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# Bis-pyrimidine acetamides: design, synthesis and biological evaluation

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## Abstract

**Background:** In the past few years, increased resistance of microorganisms towards antimicrobial agents become a serious health problem, so there is a need for the discovery of new antimicrobial agents. On the other hand, bis-pyrimidines possess various types of biological activity. In view of this, in the present study we have designed and synthesized a new series of bis-pyrimidine acetamides by Claisen–Schmidt condensation and screened for its in vitro antimicrobial and anticancer activities.

**Results:** The synthesized bis-pyrimidine acetamide derivatives were confirmed by IR, <sup>1</sup>H/<sup>13</sup>C-NMR, Mass spectral studies as well C, H, N analyses. The synthesized compounds were evaluated for their in vitro antimicrobial potential against Gram positive (*Staphylococcus aureus* and *Bacillus subtilis*); Gram negative (*Escherichia coli*, *Pseudomonas aeruginosa* and *Salmonella enterica*) bacterial and fungal (*Candida albicans* and *Aspergillus niger*) strains by tube dilution technique and the minimum inhibitory concentration (MIC) recorded in μmol/mL was comparable to reference drugs, cefadroxil (antibacterial) and fluconazole (antifungal). The in vitro anticancer activity (IC<sub>50</sub> value) determined against human colorectal carcinoma (HCT116) cancer cell line by Sulforhodamine B (SRB) technique and 5-fluorouracil used as reference drug.

**Conclusions:** The biological study demonstrated that compounds **3**, **13**, **16**, **17** and **18** were found to be most active antimicrobial agents with best MIC values than the cefadroxil (antibacterial) and fluconazole (antifungal) and compounds **12**, **16** and **18** found to have better anticancer activity against human colorectal carcinoma (HCT116) cancer cell line with best IC<sub>50</sub> value than the 5-fluorouracil (anticancer).

**Keywords:** Bis-pyrimidines, Claisen–Schmidt condensation, Antimicrobial, Anticancer, SAR

## Background

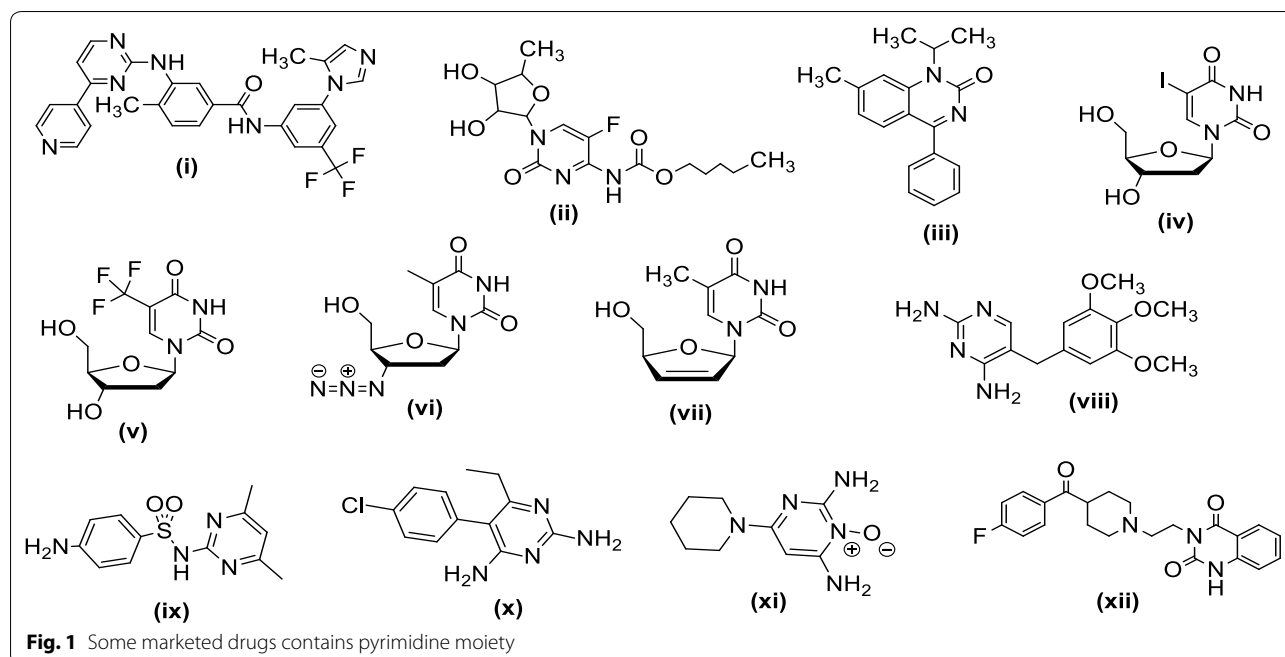
The treatment of bacterial infections remains a challenging therapeutic problem because of emerging infectious diseases as well the increasing number of multidrug resistant microbial pathogens. Despite the many antimicrobial and chemotherapeutic agents are available in market, the emergence of old and new antibiotic resistant bacterial species in the last decade lead to a substantial need for the discovery of new classes of antimicrobial compounds [1]. Cancer is one of the most serious health problems all over the world and one of the leading causes

of death. Thus, in the past for several decades, researchers have been struggling to find effective clinical approaches for the treatment of cancer and search for novel anticancer agents [2]. Among a wide variety of heterocyclic compounds that have been explored for developing medicinally important molecules, nitrogen containing heterocyclic pyrimidine derivatives occupies an important place in the field of medicinal chemistry [3]. The presence of a pyrimidine base in thymine, cytosine and uracil, which are the essential binding blocks of nucleic acids, DNA and RNA is one possible reason for their biological and therapeutical activities. Number of marketed drugs (Fig. 1) contains pyrimidine nucleus i.e. nilotinib (i) and capecitabine (ii) as anticancer; proquazone (iii) as anti-inflammatory; idoxuridine (iv) and trifluoridine (v)

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**Fig. 1** Some marketed drugs contains pyrimidine moiety

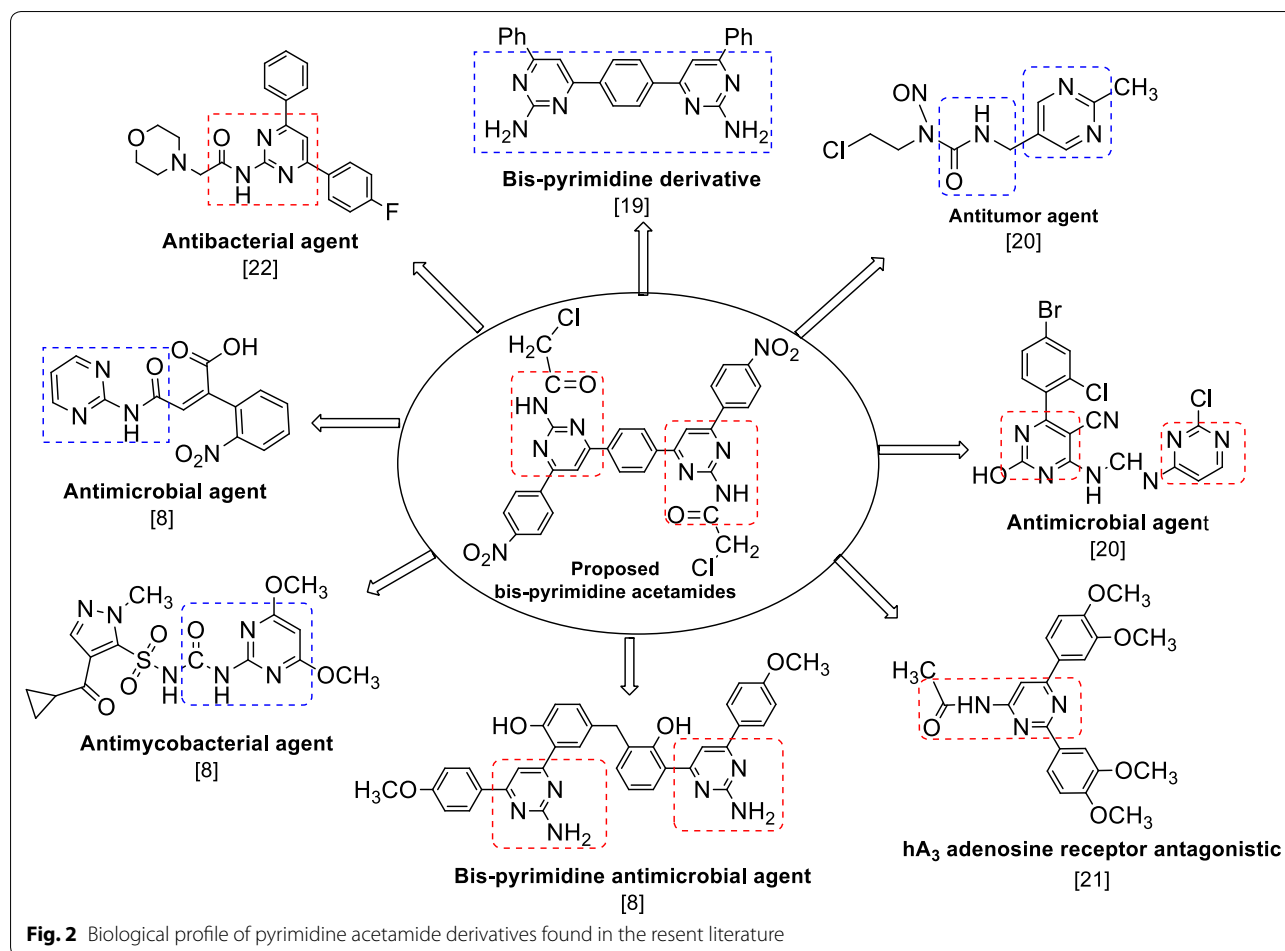
as antiviral; zidovudine (vi) and stavudine (vii) as anti-HIV; trimethoprim (viii) and sulphamethiazine (ix) as antibacterial; pyrimethamine (x) as antimalarial; minoxidil (xi) and ketanserin (xii) as antihypertensive [4]. The literature survey indicated that a wide range of pharmacological activities are exhibited by the compounds encompassing pyrimidine nucleus i.e. antibacterial [5], antifungal [6], antileishmanial [7], antimycobacterial [8], antimicrobial [9], anti-inflammatory [10], anticancer [11], antiviral [12], antitubercular [13], antimalarial [14], antioxidant activity [15], central nervous system (CNS) depressant and calcium channel blocker [8]. Based on the literature survey and biological profile of bis-pyrimidine acetamides summarized in Fig. 2 and in continuation of our efforts in searching novel antimicrobial and anticancer agents [16–18], in the present work, we hereby report the synthesis, antimicrobial and anticancer activities of a series of bis-pyrimidine acetamide derivatives.

## Results and discussion

### Chemistry

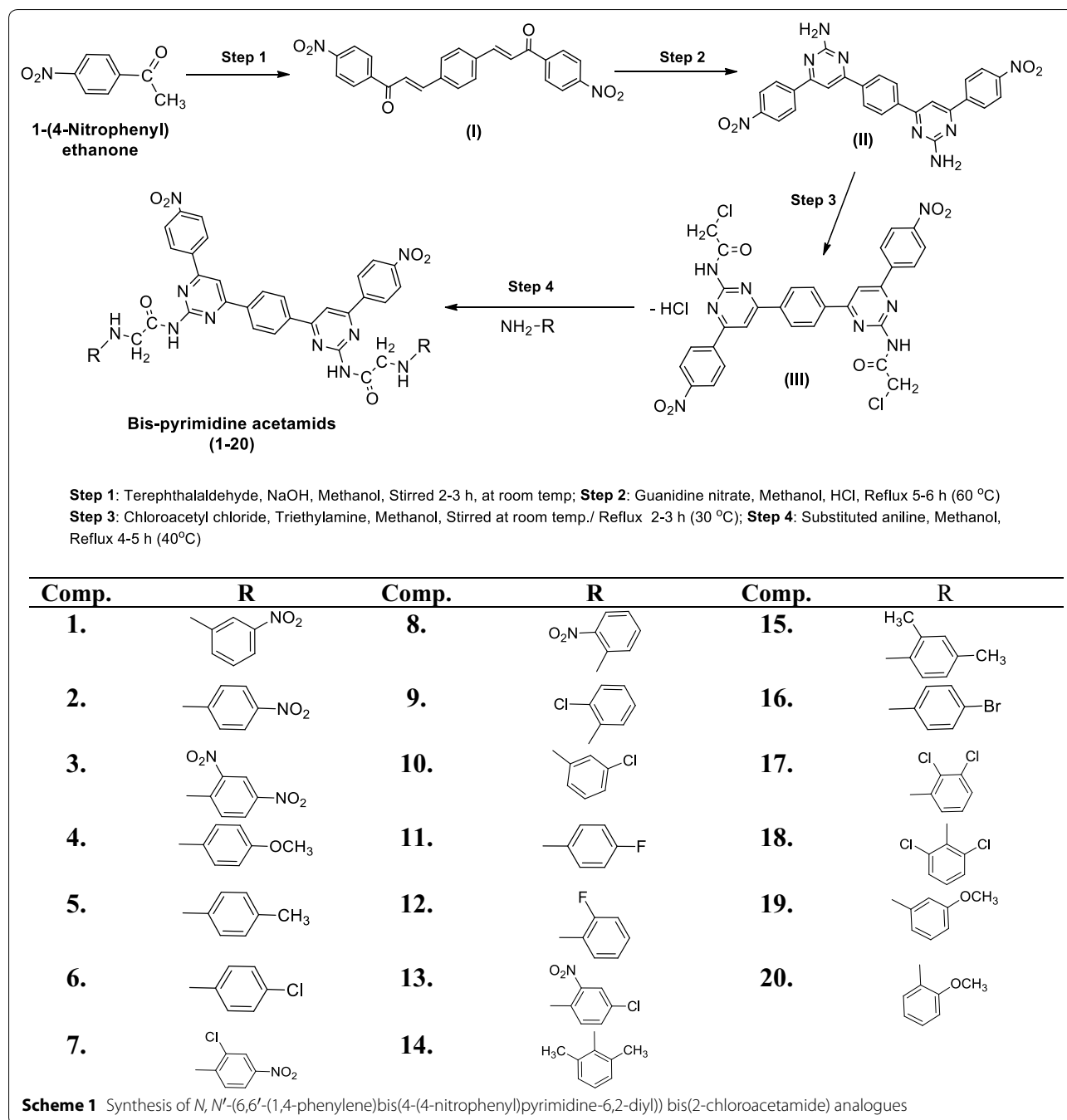
A general approach to synthesize the designed bis-pyrimidine acetamide derivatives based on Claisen–Schmidt condensation is outlined in Scheme 1. Initially, the bis-chalcone (I) was synthesized by the reaction of 1-(4-nitrophenyl)ethanone and terephthalaldehyde. The cyclization of a bis-chalcone into the corresponding bis-pyrimidine (II) was accomplished by the reaction of the bis-chalcone with guanidine nitrate. The reaction of bis-pyrimidine (II) with 2-chloroacetyl chloride resulted

in the formation of III {*N,N'*-(6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-chloroacetamide)} which on reaction with corresponding substituted aniline yielded the title compounds (1–20). The chemical structures of the synthesized compounds were established by the determination of their physico-chemical and spectroscopic data (FT-IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, Mass) and elemental analyses. The structure of the bis-chalcone was confirmed by the corresponding IR (KBr pellets, cm<sup>-1</sup>). The IR spectrum of bis-chalcone (I) showed the characteristic band at 1690 cm<sup>-1</sup> which indicated the presence of a –C=O group and characteristic bands at 3106 and 1517 cm<sup>-1</sup> indicated the presence of C–H and C=C group in aromatic ring respectively. The existence of Ar–NO<sub>2</sub> group in bis-chalcone (I) was displayed by the existence of symmetric Ar–NO<sub>2</sub> stretches in the scale of 1341 cm<sup>-1</sup> and characteristic bands at 2906 and 1598 cm<sup>-1</sup> indicated the presence of C–H and C=C group in alkyl chain respectively. Bis-pyrimidine (II) showed the characteristic bands at 3106 and 1518 cm<sup>-1</sup> for the presence of C–H and C=C group in aromatic ring respectively and characteristic bands at 3370, 1600 and 1349 cm<sup>-1</sup> for indicated the presence of C–NH<sub>2</sub>; N=CH str., of pyrimidine and C–N sym stretches of Ar–NO<sub>2</sub> group. *N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-chloroacetamide) III showed appearance of IR stretching around 3105 and 1519 cm<sup>-1</sup> in the spectral data for the presence of C–H and C=C group in aromatic ring respectively and characteristic bands at 1688, 1599, 2928, 761 and 1349 cm<sup>-1</sup>



for the  $\text{NH}-\text{C}=\text{O}$ ;  $\text{N}=\text{CH}$  str., of pyrimidine;  $\text{C}-\text{H}$  str.,  $\text{CH}_2$ ;  $\text{C}-\text{Cl}$  str., ( $\text{Ar}-\text{Cl}$ );  $\text{C}-\text{N}$  sym str. of aromatic  $\text{NO}_2$  group respectively. The structure of the bis-chalcone and its cyclized products were further confirmed by the corresponding  $^1\text{H}$ -NMR spectra. The  $^1\text{H}$ -NMR spectrum of bis-chalcone **I** showed two doublets at 7.59 ppm ( $J = 15.1$  Hz) and 8.06 ppm ( $J = 15.1$  Hz); indicating that the  $\text{CH}=\text{CH}$  group in the enone linkage is in a *trans*-conformation. The  $^1\text{H}$ -NMR spectrum of intermediate-**II** showed a multiplet signals between 7.43 and 8.40  $\delta$ , ppm confirming the cyclisation of the bis-chalcone to give bis-pyrimidine ring. The  $^1\text{H}$ -NMR spectrum of compound intermediate-**II** showed a sharp singlet at 6.99  $\delta$ , ppm due to the  $\text{NH}_2$  protons and it also showed a sharp singlet at 7.86  $\delta$ , ppm due to  $\text{HC}=\text{C}$  group, which confirmed the cyclization of the bis-chalcone into a bis-pyrimidine ring. Intermediate (**III**) showed the multiplet signals between 7.54 and 8.93  $\delta$ , ppm in  $^1\text{H}$ -NMR spectra which is indicative of aromatic proton and also exhibited sharp singlet at 7.42, 8.10, 3.66  $\delta$ , ppm due to the presence of  $\text{HC}=\text{C}$ ;  $-\text{NH}$ ;  $-\text{CH}_2$  respectively confirmed the

conversion of the bis-pyrimidine into bis-pyrimidine acetamide. The appearance of IR stretching around 1575–1569, 3086–2851 and 1580–1600  $\text{cm}^{-1}$  in the spectral data of synthesized derivatives (**1–20**) specified the existence of  $\text{C}=\text{N}$  group of pyrimidine ring;  $\text{C}-\text{H}$  and  $\text{C}=\text{C}$  group respectively. The IR absorption band in the scale of 1106–1105  $\text{cm}^{-1}$  corresponds to the  $\text{C}-\text{F}$  stretching of aromatic-fluoro compounds (**11** and **12**) and 697–536  $\text{cm}^{-1}$  corresponds to the  $\text{C}-\text{Br}$  stretching of aromatic-bromo derivative (**16**). The existence of an arylalkyl ether category ( $\text{C}-\text{O}-\text{C}$ ,  $\text{Ar}-\text{OCH}_3$ ) in derivatives, **4**, **19** and **20** are established by the existence of an IR symmetric stretches around 1107–1088  $\text{cm}^{-1}$ . Further, the existence of halogen group in compounds (**6**, **7**, **9**, **10**, **13**, **17** and **18**) is indicated by the existence of  $\text{Ar}-\text{Cl}$  stretching vibrations at 761–700  $\text{cm}^{-1}$ . The impression of IR stretching at 1692–1620  $\text{cm}^{-1}$  in the spectra of specified the existence of  $\text{NH}-\text{C}=\text{O}$  group of synthesized derivatives. The multiplet signals between 6.74 and 9.08  $\delta$ , ppm in  $^1\text{H}$ -NMR spectra is indicative of aromatic proton of synthesized derivatives (**1–20**). The compounds,



4, 19 and 20 showed singlet at 3.38–3.75  $\delta$ , ppm due to the presence of  $\text{OCH}_3$  of  $\text{Ar-OCH}_3$  in their structure. All compounds showed singlet at 7.47–7.91  $\delta$ , ppm due to the existence of  $\text{N=CH}$  in pyrimidine ring. Synthesized compounds showed appearance of IR stretching around  $1349\text{ cm}^{-1}$  which indicated the presence of  $\text{C-N}$  sym. str. of aromatic  $\text{NO}_2$  group. Compounds, 5, 14 and 15 showed singlet at 2.09–2.51  $\delta$ , ppm due to existence of  $-\text{CH}_3$  at *ortho* and *para* position. All compounds showed

singlet at 3.34–3.38  $\delta$ , ppm and 8.00–8.08  $\delta$ , ppm due to the existence of  $-\text{CH}_2-$  and  $-\text{NH}-$  groups respectively. The elemental analysis results of the synthesized bis-pyrimidine acetamide derivatives were found within  $\pm 0.4\%$  of the theoretical results. Finally, the  $^{13}\text{C-NMR}$  spectra of the bis-chalcone and the cyclized bis-pyrimidine were recorded in  $\text{DMSO-}d_6$  and the spectral signals were in good agreement with the proposed molecular structure of the synthesized compounds.  $^{13}\text{C-NMR}$

spectra details of all compounds are given in the experimental part. Characteristic molecular ion peaks were observed in the mass spectra of the bis-chalcone and the cyclized bis-pyrimidine and final bis-pyrimidine acetamide derivatives.

#### Antimicrobial activity

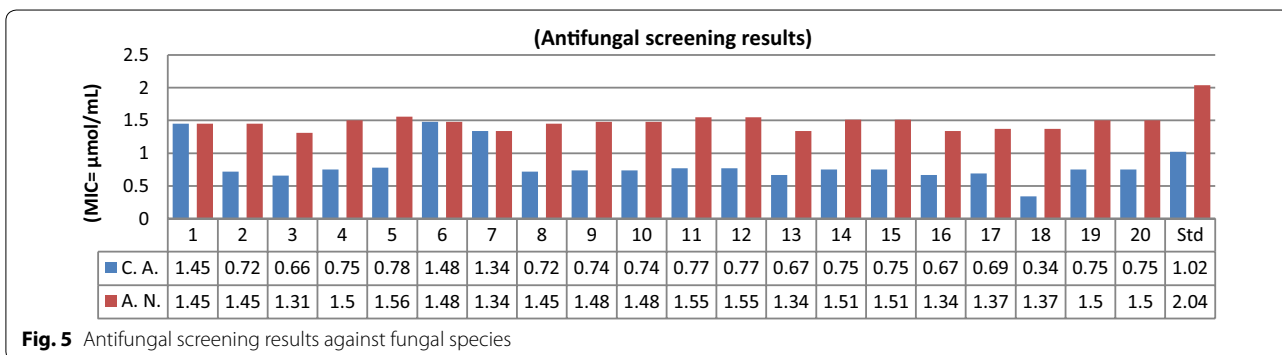
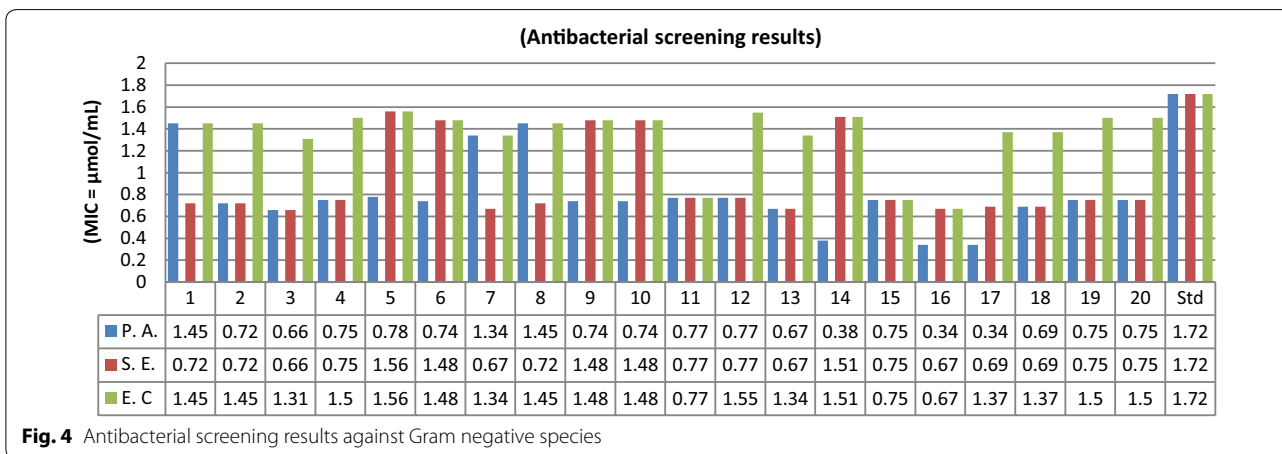
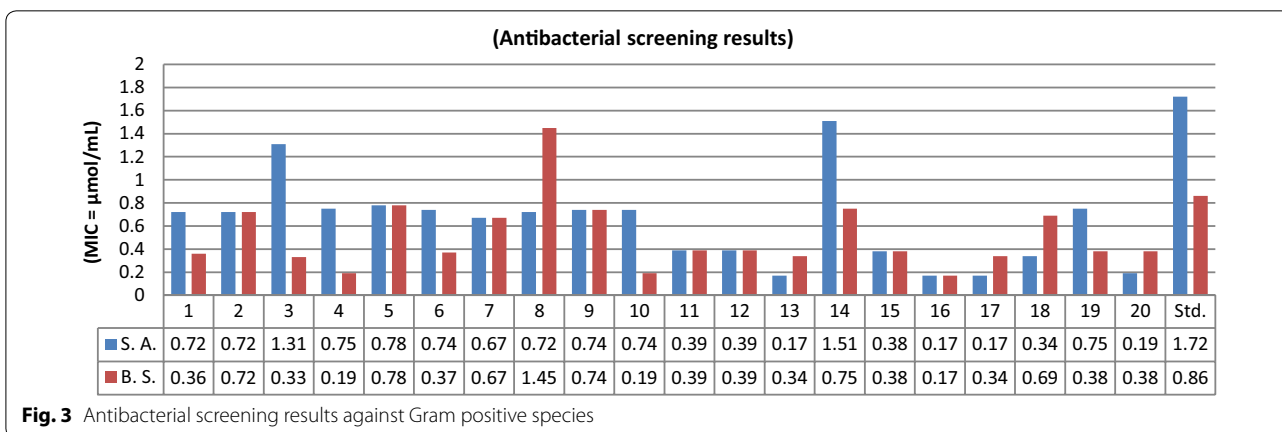
The synthesized compounds were screened for their in vitro antimicrobial activity by tube dilution method. The investigation of antimicrobial screening revealed that some of the synthesized compounds showed moderate to good antimicrobial activity against Gram positive bacterial species: *Staphylococcus aureus*, *Bacillus subtilis* and Gram negative bacterial species: *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella enterica* and fungal species: *Aspergillus niger* and *Candida albicans*. Particularly, compounds **3**, **13**, **16**, **17** and **18** have shown more promising antimicrobial activity as compared to standard drugs cefadroxil (antibacterial) and fluconazole

(antifungal). The remaining compounds displayed average to poor activity against all seven microbial species. In vitro antimicrobial activity results of synthesized compound are summarized in Table 1. Antibacterial screening results (Fig. 3) against Gram positive bacterial species demonstrated that compound **16** has showed good antibacterial activity against *S. aureus* and *B. subtilis* respectively. Compounds, **13** and **17** have sensible activity against *S. aureus*. The MIC values of **13** nearly close to MIC value of standard drugs cefadroxil while **16** and **17** have more active than standard drugs. Antibacterial screening results (Fig. 4) indicated that compound **3** possessed excellent activity against *S. enterica*. Compound **16** exhibited promising activity against *P. aeruginosa* and *E. coli*. Compound **17** was most active against *P. aeruginosa*. The MIC values of compounds **16** and **17** was more than the MIC values of standard drug cefadroxil Gram negative bacterial species. Antifungal screening results (Fig. 5) indicated that compound **3** and **18** were

**Table 1** Antimicrobial and anticancer screening results of synthesized compounds

Compounds No.	Minimum inhibitory concentration (MIC = $\mu\text{mol/mL}$ )							IC <sub>50</sub> ( $\mu\text{mol/mL}$ ) Cancer cell line
	Bacterial species					Fungal species		
	Gram positive		Gram negative					
	<i>S. aureus</i> MTCC-3160	<i>B. subtilis</i> MTCC-441	<i>P. aeruginosa</i> MTCC-3542	<i>S. enterica</i> MTCC-1165	<i>E. coli</i> MTCC-443	<i>C. albicans</i> MTCC-227	<i>A. niger</i> MTCC-281	
1.	0.72	0.36	1.45	0.72	1.45	1.45	1.45	3.86
2.	0.72	0.72	0.72	0.72	1.45	0.72	1.45	3.86
3.	1.31	0.33	0.66	0.66	1.31	0.66	1.31	3.50
4.	0.75	0.19	0.75	0.75	1.50	0.75	1.50	4.00
5.	0.78	0.78	0.78	1.56	1.56	0.78	1.56	4.16
6.	0.74	0.37	0.74	1.48	1.48	1.48	1.48	3.96
7.	0.67	0.67	1.34	0.67	1.34	1.34	1.34	3.58
8.	0.72	1.45	1.45	0.72	1.45	0.72	1.45	3.86
9.	0.74	0.74	0.74	1.48	1.48	0.74	1.48	1.98
10.	0.74	0.19	0.74	1.48	1.48	0.74	1.48	3.96
11.	0.39	0.39	0.77	0.77	0.77	0.77	1.55	1.52
12.	0.39	0.39	0.77	0.77	1.55	0.77	1.55	0.74
13.	0.17	0.34	0.67	0.67	1.34	0.67	1.34	3.58
14.	1.51	0.75	0.38	1.51	1.51	0.75	1.51	4.02
15.	0.38	0.38	0.75	0.75	0.75	0.75	1.51	2.17
16.	0.17	0.17	0.34	0.67	0.67	0.67	1.34	0.98
17.	0.17	0.34	0.34	0.69	1.37	0.69	1.37	1.22
18.	0.34	0.69	0.69	0.69	1.37	0.34	1.37	0.73
19.	0.75	0.38	0.75	0.75	1.50	0.75	1.50	4.00
20.	0.19	0.38	0.75	0.75	1.50	0.75	1.50	2.16
DMSO	0.00	0.00	0.00	0.00	0.00	0.00	0.00	–
Cefadroxil	1.72	0.86	1.72	1.72	1.72	–	–	–
Fluconazole	–	–	–	–	–	1.02	2.04	–
5-Fluorouracil	–	–	–	–	–	–	–	7.67

Std. drugs: cefadroxil—Antibacterial; fluconazole—Antifungal; 5-fluorouracil—Anticancer



found to be most effective ones against *A. niger* and *C. albicans* respectively. The rest of the compounds of the series exhibited average to poor antifungal activity. The antimicrobial activity results of synthesized bis-pyrimidine acetamide derivatives indicated that the synthesized compounds are more active than the standard drugs and

may be taken as a lead compound to discover novel antimicrobial agents.

**Anticancer activity**

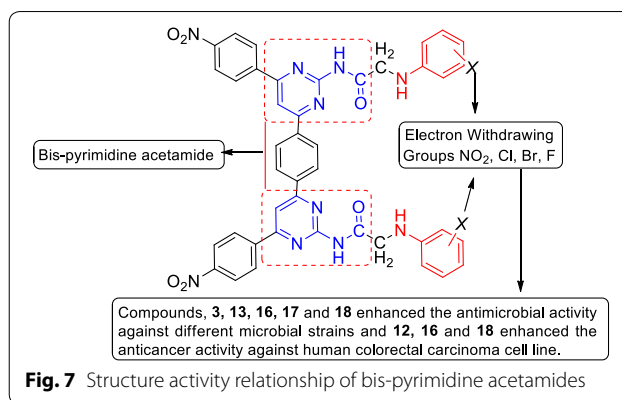
The anticancer screening ( $IC_{50} = \mu\text{mol/mL}$ ) of the synthesized bis-pyrimidine acetamide derivatives was

determined against human colorectal carcinoma [HCT-116 (ATCC CCL-247)] cancer cell line by Sulforhodamine B (SRB) technique [28] using 5-fluorouracil as reference drug and the results are presented in Table 1. Anticancer screening results (Fig. 6) revealed that in general bis-pyrimidine acetamides exhibited good anticancer potential against human colorectal cancer cell line, especially, Compounds, 12, 16 and 18 displayed more anticancer activity than the reference drug 5-fluorouracil ( $IC_{50} = 7.67 \mu\text{mol/mL}$ ) with  $IC_{50}$  values of 0.74, 0.98 and  $0.73 \mu\text{mol/mL}$  respectively.

The structure–activity relationship of the synthesized bis-pyrimidine acetamides indicated that the compounds bearing electron withdrawing group at different position of phenyl group plays an important role in enhancing the antimicrobial and anticancer potentials (Fig. 7).

### Experimental part

Preparatory materials for the research work were obtained from commercial sources and were used without further purification. All reactions were monitored by thin-layer chromatography on 0.25 mm silica gel (Merck) plates, using benzene as mobile phase and spots were observed by exposure to iodine vapours or visualized with UV light. Melting points of synthesized compounds was determined in open capillary tube. An infrared spectrum was recorded (KBr-pellets) in Bruker 12060280, Software: OPUS 7.2.139.1294 spectrometer.  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  were recorded at 600 and 150 MHz, respectively on Bruker Avance III 600 NMR spectrometer by appropriate deuterated solvents. The results are conveyed in parts per million ( $\delta$ , ppm) downfield from tetramethyl silane (internal standard).  $^1\text{H-NMR}$  spectral details of the synthesized derivatives are represented with multiplicity like singlet (s); doublet (d); triplet (t); multiplet (m) and the number hydrogen ion. Elemental analysis of the new synthesized compounds was obtained by Perkin–Elmer 2400 C, H and N analyzer. All the compounds gave C, H and N analysis within  $\pm 0.4\%$  of the theoretical results. Mass spectra were taken on Waters Micromass Q-ToF Micro instrument. The synthesized



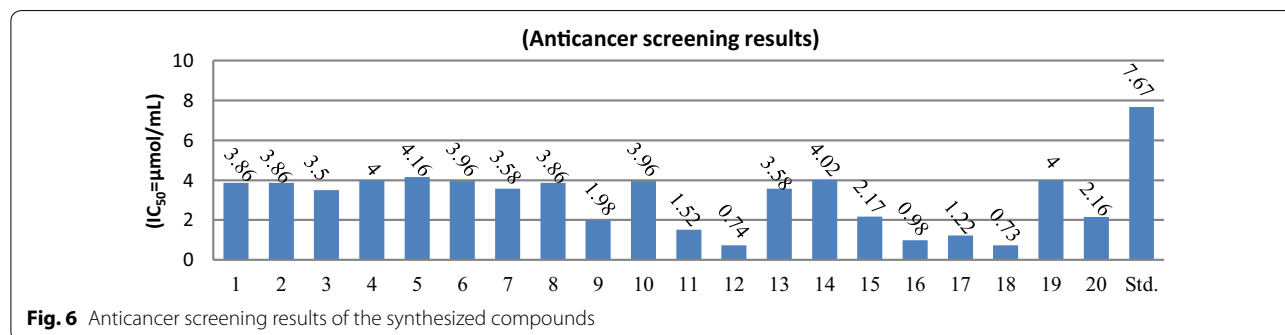
**Fig. 7** Structure activity relationship of bis-pyrimidine acetamides

compounds were characterized by the determination of their physicochemical and spectral characteristics.

### General procedure of the synthesized bis-pyrimidine acetamide derivatives (1–20)

**Step i: Synthesis of 3,3'-(1,4-phenylene)bis(1-(4-nitrophenyl)prop-2-en-1-one) (I)** A mixture of 1-(4-nitrophenyl) ethanone (0.02 mol) and terephthalaldehyde (0.01 mol) in methanol (5–10 mL) was stirred with drop wise addition of 40% sodium hydroxide solution (10 mL) at room temperature till a dark yellow mass was obtained (2–3 h). Then reaction mixture was allowed to stand overnight at room temperature and then was poured into iccold water and acidified with hydrochloric acid and the precipitated 3,3'-(1,4-phenylene)bis(1-(4-nitrophenyl) prop-2-en-1-one) was filtered, dried and recrystallized from methanol [23, 24].

**Step ii: Synthesis of 6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidin-2-amine) (II)** The solution of 3,3'-(1,4-phenylene)bis(1-(4-nitrophenyl)prop-2-en-1-one) (0.01 mol) (synthesized in previous step-i) in methanol (80 mL) was added with 0.01 mol of potassium hydroxide and 40 mL of 0.50 M solution of guanidine nitrate and refluxed for 5–6 h. The reaction mixture was then cooled and acidified with few drops of hydrochloric acid (20 mL of 0.5 M solution) and the resultant precipi-



**Fig. 6** Anticancer screening results of the synthesized compounds

tate, 6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidin-2-amine) was separated dried and recrystallized from methanol [23, 24].

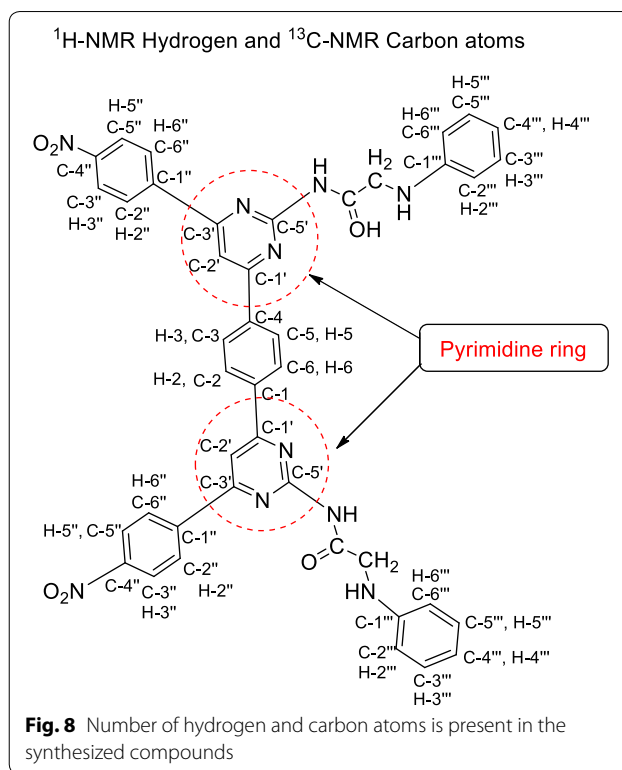
**Step iii: Synthesis of *N,N'*-(6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-chloroacetamide) (III)** In ethanol (30 mL), chloroacetyl chloride (0.02 mol) and 2–3 drops of triethylamine were added and the mixture was stirred in water bath for 10 min after that the solution of 6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidin-2-amine) (synthesized in previous step-ii) (0.01 mol) in ethanol (80 mL) was added drop wise and refluxed for 2–3 h. The reaction mixture was then cooled and poured into iccold water and resultant precipitate was filtered and washed with water, dried and recrystallized from alcohol [25].

**Step iv: Synthesis of final (1–20) bis-pyrimidine acetamide derivatives** The reaction mixture of *N,N'*-(6,6'-(1,4-phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-chloroacetamide) (0.01 mol) and substituted aniline (0.02 mol) in ethanol was refluxed for 4–5 h. The reaction progress was monitored by thin layer chromatography. After completion of reaction, the reaction mixture was poured into iccold water and the precipitated title compound was filtered, dried and recrystallized from methanol.

#### Spectral data interpretation of the synthesized compounds (Fig. 8)

**3,3'-(1,4-Phenylene)bis(1-(4-nitrophenyl)prop-2-en-1-one) (I)** IR (KBr pellets,  $\text{cm}^{-1}$ ): 3106 (C–H str., phenyl nucleus), 1517 (C=C str., phenyl nucleus), 1690 (C=O str.), 1598 (C=C str., alkyl chain), 2906 (C–H str., alkyl chain), 1341 (C–N sym str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 6.94–9.08 {m, 12H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2}, 7.59 {d, 4H, (CH)<sub>2</sub>, *J* = 15.1 Hz}, 8.06 {d, 4H, (CH)<sub>2</sub>, *J* = 15.1 Hz of CH<sub>2</sub> = CH<sub>2</sub>}; <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 129.8 (C-2, C-3, C-5, C-6), 133.4 (C-1, C-4); 148.0 (C-1'), 121.3 (C-2'), 164.7 (C = O); 145.1 (C-1''), 130.0 (C-2''), 124.9 (C-3''), 162.5 (C-4''); Elem. Anal. Calcd. C<sub>24</sub>H<sub>16</sub>N<sub>2</sub>O<sub>6</sub>; C, 67.29; H, 3.76; N, 6.54; Found: C, 67.26; H, 3.75; N, 6.50; MS ES+(ToF): *m/z* 429 [M<sup>+</sup> + 1].

**6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidin-2-amine) (II)** IR (KBr pellets,  $\text{cm}^{-1}$ ): 3107 (C–H str., phenyl nucleus), 1518 (C=C str., phenyl nucleus), 3370 (C–NH<sub>2</sub> str.), 1600 (N=CH str., of pyrimidine), 1349 (C–N sym str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 7.43–8.40 {m, 12H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2}, 7.86 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 6.97 (s, 2H, (NH)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 128.5 (C-2, C-3,



C-5, C-6), 134.6 (C-1, C-4); 157.8 (C-1', C-3', C-5'), 102 (C-2'), 149.7 (C-5') pyrimidine; 141.5 (C-1''), 126.4 (C-2'', C-6''), 124.4 (C-3'', C-5''), 148.3 (C-4''); Elem. Anal. Calcd. C<sub>26</sub>H<sub>18</sub>N<sub>8</sub>O<sub>4</sub>; C, 61.66; H, 3.58; N, 22.12; Found: C, 61.64; H, 3.51; N, 22.15; MS ES + (ToF): *m/z* 507 [M<sup>+</sup> + 1].

***N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-chloroacetamide) (III)** IR (KBr pellets,  $\text{cm}^{-1}$ ): 3105 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1688 (NH–C=O str.), 1599 (N=CH str., of pyrimidine), 2928 (C–H str., CH<sub>2</sub>), 761 (C–Cl str., Ar–Cl), 1349 (C–N sym. str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 7.54–8.93 {m, 12H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2}, 7.42 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.10 (s, 2H, (NH)<sub>2</sub>), 3.66 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 128.5 (C-2, C-3, C-5, C-6), 136.6 (C-1, C-4); 162.0 (C-1', C-3'), 108.0 (C-2'), 149.7 (C-5') pyrimidine; 141.0 (C-1''), 126.6 (C-2'', C-6''), 124.5 (C-3'', C-5''), 149.8 (C-4''), 188.0 (C = O), 44.3(CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>30</sub>H<sub>20</sub>Cl<sub>2</sub>N<sub>8</sub>O<sub>6</sub>; C, 54.64; H, 3.06; N, 16.99; Found: C, 54.60; H, 3.00; N, 16.92; MS ES + (ToF): *m/z* 660 [M<sup>+</sup> + 1].

***N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((3-nitrophenyl) amino)acetamide) (I)** Brown crystals; Yield: 70.12%; M.p.: 252–254 °C; Rf value: 90.12; IR (KBr,  $\text{cm}^{-1}$ ): 3085 (C–H str., phenyl nucleus),



1528 (C=C str., phenyl nucleus), 1679 (NH-C=O str.), 1572 (N=CH str., of pyrimidine), 2863 (C-H str., CH<sub>2</sub>), 1217 (C-NH-str.), 1347 (C-N sym. str., Ar-NO<sub>2</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.63–8.25 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-4''', H-5''', H-6''') × 2}, 7.63 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.08 (s, 2H, (NH)<sub>2</sub>), 4.0 (s, 2H, (NH)<sub>2</sub>), 3.40 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.3, 128.4 (C-2, C-3, C-5, C-6), 136.5 (C-1, C-4); 165.0 (C-1', C-3'), 109 (C-2'), 149.7 (C-5') pyrimidine; 141.0 (C-1''), 126.5 (C-2'', C-6''), 124.5 (C-3'', C-5''), 149.6 (C-4''); 149.5 (C-1''', C-3'''), 106.9 (C-2'''), 129.9 (C-5'''), 122.1 (C-6'''); 170.2 (C = O), 48.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>N<sub>12</sub>O<sub>10</sub>: C, 58.47; H, 3.50; N, 19.48; Found: C, 58.42; H, 3.49; N, 19.46; MS ES + (ToF): *m/z* 864 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-nitrophenyl) amino)acetamide) (2) Dark brown crystals; M.p.: 262–264 °C; Rf value: 0.32; Yield: 92.45%; IR (KBr, cm<sup>-1</sup>): 3086 (C-H str., phenyl nucleus), 1530 (C=C str., phenyl nucleus), 1679 (NH-C = O str.), 1573 (N=CH str., of pyrimidine), 2929 (C-H str., CH<sub>2</sub>), 1219 (C-NH- str.), 1348 (C-N sym. str., Ar-NO<sub>2</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 6.74–9.09 (m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-3''', H-5''', H-6''') × 2}, 7.04 (s, 2H, CH of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.37 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 127.3 (C-2, C-3, C-5, C-6), 138.9 (C-1, C-4); 164.0 (C-1', C-3'), 112 (C-2'), 148.3 (C-5') pyrimidine; 126.3 (C-2'', C-6''), 121.5 (C-3'', C-5''), 147.6 (C-4''); 152.5 (C-1'''), 115.3 (C-2''', C-6'''), 127.5 (C-3''', C-5'''), 135.6 (C-4'''), 168.2 (C=O), 45.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>N<sub>12</sub>O<sub>10</sub>: C, 58.47; H, 3.50; N, 19.48; Found: C, 58.41; H, 3.48; N, 19.46; MS ES + (ToF): *m/z* 864 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2,4-dinitrophenyl) amino)acetamide) (3) Brown crystals; M.p.: 257–259 °C; Rf value: 0.41; Yield: 92.67%; IR (KBr pellets, cm<sup>-1</sup>): 3211 (C-H str., phenyl nucleus), 1529 (C=C str., phenyl nucleus), 1620 (NH-C=O str.), 1675 (N=CH str., of pyrimidine), 3086 (C-H str., CH<sub>2</sub>), 1274 (C-NH- str.), 1345 (C-N sym. str., Ar-NO<sub>2</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 6.95–8.90 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-3''', H-5''', H-6''') × 2}, 7.87 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.40 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.6 (C-2, C-3, C-5, C-6), 135.05 (C-1, C-4); 164.0 (C-1', C-3'), 102 (C-2'), 149.7 (C-5') pyrimidine; 141.0 (C-1''), 127.3 (C-2'', C-6''), 124.9 (C-3'', C-5''), 148.6 (C-4''); 152.5 (C-1'''), 135.6 (C-2'''), 119.7 (C-3'''), 138.9 (C-4'''), 130.2 (C-5'''); 168.2 (C=O), 51.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>28</sub>N<sub>14</sub>O<sub>14</sub>: C, 52.95; H, 2.96; N,

20.58; Found: C, 52.85; H, 2.46; N, 20.48; MS ES + (ToF): *m/z* 954 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-methoxyphenyl) amino)acetamide) (4) Brown crystals; M.p.: 215–217 °C; Rf value: 0.53; Yield: 89.44%; IR (KBr pellets, cm<sup>-1</sup>): 3084 (C-H str., phenyl nucleus), 1529 (C=C str., phenyl nucleus), 1680 (NH-C=O str.), 1572 (N=CH str., of pyrimidine), 1221 (C-NH- str.), 1347 (C-N sym. str., Ar-NO<sub>2</sub>), 1088 (C-O-C str., -OCH<sub>3</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.04–9.09 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-3''', H-5''', H-6''') × 2}, 7.75 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.0 (s, 2H, (NH)<sub>2</sub>), 3.38 (s, 6H, (OCH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 127.3 (C-2, C-3, C-5, C-6), 138.5 (C-1, C-4); 164.0 (C-1', C-3'), 108 (C-2'), 148.7 (C-5') pyrimidine; 142.0 (C-1''), 127.5 (C-2'', C-6''), 124.9 (C-3'', C-5''), 149.6 (C-4''); 138.5 (C-1'''), 115.3 (C-2''', C-6'''), 115.0 (C-3''', C-5'''), 171.2 (C=O), 51.0 (CH<sub>2</sub>), 53.0 (*p*-OCH<sub>3</sub>); Elem. Anal. Calcd. C<sub>44</sub>H<sub>36</sub>N<sub>10</sub>O<sub>8</sub>: C, 63.46; H, 4.36; N, 16.82; Found: C, 63.44; H, 4.37; N, 16.85; MS ES + (ToF): *m/z* 834 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-(*p*-tolylamino)acetamide) (5) Brown crystals; M.p.: 250–252 °C; Rf value: 0.30; Yield: 85.43%; IR (KBr pellets, cm<sup>-1</sup>): 3084 (C-H str., phenyl nucleus), 1529 (C=C str., phenyl nucleus), 1681 (NH-C=O str.), 1569 (N=CH str., of pyrimidine), 2866 (C-H str., CH<sub>2</sub>), 1217 (C-NH- str.), 1348 (C-N sym. str., Ar-NO<sub>2</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 6.99–8.56 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-3''', H-5''', H-6''') × 2}, 7.48 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.03 (s, 2H, (NH)<sub>2</sub>), 2.51 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.8, 128.4 (C-2, C-3, C-5, C-6), 136.8, (C-1, C-4); 168.0 (C-1', C-3'), 108 (C-2'), 149.7 (C-5') pyrimidine; 141.0 (C-1''), 126.4 (C-2'', C-6''), 123.8 (C-3'', C-5''), 149.7 (C-4''); 144.5 (C-1'''), 117.0 (C-2''', C-6'''), 129.6 (C-3''', C-5'''), 188.0 (C=O), 48.0 (CH<sub>2</sub>), 20.5 (*p*-CH<sub>3</sub>); Elem. Anal. Calcd. C<sub>44</sub>H<sub>36</sub>N<sub>10</sub>O<sub>6</sub>: C, 65.99; H, 4.53; N, 17.49; Found: C, 65.92; H, 4.49; N, 17.40; MS ES + (ToF): *m/z* 802 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-chlorophenyl) amino)acetamide) (6) Brown crystals; M.p.: 168–170 °C; Rf value: 0.42; Yield: 87.58%; IR (KBr pellets, cm<sup>-1</sup>): 3084 (C-H str., phenyl nucleus), 1530 (C=C str., phenyl nucleus), 1687 (NH-C=O str.), 1603 (N=CH str., of pyrimidine), 2866 (C-H str., CH<sub>2</sub>), 1215 (C-NH- str.), 1348 (C-N sym. str., Ar-NO<sub>2</sub>), 739 (C-Cl str., Ar-Cl); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 6.35–9.08 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-3''', H-5''', H-6''') × 2}, 7.49 (s,

2H, (CH)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.36 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.4 (C-2, C-3, C-5, C-6), 134.5 (C-1, C-4); 164.0 (C-1', C-3'), 106 (C-2'), 148.3 (C-5') pyrimidine; 127.4 (C-2'', C-6''), 124.9 (C-3'', C-5''), 147.6 (C-4''); 145.5 (C-1'''), 115.1 (C-2''', C-6'''), 129.9 (C-3''', C-5'''), 126.1 (C-4'''); 165.2 (C=O), 53.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>Cl<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 59.94; H, 3.59; N, 16.64; Found: C, 59.90; H, 3.51; N, 16.60; MS ES + (ToF): *m/z* 843 [M<sup>+</sup> +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2-chloro-4-nitro phenyl)amino)acetamide) (7) Brown yellow crystals; M.p.: 170–172 °C; Rf value: 0.60; Yield: 87.12%; IR (KBr pellets, cm<sup>-1</sup>): 3085 (C–H str., phenyl nucleus), 1530 (C=C str., phenyl nucleus), 1688 (NH–C=O str.), 1603 (N=CH str., of pyrimidine), 2869 (C–H str., CH<sub>2</sub>), 1215 (C–NH– str.), 1348 (C–N sym. str., Ar–NO<sub>2</sub>), 740 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 6.48–9.08 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-3''', H-5''', H-6''') × 2}, 7.87 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.37 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 129.3 (C-2, C-3, C-5, C-6), 135.8 (C-1, C-4); 163.0 (C-1', C-3'), 113 (C-2'), 148.7 (C-5') pyrimidine; 126.3 (C-2'', C-6''), 124.9 (C-3'', C-5''), 149.3 (C-4''); 151.3 (C-1'''), 124.3 (C-2'''), 138.9 (C-4'''), 125.1 (C-3'''), 122.1 (C-5'''); 166.2 (C=O), 51.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>28</sub>Cl<sub>2</sub>N<sub>12</sub>O<sub>10</sub>: C, 54.15; H, 3.03; N, 18.04; Found: C, 54.11; H, 3.00; N, 18.12; MS ES + (ToF): *m/z* 933 [M<sup>+</sup> +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2-nitrophenyl) amino)acetamide) (8) Light Brown crystals; M.p.: 163–165 °C; Rf value: 0.34; Yield: 84.23%; IR (KBr pellets, cm<sup>-1</sup>): 3085 (C–H str., phenyl nucleus), 1530 (C=C str., phenyl nucleus), 1688 (NH–C=O str.), 1603 (N=CH str., of pyrimidine), 2868 (C–H str., CH<sub>2</sub>), 1215 (C–NH– str.), 1348 (C–N sym. str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.03–8.25 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-3''', H-4''', H-5''', H-6''') × 2}, 7.79 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.04 (s, 2H, (NH)<sub>2</sub>), 3.38 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 127.4 (C-2, C-3, C-5, C-6), 135.6 (C-1, C-4); 162.0 (C-1', C-3'), 105 (C-2'), 148.7 (C-5') pyrimidine; 141.0 (C-1''), 126.5 (C-2'', C-6''), 124.3 (C-3'', C-5''), 149.6 (C-4''); 147.5 (C-1'''), 130.1 (C-2'''), 125.9 (C-3'''), 119.1 (C-4'''), 136.2 (C-5'''); 164.2 (C=O), 50.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>N<sub>12</sub>O<sub>10</sub>: C, 58.47; H, 3.50; N, 19.48; Found: C, 58.42; H, 3.45; N, 19.41; MS ES + (ToF): *m/z* 864 [M<sup>+</sup> +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-(2-chlorophenyl) acetamide) (9) Canary yellow crystals; M.p.: 150–152 °C; Rf value:

0.58; Yield: 75.25%; IR (KBr pellets, cm<sup>-1</sup>): 3075 (C–H str., phenyl nucleus), 1521 (C=C str., phenyl nucleus), 1690 (NH–C=O str.), 1598 (N=CH str., of pyrimidine), 2851 (C–H str., CH<sub>2</sub>), 1210 (C–NH– str.), 1344 (C–N sym. str., Ar–NO<sub>2</sub>), 757 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.80–8.25 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-3''', H-4''', H-5''', H-6''') × 2}, 7.80 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.37 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.6 (C-2, C-3, C-5, C-6), 135.5 (C-1, C-4); 163.0 (C-1', C-3'), 107 (C-2'), 149.7 (C-5') pyrimidine; 141.0 (C-1''), 127.5 (C-2'', C-6''), 123.5 (C-3'', C-5''), 149.8 (C-4''); 134.5 (C-1'''), 129.1 (C-2''', C-3''', C-4'''), 127.9 (C-5'''), 133.1 (C-6'''); 156.2 (C=O), 39 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>Cl<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 59.94; H, 3.59; N, 16.64; Found: C, 59.90; H, 3.53; N, 16.61; MS ES + (ToF): *m/z* 843 [M<sup>+</sup> +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-(2-chlorophenyl) acetamide) (10) Light yellow crystals; M.p.: 138–140 °C; Rf value: 0.31; Yield: 80.22%; IR (KBr pellets, cm<sup>-1</sup>): 3074 (C–H str., phenyl nucleus), 1521 (C=C str., phenyl nucleus), 1690 (NH–C=O str.), 1597 (N=CH str., of pyrimidine), 2854 (C–H str., CH<sub>2</sub>), 1210 (C–NH– str.), 1344 (C–N sym. str., Ar–NO<sub>2</sub>), 757 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.82 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-4''', H-5''', H-6''') × 2}, 7.80 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.38 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 128.3 (C-2, C-3, C-5, C-6), 135.5 (C-1, C-4); 165.0 (C-1', C-3'), 108 (C-2'), 149.8 (C-5') pyrimidine; 142.0 (C-1''), 127.5 (C-2'', C-6''), 123.5 (C-3'', C-5''), 149.6 (C-4''); 149.5 (C-1'''), 110 (C-2'''), 134.9 (C-3'''), 120.4 (C-5'''); 163.2 (C=O), 56.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>Cl<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 59.94; H, 3.59; N, 16.64; Found: C, 59.90; H, 3.52; N, 16.67; MS ES + (ToF): *m/z* 843 [M<sup>+</sup> +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-fluorophenyl) amino)acetamide) (11) Yellow crystals; M.p.: 123–125 °C; Rf value: 0.33; Yield: 85.63%; IR (KBr pellets, cm<sup>-1</sup>): 3073 (C–H str., phenyl nucleus), 1518 (C=C str., phenyl nucleus), 1665 (NH–C=O str.), 1596 (N=CH str., of pyrimidine), 2852 (C–H str., CH<sub>2</sub>), 1210 (C–NH– str.), 1338 (C–N sym. str., Ar–NO<sub>2</sub>), 1105 (C–F str., Ar–F); <sup>1</sup>H-NMR (δ, DMSO-*d*<sub>6</sub>): 7.25–8.69 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'') × 2, (H-2''', H-3''', H-5''', H-6''') × 2}, 7.39 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.34 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR (δ, DMSO-*d*<sub>6</sub>): 129.3 (C-2, C-3, C-5, C-6), 136.7 (C-1, C-4); 161.0 (C-1', C-3'), 105 (C-2'), 149.8 (C-5') pyrimidine; 142.0 (C-1''), 126.4 (C-2'', C-6''), 124.5 (C-3'', C-5''), 147.4 (C-4''); 144.5 (C-1'''), 115.9 (C-3''', C-5'''), 119.0 (C-2''', C-6'''), 159.8 (C-5'''); 169.2 (C=O), 68.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>F<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 62.37;

H, 3.74; N, 17.32; Found: C, 62.33; H, 3.72; N, 17.35; MS ES + (ToF):  $m/z$  810 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2-fluorophenyl) amino)acetamide) (12) Gold Yellow crystals; M.p.: 170–172 °C; Rf value: 0.25; Yield: 77.12%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3108 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1665 (NH–C=O str.), 1600 (N=CH str., of pyrimidine), 2934 (C–H str.,  $\text{CH}_2$ ), 1211 (C–NH– str.), 1340 (C–N sym. str., Ar–NO<sub>2</sub>), 1106 (C–F str., Ar–F); <sup>1</sup>H-NMR ( $\delta$ , DMSO- $d_6$ ): 7.91–8.39 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'')  $\times$  2, (H-3''', H-4''', H-5''', H-6''')  $\times$  2}, 7.90 (s, 2H, (CH<sub>2</sub>)<sub>2</sub> of pyrimidine), 3.38 (s, 4H, (CH<sub>2</sub>)), 8.00 (s, 2H, (NH)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO- $d_6$ ): 129.3 (C-2, C-3, C-5, C-6), 135.5 (C-1, C-4); 162.0 (C-1', C-3'), 105 (C-2'), 149.7 (C-5') pyrimidine; 127.5 (C-2'', C-6''), 124.7 (C-3'', C-5''), 147.6 (C-4''); 130.5 (C-1'''), 153.2 (C-3'''), 116.9 (C-3'''), 121.9 (C-4'''); 188.2 (C=O), 49.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>F<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 62.37; H, 3.74; N, 17.32; Found: C, 62.34; H, 3.67; N, 17.28; MS ES + (ToF):  $m/z$  810 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-chloro-2-nitro phenyl)amino)acetamide) (13) Light yellow crystals; M.p.: 175–177 °C; Rf value: 0.16; Yield: 85.25%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3107 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1665 (NH–C=O str.), 1600 (N=CH str., of pyrimidine), 2936 (C–H str.,  $\text{CH}_2$ ), 1247 (C–NH– str.), 1341 (C–N sym. str., Ar–NO<sub>2</sub>), 761 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR ( $\delta$ , DMSO- $d_6$ ): 7.05–8.39 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'')  $\times$  2, (H-3''', H-5''', H-6''')  $\times$  2}, 7.48 (s, 2H, (CH<sub>2</sub>)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.66 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO- $d_6$ ): 128.9 (C-2, C-3, C-5, C-6), 135.5 (C-1, C-4); 165.0 (C-1', C-3'), 110 (C-2'), 149.8 (C-5') pyrimidine; 141.0 (C-1''), 126.4 (C-2'', C-6''), 124.0 (C-3'', C-5''), 149.9 (C-4''); 143.5 (C-1'''), 132.2 (C-2'''), 126.5 (C-3'''), 122.9 (C-4'''), 134.1 (C-5'''), 118.1 (C-6'''); 188.2 (C=O), 52.5 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>28</sub>Cl<sub>2</sub>N<sub>12</sub>O<sub>10</sub>: C, 54.15; H, 3.03; N, 18.04; Found: C, 54.13; H, 3.00; N, 18.01; MS ES + (ToF):  $m/z$  933 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2,6-dimethyl phenyl)amino)acetamide) (14) Gold yellow crystals; M.p.: 158–160 °C; Rf value: 0.38; Yield: 82.33%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3074 (C–H str., phenyl nucleus), 1520 (C=C str., phenyl nucleus), 1692 (NH–C=O str.), 1601 (N=CH str., of pyrimidine), 2853 (C–H str.,  $\text{CH}_2$ ), 1211 (C–NH– str.), 1343 (C–N sym. str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO- $d_6$ ): 7.94–8.39 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'')  $\times$  2, (H-3''', H-4''', H-5''')  $\times$  2}, 7.91 (s, 2H,

(CH<sub>2</sub>)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.39 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>), 2.09 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO- $d_6$ ): 128.6 (C-2, C-3, C-5, C-6), 135.5 (C-1, C-4); 162.0 (C-1', C-3'), 108 (C-2'), 149.8 (C-5') pyrimidine; 141.0 (C-1''), 126.5 (C-2'', C-6''), 123.5 (C-3'', C-5''), 149.0 (C-4''); 145.5 (C-1'''), 119.0 (C-4'''), 127.2 (C-2''', C-6'''), 127.9 (C-3''', C-5'''); 170.2 (C=O), 52.5 (CH<sub>2</sub>), 17.8 (2,6-CH<sub>3</sub>); Elem. Anal. Calcd. C<sub>46</sub>H<sub>40</sub>N<sub>10</sub>O<sub>6</sub>: C, 66.66; H, 4.86; N, 16.90; Found: C, 66.63; H, 4.81; N, 16.87; MS ES + (ToF):  $m/z$  830 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2,4-dimethyl phenyl)amino)acetamide) (15) Gold yellow crystals; M.p.: 135–137 °C; Rf value: 0.45; Yield: 89.63%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3074 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1664 (NH–C=O str.), 1597 (N=CH str., of pyrimidine), 2917 (C–H str.,  $\text{CH}_2$ ), 1208 (C–NH– str.), 1339 (C–N sym. str., Ar–NO<sub>2</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO- $d_6$ ): 6.58–8.40 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'')  $\times$  2, (H-3''', H-5''', H-6''')  $\times$  2}, 7.47 (s, 2H, (CH<sub>2</sub>)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.36 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>), 2.51 (s, 6H, (CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO- $d_6$ ): 128.9 (C-2, C-3, C-5, C-6), 136.5 (C-1, C-4); 163.0 (C-1', C-3'), 104 (C-2'), 149.8 (C-5') pyrimidine; 141.0 (C-1''), 126.4 (C-2'', C-6''), 124.5 (C-3'', C-5''), 149.8 (C-4''); 143.6 (C-1'''), 126.5, 126.2 (C-2''', C-5'''), 133.9 (C-3'''), 136.9 (C-4'''), 116.1 (C-6'''); 188.2 (C=O), 52.0 (CH<sub>2</sub>), 18.2 (o-CH<sub>3</sub>), 21.2 (p-CH<sub>3</sub>); Elem. Anal. Calcd. C<sub>46</sub>H<sub>40</sub>N<sub>10</sub>O<sub>6</sub>: C, 66.66; H, 4.86; N, 16.90; Found: C, 66.63; H, 4.87; N, 16.95; MS ES + (ToF):  $m/z$  830 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((4-bromophenyl) amino)acetamide) (16) Gold yellow crystals; M.p.: 138–140 °C; Rf value: 0.23; Yield: 87.77%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3107 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1665 (NH–C=O str.), 1599 (N=CH str., of pyrimidine), 2933 (C–H str.,  $\text{CH}_2$ ), 1209 (C–NH– str.), 1341 (C–N sym. str., Ar–NO<sub>2</sub>), 697 (C–Br str., Ar–Br); <sup>1</sup>H-NMR ( $\delta$ , DMSO- $d_6$ ): 6.51–8.69 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2'', H-3'', H-5'', H-6'')  $\times$  2, (H-2''', H-3''', H-5''', H-6''')  $\times$  2}, 7.55 (s, 2H, (CH<sub>2</sub>)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.37 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO- $d_6$ ): 128.2 (C-2, C-3, C-5, C-6), 136.7 (C-1, C-4); 160.0 (C-1', C-3'), 104 (C-2'), 149.8 (C-5') pyrimidine; 141.5 (C-1''), 126.4 (C-2'', C-6''), 123.5 (C-3'', C-5''), 149.7 (C-4''); 145.5 (C-1'''), 115 (C-2''', C-6'''), 132.0 (C-3''', C-5'''), 118.8 (C-5'''); 188.2 (C = O), 52.5 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>30</sub>Br<sub>2</sub>N<sub>10</sub>O<sub>6</sub>: C, 54.21; H, 3.25; N, 15.05; Found: C, 54.18; H, 3.20; N, 15.00; MS ES + (ToF):  $m/z$  933 [ $M^+$  +1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2,3-dichlorophenyl) amino)aceta-

*mide*) (17) Gold yellow crystals; M.p.: 195–197 °C; Rf value: 0.16; Yield: 72.01%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3108 (C–H str., phenyl nucleus), 1520 (C=C str., phenyl nucleus), 1666 (NH–C=O str.), 1599 (N=CH str., of pyrimidine), 2934 (C–H str.,  $\text{CH}_2$ ), 1211 (C–NH– str.), 1341 (C–N sym. str., Ar–NO<sub>2</sub>), 700 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 7.93–8.39 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2''), H-3'', H-5'', H-6'') × 2, (H-4''', H-5''', H-6''') × 2}, 7.91 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.38 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 128.9 (C-2, C-3, C-5, C-6), 135.1 (C-1, C-4); 162.0 (C-1', C-3'), 104.1 (C-2'), 149.0 (C-5') pyrimidine; 126.4 (C-2'', C-6''), 123.8 (C-3'', C-5''), 149.6 (C-4''); 145.3 (C-1'''), 123.6 (C-2'''), 133.9 (C-3'''), 122.9 (C-4'''), 129.1 (C-5'''), 113.1 (C-6'''); 188.2 (C=O), 52.6 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>28</sub>Cl<sub>4</sub>N<sub>10</sub>O<sub>6</sub>: C, 55.40; H, 3.10; N, 15.38; Found: C, 55.38; H, 3.07; N, 15.33; MS ES + (ToF): *m/z* 912 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((2,6-dichlorophenyl) amino)acetamide) (18) Gold yellow crystals; M.p.: 129–131 °C; Rf value: 0.33; Yield: 75.30%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3107 (C–H str., phenyl nucleus), 1520 (C=C str., phenyl nucleus), 1666 (NH–C = O str.), 1599 (N=CH str., of pyrimidine), 2936 (C–H str., CH<sub>2</sub>), 1211 (C–NH– str.), 1342 (C–N sym. str., Ar–NO<sub>2</sub>), 700 (C–Cl str., Ar–Cl); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 7.04–9.09 {m, 18H, Ar = H-2, H-3, H-5, H-6, (H-2''), H-3'', H-5'', H-6'') × 2, (H-3''', H-4''', H-5''') × 2}, 7.75 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.38 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 127.3 (C-2, C-3, C-5, C-6), 134.5 (C-1, C-4); 164.0 (C-1', C-3'), 102 (C-2'), 148.3 (C-5') pyrimidine; 126.4 (C-2'', C-6''), 124.5 (C-3'', C-5''), 148.6 (C-4''); 144.5 (C-1'''), 123.5 (C-2'''), 128.5 (C-3'''), 121.1 (C-6'''); 165.2 (C=O), 53.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>42</sub>H<sub>28</sub>Cl<sub>4</sub>N<sub>10</sub>O<sub>6</sub>: C, 55.40; H, 3.10; N, 15.38; Found: C, 76.13; H, 4.24; N, 11.12; MS ES + (ToF): *m/z* 912 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-((3-methoxyphenyl) amino)acetamide) (19) Gold yellow crystals; M.p.: 198–200 °C; Rf value: 0.21; Yield: 75.30%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3074 (C–H str., phenyl nucleus), 1519 (C=C str., phenyl nucleus), 1666 (NH–C=O str.), 1598 (N=CH str., of pyrimidine), 2836 (C–H str., CH<sub>2</sub>), 1210 (C–NH– str.), 1341 (C–N sym. str., Ar–NO<sub>2</sub>), 1105 (C–O–C str., Ar–OCH<sub>3</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 5.22–8.69 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2''), H-3'', H-5'', H-6'') × 2, (H-2''', H-4''', H-5''') × 2}, 7.41 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.01 (s, 2H, (NH)<sub>2</sub>), 3.73 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>), 3.38 (s, 6H, (OCH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 128.3 (C-2, C-3, C-5, C-6), 136.7 (C-1, C-4); 160.0 (C-1', C-3'), 106 (C-2'), 149.8 (C-5') pyrimidine; 141.5 (C-1''), 126.4 (C-2'', C-6''), 123.5 (C-3'',

C-5''), 148.3 (C-4''); 149.7 (C-1'''), 106.4 (C-2''', C-6'''), 113.3 (C-5'''); 188.2 (C=O), 54.4 (CH<sub>2</sub>), 55.1 (OCH<sub>3</sub>); Elem. Anal. Calcd. C<sub>44</sub>H<sub>36</sub>N<sub>10</sub>O<sub>8</sub>: C, 63.46; H, 4.36; N, 16.82; Found: C, 63.39; H, 4.30; N, 16.86; MS ES + (ToF): *m/z* 834 [M<sup>+</sup> + 1].

*N,N'*-(6,6'-(1,4-Phenylene)bis(4-(4-nitrophenyl)pyrimidine-6,2-diyl))bis(2-(2-methoxyphenyl) acetamide) (20) Canary yellow crystals; M.p.: 179–180 °C; Rf value: 0.32; Yield: 89.23%; IR (KBr pellets,  $\text{cm}^{-1}$ ): 3076 (C–H str., phenyl group), 1519 (C=C str., phenyl group), 1666 (NH–C=O str.), 1599 (N=CH str., of pyrimidine), 2842 (C–H str., CH<sub>2</sub>), 1211 (C–NH– str.), 1340 (C–N sym. str., Ar–NO<sub>2</sub>), 1107 (C–O–C str., Ar–OCH<sub>3</sub>); <sup>1</sup>H-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 7.14–8.39 {m, 20H, Ar = H-2, H-3, H-5, H-6, (H-2''), H-3'', H-5'', H-6'') × 2, (H-3''', H-4''', H-5''', H-6''') × 2}, 7.47 (s, 2H, (CH)<sub>2</sub> of pyrimidine), 8.00 (s, 2H, (NH)<sub>2</sub>), 3.82 (s, 4H, (CH<sub>2</sub>)<sub>2</sub>), 3.75 (s, 6H, (OCH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C-NMR ( $\delta$ , DMSO-*d*<sub>6</sub>): 128.9 (C-2, C-3, C-5, C-6), 136.7 (C-1, C-4); 164.0 (C-1', C-3'), 110.0 (C-2'), 149.8 (C-5') pyrimidine; 141.5 (C-1''), 126.4 (C-2'', C-6''), 124.5 (C-3'', C-5''), 149.7 (C-4''); 126.5 (C-1'''), 158.0 (C-2'''), 55.5 (OCH<sub>3</sub>), 113.3 (C-3'''), 128.9 (C-4'''), 121.3 (C-5'''), 133.2 (C-6'''); 188.2 (C=O), 39.0 (CH<sub>2</sub>); Elem. Anal. Calcd. C<sub>44</sub>H<sub>36</sub>N<sub>10</sub>O<sub>8</sub>: C, 63.46; H, 4.36; N, 16.82; Found: C, 63.40; H, 4.31; N, 16.85; MS ES + (ToF): *m/z* 834 [M<sup>+</sup> + 1].

#### Biological study (antimicrobial and anticancer)

The antimicrobial activity i.e. The minimum inhibitory concentration (MIC) of the synthesized compounds (1–20) was determined by tube dilution method [26] using cefadroxil (antibacterial) and fluconazole (antifungal) as reference drugs against Gram-positive [*S. aureus*, MTCC-3160 (Microbial Type Culture Collection); *B. subtilis*, MTCC-441] and Gram-negative bacteria (*E. coli*, MTCC-443; *P. aeruginosa*, MTCC-3542; *S. enterica*, MTCC-1165). The antifungal activity was assayed against yeast (*C. albicans*, MTCC-227) and mould (*A. niger*, MTCC-281). Serial dilutions of the test compounds and reference drugs were prepared in double strength nutrient broth I.P. (bacteria) or sabouraud dextrose broth I.P. (fungi) [27]. The stock solution of the test compounds and reference drugs was prepared in dimethyl sulfoxide (DMSO). Further progressive dilutions were done to obtain final concentrations of 50, 25, 12.5, 6.25, 3.125 and 1.562  $\mu\text{g/mL}$ . The samples were incubated at  $37 \pm 1$  °C for 24 h (bacteria), at  $25 \pm 1$  °C for 7 days (*A. niger*) and at  $37 \pm 1$  °C for 48 h (*C. albicans*) respectively and the results were recorded in terms of MIC. The MIC was the lowest concentration of the tested compound that yields no visible growth of microorganisms in the tube. To ensure that the solvent had no effect on the bacterial growth, a control was performed with the test medium supplemented with DMSO at the same dilutions as

used in the experiments and DMSO had no effect on the microorganisms in the concentrations studied. The anticancer screening ( $IC_{50} = \mu\text{mol/mL}$ ) of synthesized compounds was determined against human colorectal carcinoma [HCT-116 (ATCC (American Type Culture Collection) CCL-247)] cancer cell line using sulforhodamine-B (SRB) assay. In this study, the culture material was fixed with trichloroacetic acid and then stained for 30 min with 0.4% (w/v) sulforhodamine B mixed with 1% acetic acid. Unbound dye was discarded by five washes of 1% acetic acid solution and protein-bound dye was extracted with 10 mM Tris base [tris(hydroxymethyl)aminomethane] for confirmation of optical density in a computer-interfaced, 96-well microtiter plate reader [28].

## Conclusion

In summary, a series of new bis-pyrimidine acetamide molecules was synthesized in good yields and its chemical structures were confirmed by  $^1\text{H}/^{13}\text{C}$ -NMR, Mass, FT-IR studies and elemental analyses. All the synthesized compounds were tested for their in vitro antimicrobial and anticancer potentials. Among the synthesized compounds, compounds, **3**, **13**, **16**, **17** and **18** exhibited good antimicrobial potential against different microorganism (bacterial species: *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. enterica* and fungal species: *A. niger* and *C. albicans*) than the standard drugs cefadroxil and fluconazole. Similarly, compounds, **12**, **16** and **18** were found to be more effective against HCT 116 cancer cell line than the standard drug, 5-fluorouracil.

## Authors' contributions

BN and SK have designed, synthesized and carried out the antimicrobial activity of the bis-pyrimidine acetamide derivatives. KR, SAAS, SML and VM have carried out the spectral analysis, interpretation and anticancer evaluation of synthesized compounds. All authors read and approved the final manuscript.

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## Competing interests

The authors declare that they have no competing interests.

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