Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(17):10-15
(http://www.derpharmachemica.com/archive.html)

Synthesis, Characterization, Molecular Docking and Antimicrobial Activity of Nicotinic Acid Derived N-acylhydrazones

Soujanya M[1*], Rajitha G[2]

[1]*Department of Chemistry, Gokula Krishna College of Pharmacy, JNTUA, Sullurpeta-524121, Andhra Pradesh, India*
[2]*Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam (Women's University), Tirupati-517502, Andhra Pradesh, India*

ABSTRACT

A series of new nicotinic acid hydrazones were synthesized by the condensation of compound (2) with different aromatic/heteroaromatic aldehydes in acidic condition. Compound (2) was obtained by the reaction of nicotinic acid hydrazide with 4-aminoacetophenone under reflux condition and characterized by the Infra-Red (IR), Proton Nuclear Magnetic Resonance (^{1}H-NMR), Mass spectral and elemental analysis. All the title compounds were screened for antimicrobial activity (Five strains: Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Bacillus subtilis and Candida albicans), in silico and molecular docking studies. The results revealed that compounds 3f, 3d and 3g exhibited 3.12 µg/ml, 6.25 µg/ml and 12.5 µg/ml as Minimum Inhibitory Concentration (MIC) towards E. coli, P. aeruginosa, C. albicans strains respectively, which is comparable to standard (3.12 and 6.25 µg/ml as MIC respectively) and also showed good docking score (around-6.50) than standard ciprofloxacin (-4.74) predicted by XP GLIDE module of Schrodinger suite against FAB protein. All the derivatives obeys Lipinski rule of five and also compound 3c have higher Pa value towards anti-tuberculosis predicted by Prediction of Activity Spectrum of Substances (PASS) online tool.

Keywords: Nicotinic acid hydrazone, Docking, Antimicrobial activity, MIC, *In silico* screening

INTRODUCTION

During the past few decades there is a dramatic increase of Multi Drug Resistant (MDR) pathogenic strains potentiates the difficulties to treat with existing antibiotics and also slowdown the development of new synthetic antimicrobial agents. Hence it is imperative to search for new compounds for treating pathogens. It is well known from literature N-acylhydrazones (-CO-NH-N=CH-) are the versatile molecules constitutes an important class of organic compounds, exhibits significant biological activities *viz* antimicrobial [1], anti-inflammatory [2], anticancer [3], antitubercular [4], antiprotozoal [5], analgesic [6], antiplatelet [7], antioxidant [8] activities etc., due to the presence of azomethine group which is connected to the carbonyl group. On the other hand literature review explores nicotinic acid (pyridine 3-carboxylic acid) found in plants and animals, have important role in biological system and their derivatives possess antimicrobial [9], anti-inflammatory [10], antioxidant [11], antitubercular [12] activities etc. It is worthy to note, the importance of computational techniques for the prediction of various activities explored by new ligand molecules plays an important role and also accelerates the drug discovery process which can save the time and resources [13].

In view of above mentioned facts, herein we report the synthesis, characterization, antimicrobial evaluation of title compounds to treat the remarkable adaptability of the bacterial strains followed by *in silico*, molecular docking studies.

MATERIALS AND METHODS

All the melting points reported in this series were determined in open capillaries using Thermonik Pricision Melting Point Cum Boiling Point Apparatus C-PMB and are uncorrected. Homogeneity of the compounds was checked by using pre coated Thin Layer Chromatography (TLC) plates. The IR spectra were recorded using KBr pellets on a Perkin-Elmer 1760 Spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker Advance 400 MHz spectrophotometer using Tetramethylsilane (TMS) as an internal standard. Chemical shift (δ) values are reported in δ (ppm). Mass spectra were recorded on an Apex Mass spectrophotometer and all the solvents and chemicals were procured from Sigma Aldrich, used without further purification. The molecular docking was done by using XP GIDE module of Schrodinger suite.

Synthesis of N'-(1-(4-aminophenyl)ethylidene)nicotinohydrazide 1: Nicotinohydrazide (10 mmol), 4-aminoacetophenone (10 mmol), few drops of glacial acetic acid were taken in methanol (20 ml) and reflux on water bath at 100°C for 1 h. On cooling forms the shining yellow color crystalline solid, which was filtered, washed and used for further steps without recrystallization. Yield: 76%; mp: 200-202°C; IR (KBr, ν_{max}/cm^{-1}): 3271 (NH), 3023 (aromatic C-H), 2963 (C-H of CH_3), 1662 (C=O), 1597 (C=N).

^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 2.26 (s, 3H, -CH_3), 4.04 (bs, 2H, NH_2), 6.50-9.02 (m, 8H, Ar-H), 10.75 (s, 1H, CONHN); Anal. Calcd. For $C_{14}H_{14}N_4O$: C, 69.13; H, 5.55; N, 22.03; Found: C, 69.34; H, 5.10; N, 20.10.

General procedure for the synthesis of N'-(1-(4-acetamidoophenyl)ethylidene) nicotinohydrazide 2: A mixture of compound 1 (20 mmol) and acetic anhydride (10 ml) was transferred in to round bottom flask. Then the reaction mixture was heated on steam bath for 1 h, allowed to stand at room temperature for 2-3 h. The light yellow color solid was filtered, recrystallized from ethanol. Yield: 64%; mp: 164-166°C. IR (KBr, ν_{max}/cm^{-1}): 3283 (NH), 3056 (Ar C-H), 2983 (C-H of CH_3), 1674 (C=O), 1588 (C=N). ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 2.72-2.24 (s, 6H, -CH_3), 6.92-8.92 (m, 8H, Ar-H), 9.84-10.63 (s, 2H, CONHN); EI-MS m/z: 297 (M+1). Anal. Calcd. For $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44; N, 18.91; Found: C, 63.98; H, 5.13; N, 19.08.

General procedure for the synthesis of N'-(1-(4-(substituted benzylideneamino)phenyl) ethylidene) nicotinohydrazide 3a-g: A mixture of compound 1 (10 mmol), aromatic/heteroaromatic aldehyde (10 mmol) in ethanol (15 ml) acidified with glacial acetic acid were refluxed on water bath for 30 min to 1 h till a different spot on TLC may appears. On cooling, solid get separated, washed with alcohol, collected by filtration and recrystallized from methanol.

N'-(1-(4-(benzylideneamino)phenyl)ethylidene)nicotinohydrazide 3a: Yield: 53%; mp: 203-205°C; IR (KBr, ν_{max}/cm^{-1}): 3216 (NH), 3019 (Ar C-H), 2971 (C-H of CH_3), 1691 (C=O), 1611 (C=N). ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 2.41 (s, 3H, -CH_3), 7.40-8.92 (m, 12H, Ar-H), 8.31 (s, 1H, HC=N), 10.74 (s, 1H, CONHN); Anal. Calcd. For $C_{21}H_{18}N_4O$: C, 73.67; H, 5.30; N, 16.36; Found: C, 73.18; H, 5.22; N, 16.18.

N'-(1-(4-(4-methoxybenzylideneamino)phenyl)ethylidene)nicotinohydrazide 3b: Yield: 69%; mp: 228-230°C; IR: (KBr, ν_{max}/cm^{-1}): 3231(NH), 3078 (Ar C-H), 2992 (C-H of CH_3), 2904 (C-H of OCH_3), 1656 (C=O), 1603 (C=N). ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 2.39 (s, 3H, -CH_3), 3.61 (s, 3H, -OCH_3), 6.92-9.05 (m, 12H, Ar-H), 8.28 (s, 1H, HC=N), 10.76 (s, 1H, CONHN); Anal. Calcd. For $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04; Found: C, 71.12; H, 5.56; N, 15.38.

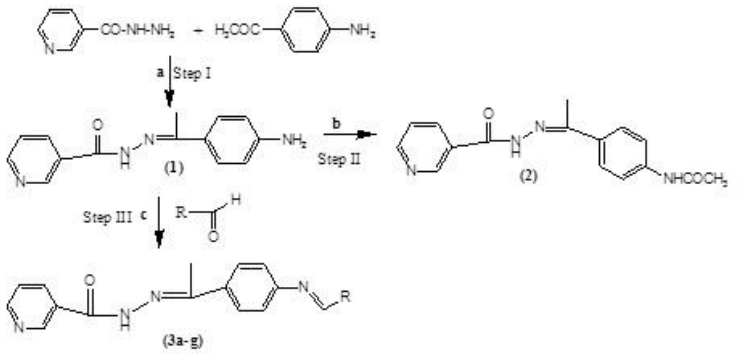
N'-(1-(4-(3-nitrobenzylideneamino)phenyl)ethylidene)nicotinohydrazide 3c: Yield: 71%; mp: 212-214°C; IR: (KBr, ν_{max}/cm^{-1}): 3274 (NH), 3091 (Ar C-H), 2947 (C-H of CH_3), 1677 (C=O), 1569 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.51 (s, 3H, -CH_3), 7.42-9.064 (m, 12H, Ar-H), 8.25(s, 1H, HC=N), 10.98 (s, 1H, CONHN); EI-MS m/z: 388 (M+1). Anal. Calcd. For $C_{21}H_{17}N_5O_3$: C, 65.11; H, 4.42; N, 18.08; Found: C, 65.42; H, 4.16; N, 17.89.

N'-(1-(4-(2-hydroxy benzylideneamino)phenyl)ethylidene)nicotinohydrazide 3d: Yield: 57%; mp: 215-217°C; IR: (KBr, ν_{max}/cm^{-1}): 3317 (OH), 3219 (NH), 3078 (Ar C-H), 2953 (C-H of CH_3), 1652 (C=O), 1561 (C=N). ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 2.37 (s, 3H, -CH_3), 7.20-8.98 (m, 12H, Ar-H), 8.20 (s, 1H, HC=N), 9.47 (Ar-OH) 10.32 (s, 1H, CONHN); Anal. Calcd. For $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 18.08; Found: C, 70.52; H, 4.90; N, 18.26.

N'-(1-(4-(4-chloro benzylideneamino)phenyl)ethylidene)nicotinohydrazide 3e: Yield: 61%; mp: 263-266°C; IR: (KBr, ν_{max}/cm^{-1}): 3197 (NH), 3062 (Ar C-H), 2982 (C-H of CH_3), 1648 (C=O), 1609 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.41 (s, 3H, -CH_3), 7.20-9.13 (m, 12H, Ar-H), 8.30 (s, 1H, HC=N), 10.83 (s, 1H, CONHN); Anal. Calcd. For $C_{21}H_{17}ClN_4O$: C, 66.93; H, 4.55; N, 14.87; Found: C, 66.62; H, 4.71; N, 14.46.

N'-(1-(4-((pyridin-4-yl)methyleneamino)phenyl)ethylidene)nicotinohydrazide 3f: Yield: 60%; mp: 193-195°C; IR: (KBr, ν_{max}/cm^{-1}): 3284 (NH), 3041 (Ar C-H), 2976 (C-H of CH_3), 1627 (C=O), 1562 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.42 (s, 3H, -CH_3), 7.10-9.05 (m, 12H, Ar-H), 8.14 (s, 1H, HC=N), 10.92 (s, 1H, CONHN); EI-MS m/z: 344 (M+1). Anal. Calcd. For $C_{20}H_{17}N_5O$: C, 69.93; H, 4.99; N, 20.40; Found: C, 69.72; H, 4.83; N, 20.56.

N'-(1-(4-(2,4-chloro benzylideneamino)phenyl)ethylidene)nicotinohydrazide 3g: Yield: 71%; mp: 210-213°C; IR: (KBr, ν_{max}/cm^{-1}): 3217 (NH), 3043 (Ar C-H), 2979 (C-H of CH_3), 1652 (C=O), 1597 (C=N). ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.40 (s, 3H, -CH_3), 7.22-9.24 (m, 11H, Ar-H), 8.32 (s, 1H, HC=N), 10.91 (s, 1H, CONHN); Anal. Calcd. For $C_{21}H_{16}Cl_2N_4O$: C, 61.33; H, 3.92; N, 13.62; Found: C, 61.24; H, 3.71; N, 13.47.



3a R=Phenyl; **3b** R=4-Methoxy phenyl; **3c** R=3-nitro phenyl; **3d** R=2-hydroxy phenyl; **3e** R=4- chloro phenyl; **3f** R=4-pyridyl; **3g** R=2,4-di chloro phenyl.

a:Methanol, glacial acetic acid; **b**: Acetic anhydride; **c**: Ethanol, glacial acetic acid

Scheme 1

Antimicrobial assay

All the title compounds were assayed *in vitro* for antimicrobial activity against two Gram-negative bacterial strain (*Escherichia coli*, *Pseudomonas aeruginosa*), Gram-positive (*Staphylococcus aureus, Bacillus subtilis*) and one fungal strain (*Candida albicans*). The culture was obtained by inoculation of respective bacteria in double strength nutrient broth-I.P. followed by incubation at 37°C for 24 h.

The stock solution (200 µg/ml) of title compounds were serially diluted in tube [14] containing 1 ml of sterile double strength nutrient broth I.P. to get a concentration of 100, 50, 25, 12.5, 6.25 and 3.125 µg/ml concentrations and then inoculated with 100 µl of suspension of respective organisms in sterile saline. The tubes were incubated at 37°C for 24 h and determine the MIC, which is the lowest concentration of the drug where the tubes remain clear, indicate the growth of organism was completely inhibited at that concentration. The antifungal activity of title compounds were determined by serial dilution method which is followed to antibacterial assay using Sabouraud dextrose broth-I.P and the tubes were incubated at 37°C for 48 h and then calculate the MIC.

***In silico* absorption, distribution, metabolism and excretion (ADME) prediction**

The ADME properties of title compounds (1, 2 & 3a-g) were analyzed by employing Molinspiration online tool [15] (http://www.molinspiration.com/cgi-bin/properties), in order to check their Lipinski rule of five, % oral absorption and also the toxicity profile, overall drug likeness score were calculated by OSIRIS program (http://www.organic-chemistry.org/prog/peo/). Prediction of Activity Spectrum of Substances (PASS) is another *in silico* computer program to predict the biological activity spectrum for a compound on the basis of its structural formula. Biological activity spectrum for a substance is a list of biological activity types for which the probability to be revealed (Pa) and the probability not to be revealed (Pi) are calculated. Pa and Pi values are independent and their values vary from 0.000-1.000. If Pa>0.7, the compound is likely to reveal its activity in experiments, but in this case the chance of being the analogue of the known pharmaceutical agent is high [16]. The % oral absorption was calculated according to the formula [17].

$$\%ABS=109-(0.345 \times TPSA)$$

Molecular docking

Further all the title compounds (1, 2 and 3a-e) were undergone molecular docking studies with *E. coli* FAB protein (β-ketoacyl-acyl carrier protein synthase III) retrieved from the Protein Data Bank (PDB) incorporated with inhibitor. The 3D crystal structure of target (PDB ID: 5BNM) was imported in to maestro v 9.0. Receptor grid was generated according to GLIDE protocol and all the ligands, standard were docked by using XP GLIDE module of Schrodinger suite.

XP G Score=0.065 × Van Der Waals energy+0.130 × Coulomb energy+Lipophilic term+H bonding+metal binding+Buryp P+Rot B+Polar interactions [18].

RESULTS AND DISCUSSION

Chemistry

All the title compounds were synthesized according to the reaction outlined in Scheme 1. Nicotinic acid hydrazide was refluxed with 4-amino acetophenone in acidic condition to yield compound (1) with good yield, purity and act as a precursor for the synthesis of remaining compounds. Compound (1) was refluxed with acetic anhydride for one hour yield compound (2) and also the nucleophilic addition of compound (1) N'-(1-(4-aminophenyl)ethylidene)nicotinohydrazide with functionalized aromatic/heteroaromatic aldehydes in ethanol acidified with a few drops of acetic acid yields the title compounds (3a-f). The IR data suggest appearance of bands in the region of 1627-1691 cm^{-1}; 1561-1611 cm^{-1} indicates the presence of C=O, C=N respectively with in the title compounds. The appearance of IR band around 3200 cm^{-1}, 3300 cm^{-1} showed the presence of NH linkage of amide bond of hydrazide and hydroxy group (3d). The appearance of peaks between 2947-3091 cm^{-1} indicates the presence of aromatic, aliphatic C-H of title compounds. The ^{1}H-NMR data reveals appearance of singlet around δ=10, δ=8.2 confirmed the presence of NH of hydrazide and formation of azomethine (CH=N) proton. And also it is important to note appearance of a singlet and one doublet at higher ppm, corresponding to C_1, C_6 protons of pyridine, as they are in close proximity of aromatic OH (3d). Moreover shifting of aromatic proton towards higher region (deshielding) confirmed the presence of NO_2 group (3c). Furthermore the absence of signal corresponding to the free aromatic NH_2 at δ=4.42 supports the formation of compounds (3a-g). The appearance of molecular ion peaks (M+1) at 297, 388 and 344 indicates the formation of compounds 2, 3c and 3f respectively.

The antibacterial data of title compounds was tabulated (Table 1) reveals compound 3f and 3d exhibited higher sensitivity (MIC: 3.12 µg/ml and 6.25 µg/ml) towards *E. coli*, *P. aeruginosa* strains respectively which is comparable to standard. Against *S. aureus*, *B. subtilis* compound 3g and 3d emerged as most active compound having 6.25 µg/ml and 12.5 µg/ml as MIC compared to other derivatives. The SAR analysis of antimicrobial result reveals the type of substitution at the azomethine end have considerable impact on the activity and it is interesting to note that compound (3g) bearing pyridyl group exhibited greater activity against tested strains than phenyl derivatives (3a). This might be due to the presence of one more pyridyl substitution potentiates the activity profile of drug. And also it is important to note presence of hydroxyl group on benzylidene ring potentiates the activity, probably by polar interaction with the target. It is noteworthy, compounds (3a-g) able to exhibits good activity than compounds (1, 2) clearly indicates the contribution of azomethine group towards the antibacterial and antifungal profile. On the other hand the antifungal data revealed compound 3g bearing halogens were able to produce good activity (MIC: 12.5 µg/ml) against *C. albicans* than other derivatives is due to the higher lipophilicity of compound and this result was similar to Daniela et al., and remaining all showed moderate activity (Tables 2 and 3) [19].

The *in silico* data reports all the compounds obeys the Lipinski rule of five explains the oral bioavailability of title compounds assessed by Molinspiration online kit, showed good oral bioavailability between 70-86% and also have good bioactive scores towards the enzyme inhibition than others types of mechanisms. Further all the derivatives free from potential toxicity except 3b, 3c predicted by using OSIRIS, depicted in Table 2 which is the major hurdle to introduce the synthetic compounds in to the market as new drug and all the compounds have good drug likeness score between 1.77-4.47. It is important to note, PASS data provides the possible activities to further evaluated the compounds for the predicted activities depicted in Table 4 and all the compounds have higher Pa value towards anti-tuberculosis, antimycobacterial.

Further the study was continued with the molecular docking studies with FAB protein coded with 5BNM and the data reveals all the derivatives except 3a-c elicited good docking score (-6.00 to -6.48) than the standard drug ciprofloxacin (-4.74) predicted by using XP GLIDE. Compound (3f) showed higher affinity towards the target, it might be due to the complete fitting of molecule with in the hydrophobic cavity of target protein and this data provides the possible pose and type of interactions within the protein environment (Figures 1-4).

Table 1: Antimicrobial activity and docking sores of title compounds (1, 2, 3a-g)

		MIC (µg/ml)					Molecular docking	
		Gram-negative		Gram-positive		Fungal		
S. No.	Com code	*Escherie a coli*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*	*Bacillus subtilis*	*Candida albicans*	Docking score	Binding free energy (kcal/mol)
1	**1**	>100	50	>100	>100	>100	-	-
2	**2**	>100	>100	>100	>100	>100	-	-
3	**3a**	>100	50	>100	>100	>100	-4.10	-41.20
4	**3b**	50	>100	>100	50	25	-4.32	-44.10
5	**3c**	25	50	50	25	>100	-3.43	-35.58
6	**3d**	12.5	6.25	25	12.5	>100	-6.44	-53.62
7	**3e**	25	50	50	50	50	-6.00	-50.45
8	**3f**	3.12	12.5	12.5	25	50	-6.48	-49.18
9	**3g**	6.25	25	6.25	50	12.5	-6.27	-40.66
10	**STD**	6.25	6.25	3.12	3.12	6.25	-4.74	-55.98

(-) not tested

Table 2: Molecular descriptors of title compounds (1, 2, 3a-f)

S. No.	C code	Log P	Log S	TPSA	% abs	n- Hba	n-hbd	n-ROTB	Mw	Mu	Tu	Ir	Re	Dl
1	**1**	0.85	-3.36	80	81	5	3	3	254	G	G	G	G	3.21
2	**2**	0.99	-3.62	83	80	6	2	4	296	G	G	G	G	4.07
3	**3a**	3.31	-4.82	66	86	5	1	5	342	G	G	G	G	3.66
4	**3b**	3.37	-4.84	75	83	6	1	6	372	R	G	G	G	3.62
5	**3c**	3.24	-6.67	112	70	8	1	6	387	R	R	G	G	1.77
6	**3d**	3.25	-4.53	86	79	6	2	5	358	G	G	G	G	3.64
7	**3e**	3.94	-5.20	66	86	5	1	5	376	G	G	G	G	4.47
8	**3f**	2.02	-4.03	79	81	6	1	5	343	G	G	G	G	3.66
9	**3g**	4.59	-6.30	66	86	5	1	5	344	G	G	G	G	3.69

Log P: Lipophilicity; Log S: Solubility; TPSA: Total Polar Surface Area; n-Hba: No of hydrogen bond acceptors; n-Hbd: No of hydrogen bond donars; n-ROTB: No of Rotatable Bonds; Mw: Molecular weight; Mu: Mutagenic; Tu: Tumorigenic; Ir: Irritant; Re: Reproductive effect; Dl: Drug-likeness; G: No Risk; R: High Risk

Table 3: Bioactive scores of title compounds (1, 2, 3a-g)

S. No.	Com code	GPCRL	ICM	KI	NRL	PI	EI
1	**1**	-0.39	-0.67	-0.47	-0.75	-0.48	-0.19
2	**2**	-0.37	-0.76	-0.47	0.66	-0.46	-0.35
3	**3a**	-0.56	-0.94	-0.45	-0.67	-0.58	-0.36
4	**3b**	-0.56	-0.94	-0.45	-0.63	-0.60	-0.38
5	**3c**	-0.64	-0.90	-0.54	-0.68	-0.65	-0.43
6	**3d**	-0.52	-0.97	-0.43	-0.56	-0.52	-0.33
7	**3e**	-0.54	-0.91	-0.46	-0.66	-0.61	-0.38
8	**3f**	-0.55	-0.93	-0.43	-0.67	-0.58	-0.35
9	**3g**	-0.56	-0.91	-0.46	-0.70	-0.62	-0.39

GPCR: G-protein coupled receptor ligand; ICM: Ion Channel Modulator; KI: Kinase Inhibitor; NRL: Nuclear Receptor Ligand; PI: Protease Inhibitor; EI: Enzyme Inhibitor

Table 4: **Prediction of activity spectrum of substances scores of title compounds (1, 2, 3a-g)**

S. No.	Com code	I		II		III		IV		V	
		Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi	Pa	Pi
1	**1**	0.7	0.003	0.7	0.004	-	-	-	-	0.7	0.02
2	**2**	0.7	0.004	0.7	0.005	0.6	0.009	-	-	0.6	0.04
3	**3a**	0.8	0.030	0.8	0.004	0.7	0.008	0.7	0.004	0.7	0.01
4	**3b**	0.8	0.003	0.8	0.004	-	-	0.5	0.007	0.6	0.05
5	**3c**	0.9	0.002	0.8	0.003	0.7	0.011	0.5	0.006	-	-
6	**3d**	0.8	0.002	0.8	0.003	-	-	-	-	0.6	0.04
7	**3e**	0.8	0.003	0.8	0.004	0.6	0.013	0.6	0.005	0.6	0.03
8	**3f**	0.8	0.002	0.8	0.003	0.8	0.004	0.6	0.005	0.8	0.008
9	**3g**	0.7	0.004	0.7	0.004	-	-	0.6	0.005	0.7	0.004

I: Antituberculosis; II: Antimycobacterial; III: Phosphatidylserine decarboxylase inhibitor; IV: Thiol protease inhibitor; V: Taurine dehydrogenase inhibitor; Pa: Probability to be active; Pi: Probability to be active

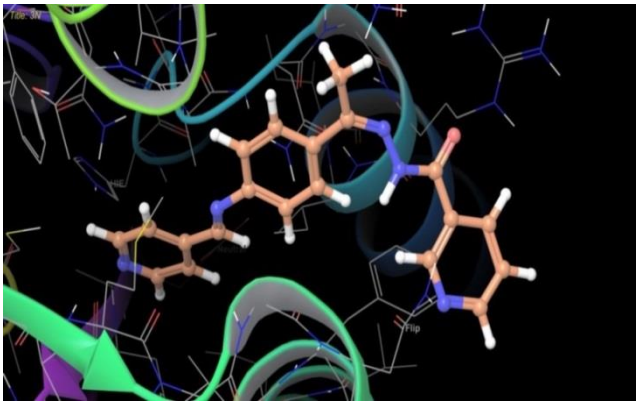


Figure 1: 2D interaction of 3f with active site of 5BNM target

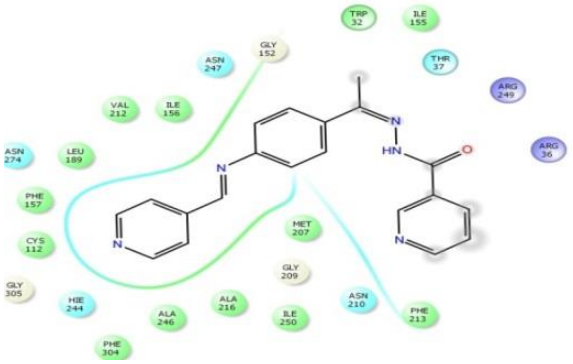


Figure 2: 3D interaction of 3f with active site of 5BNM target

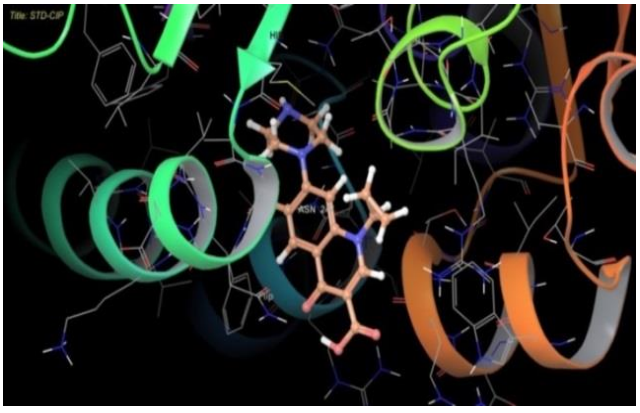


Figure 3: 3D interaction of standard with active site of 5BNM target

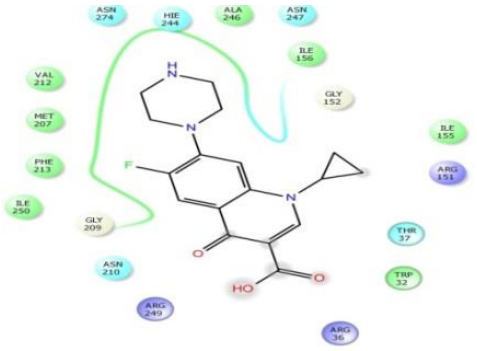


Figure 4: 2D interaction of standard with active site of 5BNM target

CONCLUSION

In the present study we develop a facile synthetic route for the synthesis of new N-acylhydrazone, screened for antimicrobial activity and further interaction with the target was explored by docking studies. Among all, compound 3f and 3g exhibited good antibacterial and antifungal activities, could be selected as a lead compounds for further development of potent antimicrobial agent and it supported by molecular docking results. It is interesting to note compound 3c need further studies to prove the molecule as anti-tubercular agent predicted by PASS tool.

ACKNOWLEDGEMENTS

The authors are Thankful Laila impex, Vijayawada and DST, Sri Venkateshwara University for providing spectral data.

REFERENCES

[1] M. Lilia, B. Coralia, B. Ion, C.D. Carmen, H. Anamaria, B. Otilia, I. Petre, P. Anca, T. Arnaud, Z. Irina, *Bioorg. Med. Chem*., **2015**, 23, 401-410.
[2] G. Murineddu, G. Loriga, E. Gavini, A.T. Peana, A.C. Mule, C.A. Pinna, *Arch. Pharm*., **2001**, 334, 393-398.
[3] P.R. Kamath, D. Sunil, A.A. Ajees, K.S.R. Pai, S. Biswas, *Eur. J. Med. Chem*., **2016**, 14, 134-147.
[4] L. Bukowski, M. Janowiec, *Pharmazie*., **1996**, 51, 27-30.
[5] A. Inam, S.M. Siddiqui, T.S. Macedo, D.R. Moreira, A.C. Leite, M.B. Soares, A. Azam, *Eur. J. Med. Chem*., **2014**, 75, 67-76.
[6] G. Rajitha, K.V.S.R.G. Prasad, A. Umamaheswari, D. Prardhan, K. Bharathi, *Med. Chem. Res*., **2014**, 23, 5204-5214.
[7] L.M. Lima, F.S. Frattani, J.L. Dos Santos, H.C. Castro, C.A.M. Fraga, R.B. Zingali, E.J. Barreiro, *Eur. J. Med. Chem*., **2008**, 43, 348-356.
[8] G. Rajitha, N. Saideepa, Praneetha, *Indian. J. Chem*., **2011**, 50, 729-733.
[9] R.Y. Morjan, A.M. Mkadmh, I. Beadham, A.A. Mattar, J. Raftery, R.G. Pritchard, A.M. Awadallah, J.M. Gardiner, *Bioorg. Med. Chem. Lett*., **2014**, 24, 5796-800.
[10] M.A. Godin, W.C. Ferreira, L.T.S. Rocha, R.G. Ferreira, A.L.L. Paiva, L.A. Merlo, E.B.N. Jr, L.F.S. Bastos, M. Coelho, *Pharmacol. Biochem. Behav*., **2012**, 101, 493-498.
[11] J.P. Kamat, T.P. Devasagayam, *Redox. Rep*., **1999**, 4, 179-184.
[12] M.W. Eldehna, F. Mohamed, M. Marwa, A. Aziz, H.A.A. Abdel-Aziz, *Molecules*., **2015**, 20, 8800-8815.
[13] Y.P. Zhoua, C.B. Cai, S. Huanb, J.H. Jiang, H.L. Wu, G.L. Shen, R.Q. Yu, *Anal. Chim. Acta*., **2007**, 593, 68-74.
[14] J.G. Cappucino, N. Sherman, Addison Wesley Longman Inc., Redwood City, **1999**, 263.
[15] R.E. Buntrock, *J. Chem. Inf. Model*., **2002**, 42, 1505-1506.
[16] V. Poroikov, D. Akimov, E. Shabelnikova, D. Filimonov, *SAR. And. QSAR. In. Environmental. Research*., **2001**, 12, 327-344.
[17] B. Vishwanathan, B.M. Gurupadayya, K. Venkata Sairam, *Bangladesh. J. Pharmacol*., **2016**, 11, 67-74.
[18] P. Chaitanya, G. Deepak Reddy, G. Varun, L.M. Srikanth, V.V.S.R. Prasad, A. Ravindernath, *Med. Chem.*, **2014**, 10, 711-723.
[19] S. Daniela, B. Bruna, B. Adriana, C. Simone, D.A. Melissa, R. Daniela, M. Emanuela, P. Lucia, Z. Alessandra, *Eur. J. Med. Chem*., **2012**, 53, 246-253.