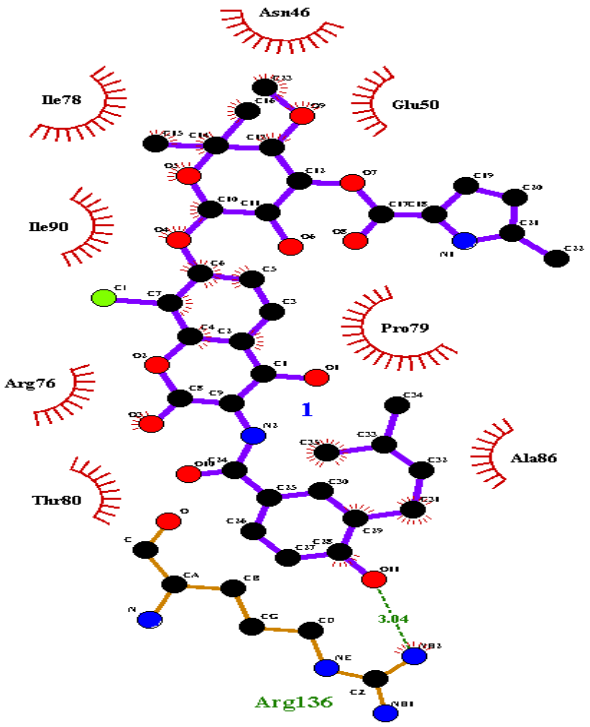
Table 3: Energy-based interactions and hydrogen bonds for five novel Schiff base derivatives and chlorobiocin docked into DNA gyrase.

Compound No.	Structure	Estimated Free Energy of Binding (Kcal/mol)	Hydrogen Bond	Interactive amino acids
Chlorobiocin		-1.99	Arg136 (3.04 Å)	Asn46, Glu50, Pro79, Ala86, Thr80, Arg76, Ile90, Ile78
3a		-5.69	-	Asp73,Val43, Thr165, Ala47,Ile78,Gly77, Pro79, Glu50,Val120, Val167,Val71
3b		-5.93	Asn46 (3.15 Å)	Glu50, Gly77, Ile78,Ala47, Thr165, Val71,Val167, Val43,Asp73,Val120
3c		-5.12	Asn46 (3.22 Å)	Glu50, Gly77, Ile78, Val71, Asp73, Ala47, Val43, Val167
3d		-5.37	-	Pro79, Glu50, Gly77, Ile78, Val71, Ala47, Gln72, Thr165, Asn46, Val120, Val43, Asp73
3e		-5.33	-	Pro79, Glu50, Ile78, Asn46, Val167, Val71, Val120, Asp73, Thr165, Ala47, Val43, Gln72, Gly77

3.2.2. Antifungal activity

Compounds also showed reasonably good antifungal activity. Compound 3a showed 73% zone of inhibition and 3b, 3c, 3d and 3e showed 68%, 64%, 70% and 64% respectively against *Candida albicans* fungus. Compound 3a was having highest anti fungal potential with the percentage inhibition of 70% against *Aspergillus clavatus* (table 6).

Compounds 3a-e has shown reasonably good antifungal activities against *Candida albicans* and *Aspergillus clavatus* compared to standard drug (Griseofulvin). Zone of inhibition for griseofulvin against fungi is tabulated in Table 7.



Hydrogen bonds are shown by green dashed line

Fig. 1: Docked conformation of compound chlorobiocin in the binding site of DNA gyrase

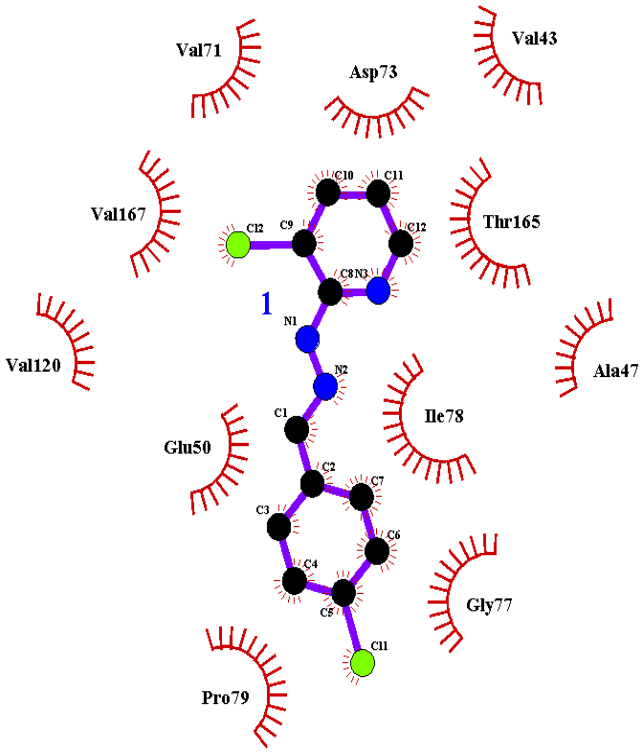
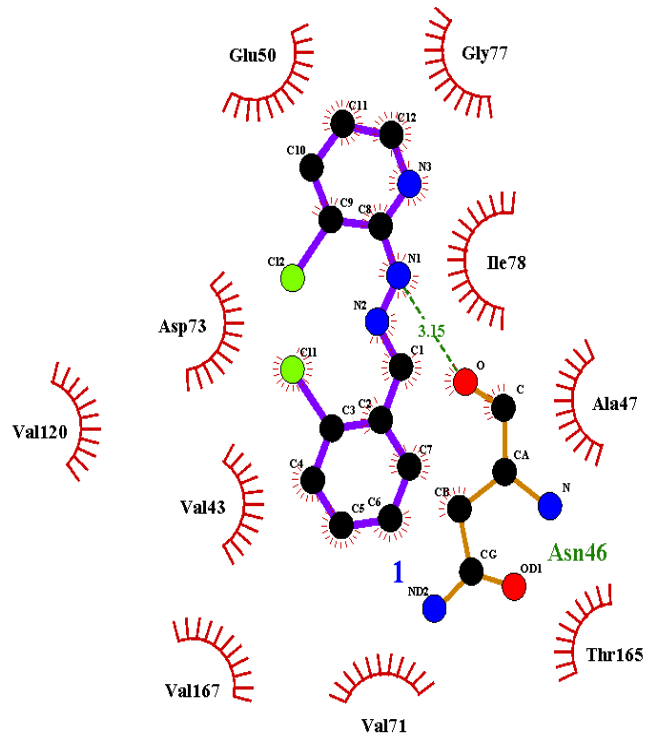
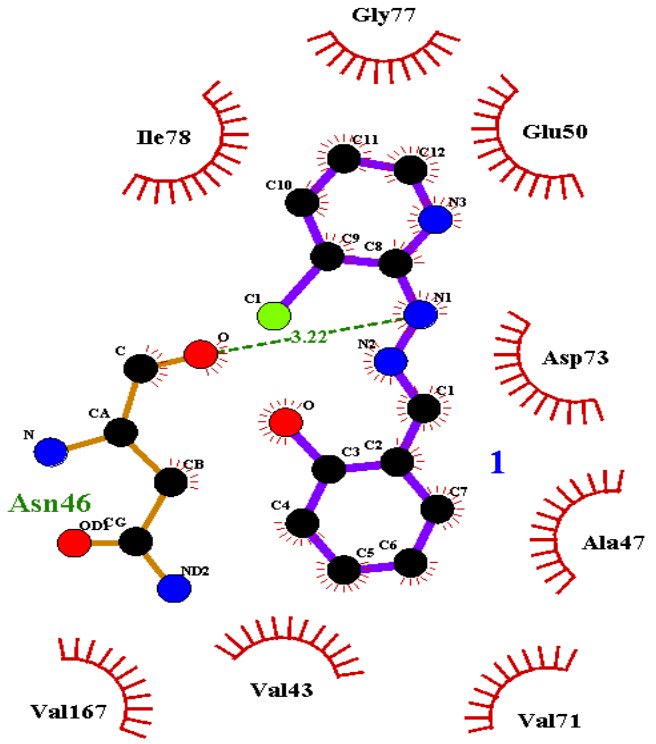


Fig. 2: Docked conformation of compound 3a in the binding site of DNA gyrase.



Hydrogen bonds are shown by green dashed line

Fig. 3: Docked conformation of compound 3b in the binding site of DNA gyrase



Hydrogen bonds are shown by green dashed line

Fig. 4: Docked conformation of compound 3c in the binding site of DNA gyrase

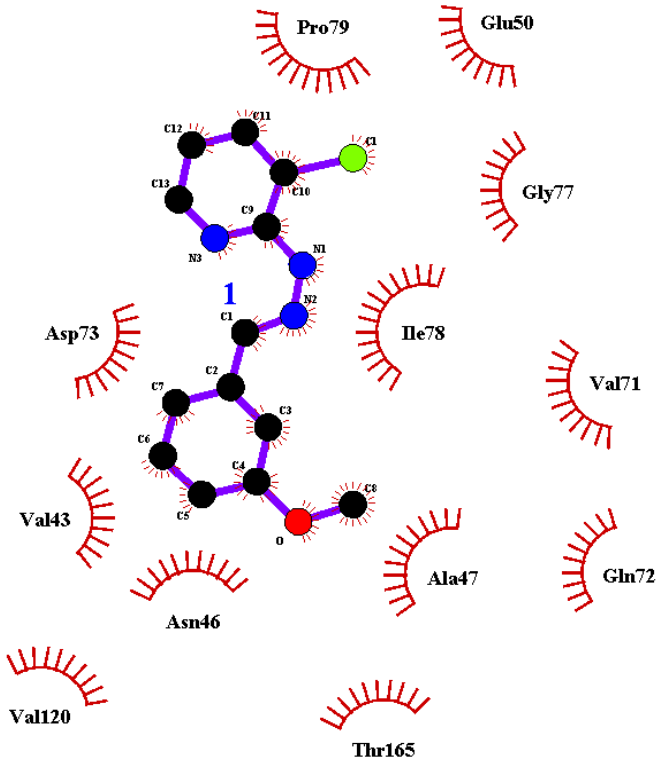


Fig. 5: Docked conformation of compound 3d in the binding site of DNA gyrase

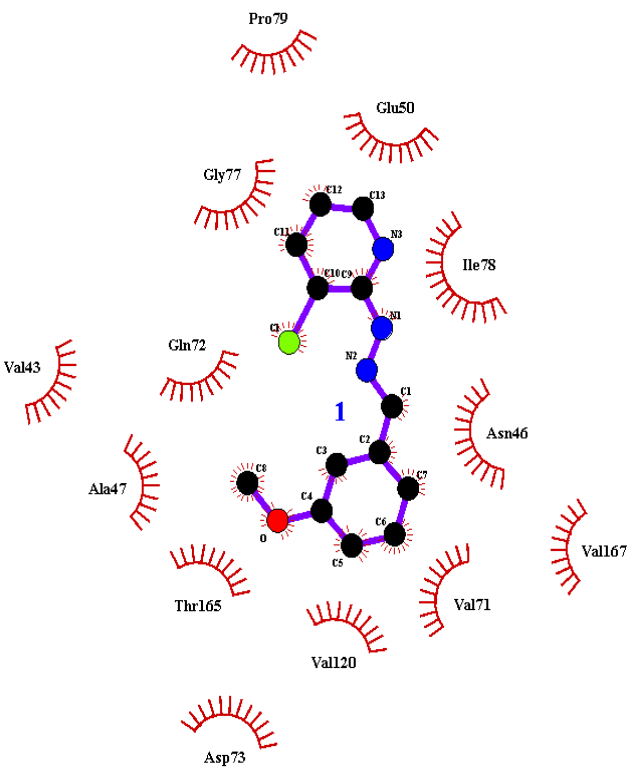


Fig. 6: Docked conformation of compound 3e in the binding site of DNA gyrase

Table 4: Antibacterial activity of samples

Group	Concentration	Zone of inhibition in mm (%)			
	(µg/ml)	*S. aureus*	*S. pyogenes*	*E. coli*	*P. aeruginosa*
3a	25 µg/ml	16 (58%)	18 (73%)	18 (63%)	13 (51%)
3b	25 µg/ml	19 (66%)	27 (86%)	18 (63%)	16 (46%)
3c	25 µg/ml	18 (63%)	13 (51%)	22 (79%)	14 (56%)
3d	25 µg/ml	16 (58%)	25 (78%)	18 (63%)	19 (59%)
3e	25 µg/ml	15 (54%)	22 (67%)	17 (61%)	18 (56%)

Table 5: Antibacterial properties of standard antibacterial (zone of inhibition in mm)

Drug	Concentration (µg/ml)	Micro Organisms			
		Zone of barrierin mm			
		S. aureus	*S. pyogenes*	*E. Coli*	*P. aeruginosa*
Cefixime	5	22	19	18	20
	25	29	26	25	28
	50	33	35	36	37

Table 6: Antifungal activity of samples

Group	Concentration	Zone of inhibition in mm (%)	
	(µg/ml)	*Candida albicans*	*Aspergillus clavatus*
3a	25 µg/ml	23 (73%)	22 (70%)
3b	25 µg/ml	21 (68%)	20 (64%)
3c	25 µg/ml	20 (64%)	21 (68%)
3d	25 µg/ml	22 (70%)	18 (55%)
3e	25 µg/ml	20 (64%)	21 (68%)

Table 7: Antifungal activity of anti fungal drugs standards *(zone of inhibition in mm)*

Standard Drug	Concentration (µg/ml)	Micro Organisms	
		Zone of barrier in mm	
		Candida Albicans	*Aspergillusclavatus*
Griseofulvin	5	34	35
	25	47	43
	50	52	55

4. CONCLUSION

Schiff bases were prepared from 3-Chloro-2-hydrazinopyridine and substituted benzaldehyde in the presence of graphene oxide catalyst. These compounds were characterized by FT-IR, NMR and Mass spectroscopy. The 2-(benzlidene)-1-(3-chloropyridin-2-yl) hydrazine derivatives has shown reasonably good antibacterial activities and antifungal activities against different pathogens. Docking studies confirmed that 2-(benzlidene)-1-(3-chloropyridin-2-yl)hydrazine derivatives have better interaction with DNA gyrase compare to standard antibiotic drug chlorobiocin, which is probably attributed to hydrogen bonding. It would be an important cost effective greener route for the preparation of clinical drugs for pharmaceutical industries.

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