Synthesis, antibacterial studies, and molecular modeling studies of 3,4-dihydropyrimidinone compounds

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Received: 4 May 2015 / Accepted: 10 June 2015 / Published online: 4 July 2015
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Abstract The syntheses of dihydropyrimidinones (DHPMs) using solvent-free grindstone chemistry method. All the synthesized compounds exhibited significant activity against pathogenic bacteria. The current effort has been developed to obtain new DHPM derivatives that focus on the bacterial ribosomal A site RNA as a drug target. Molecular docking simulation analysis was applied to confirm the target specificity of DHPMs. The crystal structure of bacterial 16S rRNA and human 40S rRNA was taken as receptors for docking. Finally, the docking score, binding site interaction analysis revealed that DHPMs exhibit more specificity towards 16S rRNA than known antibiotic amikacin. Accordingly, targeting the bacterial ribosomal A site RNA with potential drug leads

promises to overcome the bacterial drug resistance. Even though, anti-neoplastic activities of DHPMs were also predicted through prediction of activity spectra for substances (PASS) tool. Further, the results establish that the DHPMs can serve as perfect leads against bacterial drug resistance.

Keywords Grindstone chemistry · Ribosomal RNA · Bioactivity · Molecular modeling

Introduction

The increasing use of antibiotics for antibacterial therapy has inevitable development and expansion of antibiotic resistance in microorganisms, particularly in human pathogens. Further, most pathogens are developing the tendency to accumulate multiple resistances under antibiotic pressure and selection. For an example, methicillin-resistant *Staphylococcus aureus* (MRSA) are acquired resistance to all classes of antibiotics, which are most likely responsible for the failure of antibiotic therapeutics [1]. There has been an intense need to identify the potential drugs with novel binding site and inhibitor mechanisms. Recent studies are conferred that rRNA as an attractive drug target for multiple drug-resistant bacterial strains [2]. Subsequently, rRNA actively involved in wide range of biological process such as the storage and propagation of genetic information and protein synthesis [3]. In order to choose the novel targets towards RNA, rRNA is one of the good candidates, as well-studied drug targets for their active site [4]. Aminoglycosides are group of extensively studied antibiotics that specifically bind with A site of 16S rRNA in the bacterial ribosome [5]. Unfortunately, aminoglycosides are nonspecifically bind to the other RNA molecules and cause the nephro- and ototoxicity. This factor confined the clinical usage of aminoglycosides [2]. However, the rRNA-aminoglycoside

Electronic supplementary material The online version of this article (doi:10.1007/s12154-015-0142-4) contains supplementary material, which is available to authorized users.

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binding interaction provides the key features to synthesize the novel and potent rRNA binding small molecules and could diminish constancy of bacterial protein synthesis [2, 6]. The specific rRNA binding affinity of novel dihydropyrimidinone (DHPM) compounds were validated by combined approach of computational simulation. The derivatives of DHPMs are reported to exhibit a broad spectrum of biological activities such as antihypertensive agents, anticancer, anti-bacteria, anti-malarial agents, and anti-inflammatory agents and act as calcium channel blockers, neuropeptide γ -antagonists [7]. These observations have prompted to undertake the designing of new DHPMs derivatives against microbial resistance. Hence, the objectives of the studies are an efficient and green water assisted protocol for the synthesis of medicinally important 3, 4-DHPMs under grindstone chemistry technique. In addition to this, we addressed the *in silico* and *in vitro* of antibacterial evaluation of synthesized compounds.

Materials and methods

Grid stone synthesis

Various aromatic aldehydes (Table 1) using cupric chloride (Fig. 1) are substituted to develop rapid, efficient, and an inexpensive procedure for the synthesis of various novel biological active 3,4,-dihydropyrimidin-2-(1*H*)-ones by condensation of some novel 1,3-dicarbonyl compounds with urea/thiourea. The synthesized compound structures were established by elemental and spectral studies.

General procedure for the preparation of 4-(aryl)-6-methyl-2-oxo-*N*-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxamides

A mixture of an aromatic aldehyde (10 Mmol), *N*-phenylacetoacetamide (10 Mmol), urea (10 Mmol), cupric chloride (10 Mmol), and 2–3 drops of conc. HCl was ground together to give a syrup under solvent-free condition which was left overnight. The contents were poured into ice-cold water and the product that separated was filtered, dried, and crystallized, and their isolated yields and melting points are given in Table 1. All the compounds have been synthesized as per the procedure [8] described in Fig. 1. A mixture of an aromatic aldehyde, *N*-phenylacetoacetamide, urea/thiourea, cupric chloride, and few drops of conc. HCl was ground together to give a syrupy liquid which on standing for overnight the desired product dihydropyrimidinones (DHPMs) were synthesized. The color of the products was ranging as follows: colorless, yellow, to orange red. Most of the compounds are soluble in common organic solvents and few of them in DMSO.

Compounds of similar type have been synthesized by various methods and also give similar type of products. The reported DHPM was prepared in the presence of polyphosphate ester (PPE) [9] or without PPE [10] under microwave condition and also synthesized in presence of Bromosuccinimide (NBSN) under the same condition [11]. Also, this compound has been prepared using ruthenium (II) chloride as a catalyst [12, 13]. In all the above methods, the catalyst used is expensive; however, the current method cupric chloride is used as a catalyst which is easily available, inexpensive, non-toxic, and eco-friendly. Although, our compounds of interest are prepared by simple mixing of aromatic aldehyde, *N*-phenylacetoacetamide, urea, and cupric chloride under room temperature. On comparison with the above synthetic strategy, our compounds have been obtained by purely greener technique.

Spectral analysis of synthesized compounds

The synthesized compounds were well characterized on the basis of IR and NMR spectral techniques. The IR and ^1H NMR spectra of the synthesized DHPMs bear close resemblance. In the ^1H NMR spectrum of compound c [14] (a representative example), the three-proton singlet at δ 2.13 is assigned to allylic methyl (CH_3 -6), while the three-proton singlet at δ 3.73 is ascribed to methoxyl of the C-4 of phenyl group. The one-proton singlet at δ 5.47 is due to C-4 proton of the dihydropyrimidinone ring. Of the three downfield one-proton singlets, the broad singlet at δ 8.74 is assigned to N_1H of the DHPM, while the one at δ 9.17 is attributed to NH of amide and the broad far downfield singlet at δ 10.0 is due to N_3H . These assignments are in good agreement with published data [8, 15] and further supported by its ^{13}C NMR data.

Molecular modeling studies

Different series of 3,4-dihydropyrimidinone structures were constructed using ChemAxon's Marvin Sketch chemical software (<http://www.chemaxon.com/products/marvin/marvinsketch/>) and were used for further evaluation.

Optimization and energy minimization of RNA and ligand

All the compounds were prepared for structural optimization and conformer generation using LigPrep [16]. The OPLS-2005 force field was applied to obtain the optimized and energy minimized conformers of compounds. Before the energy minimization process of ligand structures, following steps were taken: addition of implicit hydrogen atoms; neutralization of charged groups; and generation of various ionization,

Table 1 The synthesis of dihydropyrimidinones in the presence of cupric chloride dehydrate data

Entry	Compound	Aldehydes	Urea/Thiourea	Yield (%)	m.p (°C)
1	A			89.3 (58)	230-238 lit ²⁰ (246-248)
2	B			73.5	164-166
3	C			92.1 (67)	245-248
4	D			93.0	132-134
5	e			81.2	134-135
6	f			95.7 (75)	221-224 lit ²¹ (213-215)
7	g			97.3	108-110
8	h			82.7 (65)	228-230 lit ²² (227-231)
9	i			93.9	148-150
10	j			76.4	118-119

Fig. 1 Grindstone chemistry pathway for DHPM synthesis [17].

tautomerization, and chirality states of the ligand molecule [17].

In this study, the crystal structure of bacterial ribosomal A site and amikacin (PDB ID: 2G5Q) and human 40S ribosomal RNA (PDB ID: 3J3D) were retrieved from Protein Data Bank. The RNA structures underwent the preparation and refinement steps using OPLS-2005 force field. Subsequently, the restrained minimization of rRNA structure was continued until the average root-mean-square deviation (ARMSD) of heavy atom reached 0.30 Å [18, 3].

Prediction of binding pocket of 40S ribosomal RNA

The drug binding pocket of human rRNA was predicted by using SiteMap module of Schrodinger. SiteMap provides the information about ligand binding sites on the protein or DNA/RNA receptors. Sitemap operates in a manner of analogous to Goodford's GRID algorithm to define the sites. The algorithm automatically investigates and identifies the possible binding pockets from the receptor and represents the active site for docking simulation. The charge density was calculated by OPLS-2005 force field on the rRNA receptor. The grid point spacing was defined as 1 Å [19].

Molecular docking simulation

The Glide algorithm utilizes the pre-computed grid box containing the shape and properties of active sites. The Coulomb and van der Waals electric field of the protein also gathered at grid box [20]. During the grid generation, the ligand was removed from the receptor and binding region was defined by cognate binding ligand pose. The grid box size was defined with $10 \times 10 \times 10$ Å radius around the ligand from active site. Soften potential van der Waals radii scaling factor was not employed for rRNA docking. The ligands were docked with active site using Glide extra precision (XP) docking an exhaustive search of possible positions and orientations over the active site of rRNA [3]. OPLS-2005 force field was

employed for refinement of docking solutions including torsional and rigid body movements of the ligand used. In XP docking, the GlideScore is more accurate at minimizing false positives and can be especially useful in lead optimization. The small numbers of lowest energy poses are taken for Monte Carlo simulation [20]. Finally, the binding affinity of receptor-ligand was ranked by GlideScore and poses in ligand databases. The docked models were ranked using Emodel energy, composite scoring of receptor-ligand molecular mechanics interaction and ligand strain energy [18].

Drug-like property assessment of compounds

Pharmacokinetic parameters of absorption, distribution, metabolism, and excretion (ADME) were analyzed to examine the drug-like properties of synthesized compounds and known amikacin. QikProp predicts the physicochemical properties and pharmacologically relevant properties of the lead molecule [21]. All the unknown and known molecules were neutralized before the QikProp analysis. QikProp follows the BOSS program with OPLS-AA force field to perform Monte Carlo statistical mechanics simulations on organic solutes in a periodic box of explicit water molecules. This simulation leads to configurational average for number of pharmacological descriptors; correlations of these descriptors to experimentally determined properties were compared [21, 22]. The program was performed with normal mode to investigate the pharmacological properties of the known and screened compounds.

Biological activity spectrum by PASS—prediction

Biological activity spectrum (BAS) of chemical compounds comprises the different types of pharmacological effects; molecular mechanism of action; and toxicity effects such as mutagenicity, carcinogenicity, teratogenicity, and embryogenicity. The structural information of the compounds is accounted to predict the drug-likeness of candidates with

specific biological targets. The online version of PASS program was applied for selecting the compounds with desirable and without toxicity of biological activities among the 250,000 compounds from NCI database [23, 24]. The NCI database includes drugs, drug candidates, leads, and toxic substances. Prediction of activity spectra for substances (PASS) analyze the structure activity relationship (SAR) of training set compounds with database compounds whose biological activity is determined experimentally. The structure descriptor Multilevel Neighbourhood of Atom (MNA) is used in PASS to illustrate the chemical structures. Depending on the statistics of MNA descriptors of the training set descriptors for active and inactive compounds from the original training set, two probabilities are calculated for each activity: P_a the probability of the compound being active and P_i the probability of being inactive [24]. The P_a and P_i values vary from 0 to 1, and $P_a + P_i < 1$, since these probabilities are calculated independently. P_a and P_i can be considered to be measures of the compound under study belonging to the classes of active and inactive compounds, respectively. The most probable activities for a given compound are characterized by P_a values close to 1 and P_i values close to 0 [25].

Antibacterial potential of synthesized compounds

The bacterial strains used for the screening such as *Salmonella typhi* (Gram-negative) and *S. aureus* (Gram-positive) were procured from Microbial Type Culture Collection (MTCC), Chandigarh, India, and maintained in the laboratory in slopes of nutrient agar at 4 °C. The antimicrobial activity of compounds was tested against the abovesaid organisms following the standard disc diffusion method [26, 27]. Briefly, the microorganism inoculum was prepared from 12 h broth cultures and the suspensions are then adjusted to a turbidity of 0.5 McFarland. Susceptibility tests are then conducted using the

standard broth microdilution method in Mueller-Hinton broth with an inoculum of $\sim 5 \times 10^4$ CFU mL⁻¹. Mueller-Hinton agar plates inoculated by culture and the compound (10 µg/mL) loaded 6-mm disc were placed on the plate that was incubated without agitation for 24 h at 37 °C. DMSO was used as respective solvent system. Each test compounds were dissolved in DMSO. Later, we soaked the sterile discs on the respective test compounds and wait for few minutes than placed on the inocula seeded plates. DMSO soaked disc was used as negative control. The susceptibility of the bacteria to the test compounds was determined by the formation of an inhibitory zone. The plates were then incubated at 37 °C for 24 h and observed for clear zone of inhibition, and the inhibition zone was measured in millimeter. Six replications were maintained for each category [28].

Results and discussion

A novel green synthesis and environmentally benign water assisted protocol for the synthesis of 3,4-DHPMs in good to excellent yields without using additional solvents. Moreover, the catalyst used is easily available and inexpensive. The required DHPMs were readily prepared by grindstone chemistry technique catalyzed by CuCl₂·2H₂O and conc. HCl (Fig. 1). Adopting the above technique, five dihydropyrimidine-2*H*-ones (Table 1 (a–e)) and five dihydropyrimidine-2*H*-thiones (Table 1 (f–j)) have been prepared and characterized by IR and ¹H NMR.

Compounds of similar type have been synthesized by various methods and also give similar type of products. The reported synthesis showed dihydropyrimidinones prepared in the presence of PPE [9] or without PPE [10] under microwave

Fig. 2 Extra precision Glide docking (2G5Q) with **a** amikacin and **b** compound j

Table 2 Glide XP docking analysis of DHPM derivatives with bacterial 16SrRNA

Compound code	H-bond	π - π stacking	π -cation interaction	Nucleotides	Glide XP score	Glide energy	Glide Emodel
Amikacin	11	–	–	A16, A17, G18, G15, U19, C20, G21	–10.65	–83.27	–105.48
A	2	1	–	G15, A17	–5.74	–37.42	–48.28
B	2	1	–	G15, A17	–5.26	–36.60	–44.46
C	2	1	–	G15, A17	–4.12	–35.26	–43.28
D	1	2	1	G15, G18, A17	–5.05	–35.78	–40.25
E	2	2	–	G15, A17	–5.85	–39.12	–48.85
F	3	2	–	G15, G18, A17	–7.12	–52.83	–58.62
G	3	1	–	G15, G18, A17	–7.25	–50.85	–62.29
H	3	2	–	G15, G18, A17	–6.52	–45.23	–51.63
I	3	1	1	G15, G18, A17	–7.65	–65.32	–72.52
J	3	1	–	G15, G18, A17	–8.48	–79.39	–89.26

condition and also synthesized in presence of NBSN under same condition [11]. Also, this compound has been prepared using ruthenium (II) chloride as catalyst [12]. In all the above methods, the catalyst is expensive, but in this method, cupric chloride is used as a catalyst which is easily available, inexpensive, non-toxic, and eco-friendly. Moreover, the classical Biginelli reaction requires long reaction times (20 h) and often suffers from low yields of products in case of substituted aromatic and aliphatic aldehydes [12].

On comparison with the above synthetic strategy, around ten different compounds have been synthesized and total percentage of yield of the final compounds were calculated (Supplemental Information 1). Detailed spectral data are presented in the experimental section. The IR and ^1H NMR spectra of the synthesized DHPMs bear close resemblance (Supplemental Information 2). In the ^1H NMR spectrum of compound c [14], the three-proton singlet at δ 2.13 is assigned to allylic methyl (CH_3 -6), while the three-proton singlet at δ

3.73 is ascribed to methoxyl of the C-4 of phenyl group. The one-proton singlet at δ 5.47 is due to C-4 proton of the dihydropyrimidinone ring. Of the three downfield one-proton singlets, the broad singlet at δ 8.74 is assigned to N_1H of the DHPM, while the one at δ 9.17 is attributed to NH of amide and the broad far downfield singlet at δ 10.0 is due to N_3H . These assignments are in good agreement with published data [8] and further supported by its ^{13}C NMR data.

Docking analysis

The RMSD value was calculated to estimate the quality of the docking protocol; the RMSD of Glide XP docking is 1.1 Å. The minimum deviation value explained that docking protocol highly resembled the crystal structure of RNA-amikacin complex. The known amikacin exhibited 11 hydrogen bond interactions with A site of 16S rRNA. Further, DHPM derivative hits were docked with Glide XP mode docking. Finally,

Fig. 3 2D interaction maps of hydrogen bond and π - π stacking between bacterial rRNA and synthesized compound. **a** Compound d. **b** Compound i

Fig. 4 Extra precision Glide docking of human rRNA (3J3D) with **a** amikacin and **b** compound j

ten compounds (a–j) were chosen in order to best scoring and docking poses. The Glide Emodel energy scores of amikacin and compound j were -105.48 and -89.26 kcal/mol, respectively. The active site interaction maps of amikacin and best docked compound j are illustrated in Fig. 2. The best minimum Glide energy score was observed from compound j (-79.39 kcal/mol). All the compounds exhibited better energy score and binding poses similar to amikacin. The detail of energy score, nucleotide interaction, hydrogen bond interaction, and non-hydrogen bond interactions are described in Table 2. All the compounds resembled the crucial nucleotide interaction with G15, A17, and G18. Even though, all the DHPM derivatives formed the strong hydrophobic π - π interaction with guanine nucleotides G15 and G18. The non-bonded π - π stacking is one of the essential interactions formed between aromatic ring atoms [29]. In addition to that, compounds d and i exhibited the significant π -cation interaction with nucleotides G15 and G18, respectively (Fig. 3). The one more significant salt bridge interaction was observed

between compound d and A17 nucleotide (Fig. 3a). The aromatic ring structure of the ligand formed the π -cation interaction; this interaction also significantly stabilizes the protein-ligand or DNA/RNA-ligand interaction [30, 31]. The structural account of active site and its interaction would enhance the probability of catalytic inactivity mechanism. Finally, all the DHPM derivatives showed the better hydrogen bond and non-hydrogen bond interaction with A site of rRNA which mimics the amikacin. The obtained binding score value could possibly follows the experimental antibacterial activity. Later, we calculate the total activity (= biological inhibition zone–docking energy); interestingly, we observed the same trend (Supporting information 3). Moreover, a result of antibacterial activity could be several targets within the bacterial cell leading to growth inhibition [1]. Further, specific molecular level technique would be needed to confirm the binding mechanism of the DHPM derivatives.

Series of docking studies were also performed for human 40S rRNA as a target. Interestingly, amikacin drug exhibited

Table 3 Glide XP docking analysis of DHPM derivatives with human 40S rRNA

Compound code	H-bond	π - π stacking	Nucleotides	Glide XP score	Glide energy	Glide Emodel energy
Amikacin	14	–	U93, G94, C96, G95, G431, G432, A433, G434, C450	-11.97	-204.63	-375.062
A	1	–	C497	-3.93	-17.24	-32.82
B	2	–	C430, G431	-2.02	-13.82	-24.42
C	1	–	G94	-2.33	-11.78	-22.22
D	2	–	A433, A448	-2.01	-11.16	-22.52
E	1	–	C450	-2.62	-12.45	-25.35
F	1	–	A448	-0.89	-10.83	-18.72
G	1	–	A448	-0.62	-8.85	-15.29
H	–	1	A433	-1.91	-10.93	-20.33
I	1	–	C450	-0.72	-9.32	-17.72
J	1	–	C496	-0.44	-7.39	-14.56

Table 5 Biological activity spectrum of DHPM derivatives

Compound	Biological activity			
	Antibacterial		Anti-neoplastic	
	Pa ^a	Pi ^b	Pa	Pi
a	0.307	0.003	0.427	0.002
b	0.354	0.008	0.353	0.018
c	0.283	0.004	0.455	0.010
d	0.245	0.004	0.282	0.029
e	0.260	0.060	0.647	0.020
f	0.322	0.142	0.647	0.005
g	0.340	0.100	0.597	0.005
h	0.257	0.108	0.639	0.050
i	0.352	0.110	0.594	0.004
j	0.337	0.001	0.545	0.007

^a Pa–probability “to be active”^b Pi–probability “to be inactive”

higher binding affinity and as synthesized DHPM derivative j showed relatively low binding affinity towards human rRNA site (Fig. 4 and Table 3, respectively). The obtained results indicate that the proposed DHPM derivative acts as the better drug leads for bactericidal activity.

ADME property analysis

The better scored and posed synthesized compounds were further evaluated to predict the physicochemical and biological features. The molecular weight, water solubility, percentage of human oral absorption, and volume parameters were

chosen for the prediction. The known and DHPM derivatives molecular weight range from 307.45 to 585.60. Volume parameter is explained as total solvent-accessible volume in cubic angstroms and exhibited range from 694.19 to 843.64. The total solvent-accessible surface (SASA) ranged from 637.19 to 843.64, and QPlogPw coefficient range from 11.27 to 53; all the predicted values accomplished the desired range (Table 4). The screened compounds also exhibited the most significant value of percentage of human oral absorption ranging from 75.33 to 100. All the pharmacokinetic parameters showed the favorable range that is suitable for human use, thereby promising their potential as drug-like candidates.

PASS prediction

The synthesized compounds were evaluated for their biological activity. All the compounds showed significant range of Pa value close to 1 and Pi value close to 0. PASS prediction of all DHPM derivatives showed antibacterial and anti-neoplastic activity (Table 5) [32].

Antibacterial activity of synthesized compounds

All the synthesized compounds a–j were examined for antibacterial activity. Among these, compounds f, g, i, and j exhibited high activity against *S. aureus*; compounds a, b, e, and c [14] showed moderate activity against *S. aureus*. Compounds a–j showed moderate activity against bacteria *S. typhi* [14, 33, 34]. The significant range of zone of inhibition observed from DHPMs was described in Supplemental Information 3. However, it also possessed few side effects [35, 36]. The docking studies of amikacin with human 40S rRNA had

Table 4 Comparative ADME property analysis of the DHPM derivatives and amikacin

Compound	Molecular weight ^a	SASA ^b	Volume ^c	Human oral absorption (%) ^d	QPLogPW ^e
Amikacin	585.60	843.64	1645.21	0.00	53.00
a	307.35	700.00	1312.20	92.24	11.70
b	341.79	725.40	1357.44	95.00	11.56
c	337.37	637.19	1158.56	86.85	11.27
d	352.34	735.72	1385.91	75.33	12.79
e	351.36	673.39	1301.65	95.38	12.45
f	323.41	731.07	1358.36	100	12.45
g	357.86	713.75	1333.37	100	12.44
h	353.44	639.57	1171.36	91.32	12.79
i	368.41	723.98	764.68	85.56	14.17
j	367.42	686.90	694.16	100	14.05

^a Molecular weight (acceptable range 130.0–725.0)^b Total solvent-accessible surface area (SASA) (acceptable range 300.0–1000.0)^c Volume (acceptable range 500.0–2000.0)^d Percent human oral absorption—>80 % is high and <25 % is poor^e Predicted water/gas partition coefficient (QPlogPw) (acceptable range 4.0–45.0)

shown higher interaction. But for the DHPM derivatives, specific interaction towards bacterial 16S rRNA and less interaction with 40S rRNA had been exhibited. Presumably, DHPM derivatives could have the minimized specific interaction towards 16S rRNA and drug resistance; it could possibly minimize the side effect. Hence, DHPM derivatives could be the better candidate than amikacin. Therefore, further investigations would be required to document the effectiveness and side effect profile of the DHPM derivatives. This could be considered as an initial part of a future multicenter trial.

Conclusion

In the present study, green and environmentally benign water assisted protocol was used for the synthesis of 3,4-DHPMs. Moreover, the catalyst used is easily available and inexpensive. The required DHPMs were readily prepared by grindstone chemistry technique catalyzed by $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ and conc. HCl. Adopting the above technique, five dihydropyrimidine-2*H*-ones (a–e) and five dihydropyrimidine-2*H*-thiones (f–j) have been prepared and characterized by IR and ^1H NMR. Furthermore, DHPM derivative contains carbamoyl group in 5-position. These observations have prompted us to undertake the synthesis of new DHPMs derived from *N*-phenylacetamide as 1,3-dicarbonyl component with a great interest to evaluate them for antibacterial activities. All the derivatives were bind with rRNA of both the Gram-positive and Gram-negative strains, respectively. The binding affinity of derivatives with bacterial and human rRNA was validated through docking analysis. Molecular docking studies showed that all the derivatives retained the specific integrity with bacterial and human rRNA binding pocket, respectively. Bacterial 16S rRNA-DHPM complex association showed better interaction and good energy score than known amikacin. Although, human 40S rRNA-DHMP binding complex exhibited less binding energy score and atomic interaction than known amikacin. These results indicate that the synthesized compounds possessed the specific interaction towards bacterial rRNA and do not disturb the human rRNA function. In addition, ADME properties analyses including physico-chemical descriptors as well as pharmacokinetic parameters are within the acceptable range defined for human use, thereby indicating their potential as drug-like molecules. Most of the compounds also showed anti-neoplastic activity by PASS biological activity prediction. Finally, the synthesized compounds would act as potential antibacterial inhibitors as well as anti-neoplastic activity.

Acknowledgments The author SKS thank the Department of Science and Technology (DST) for Fast Track grant (SR/FT/CS-66/2010) and the Department of Biotechnology (DBT), New Delhi, BT/502/NE/TBP/2013. One of the authors, SKK, thanks the Conacyt and SEP of Mexican Govt.

Conflict of interest The authors declare that they have no competing interests.

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