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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

A new class of bactericidal agents against *S. aureus*, MRSA and VRE derived from bisindolylmethane

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Abstract A series of bisindolylmethanes (BIMs) (**1a–7j**) including hybrid BIMs **6a–6c** were prepared for bioevaluation. The results of initial antimicrobial screening of compounds **1a–6c** showed compounds **2b**, **2m**, **4a** and **5b** to be the most potent inhibitors, exhibiting MIC as well as MBC values equal to or less than that of ciprofloxacin (0.5–2 μg/mL) against *Staphylococcus aureus*, MRSA and VRE. Compound **2m** was selected further to study the effect of *N,N′* disubstitution towards antibacterial and antitumor activity. It was observed that substitution at *N,N′* position (**7a–7j**) of **2m** diminishes its antibacterial activity though in vitro antitumour activity against a panel of prostate, cervical and lung cancer cell lines remains more or less intact.

Keywords Bisindolylmethanes · Antimicrobial · MRSA · VRE · MBC · Antiproliferative

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Introduction

The widespread and inappropriate use of antibiotics has given rise to the development of resistance in a variety of pathogenic microorganisms (Hancock, 2005). Bacterial pathogens such as methicillin-resistant *Staphylococcus aureus*; vancomycin-resistant enterococci (VRE); multi-drug-resistant *Escherichia coli, Pseudomonas aeruginosa* and *Acinetobacter baumannii* have acquired the status of superbugs (Rybak, 2004). While it is easy to find compounds that kill bacteria, it is hard to find novel antibacterial classes worthy of development. The arsenal of antibacterial agents is restricted to antibiotics like linezolid, daptomycin, quinupristin–dalfopristin, tigecycline and ceftobiprole as promising agents against VRE and MRSA (Aksoy and Unal, 2008). Nevertheless, these antibiotics have limitation regarding poor absorption and serious side effects. Particularly linezolid, the most potent and frequently used antibiotic, is bacteriostatic against most susceptible organisms but displays poor bactericidal activity against some strains (Ament *et al*., 2002).

Indole and its derivatives are known as an important class of heterocyclic compounds in pharmaceutical as well as synthetic chemistry (Sundberg, 1996). The most ubiquitous of the known bioactive alkaloids are based on the indole moiety. Particularly bisindolylmethanes (BIMs) widely occur in various natural products isolated from marine sponge alkaloids (Oh *et al*., 2006) and exhibit a wide range of biological activities (Azmi *et al*., 2008; Rahman and Sarkar, 2005; Gong et al., 2006). In our earlier communication, we designed synthesis of *N,N′*-glycoside derivatives of BIMs for their antiproliferative potential against various cancer cell lines (Sharma *et al*., 2012). However, use of BIM and its derivatives for antibacterial activities is limited (Kamal *et al*., 2009). In a programme

directed towards the synthesis of indole-based new chemical entities which will be bacteriostatic as well as bactericidal, we synthesize BIM derivatives which are inhibitors of *S. aureus*, MRSA and VRE. Further their SAR has been carried out for antimicrobial and anticancer properties.

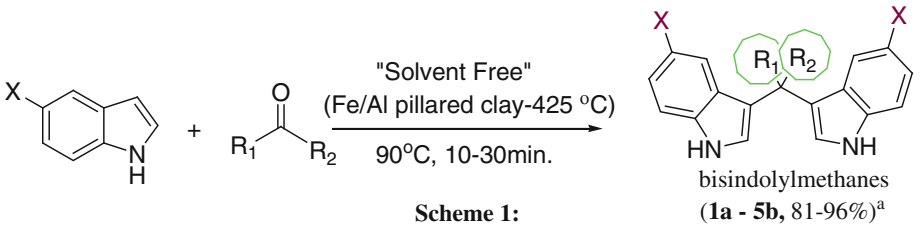
Results and discussion

BIMs with a common structure (Scheme 1, Table 1) were synthesized using our previously developed Fe/Al-pillared catalyst (Sharma *et al*. 2013). Variations were made both in the five position of indole and R_1, R_2 mentioned in the Scheme 1.

Due to considerable antifungal (Goel *et al*., 2012) and antibacterial (Ronad *et al*., 2010) properties of benzopyrans we then used ketone derived from benzopyran core with indole to obtain new hybride molecules (**6a–6c**) in moderate yield (Scheme 2) under optimized condition (Sharma *et al*., 2013).

For SAR studies, title compounds (**1a–6c**) were evaluated in vitro for antimicrobial activities. Table 2 shows the antibacterial activity as minimum inhibitory concentration (MIC) of the synthesized compounds. BIMs containing 5-bromoindole (viz. **2a**) were found to be more active than those with unsubstituted indole (**1a**). Keeping 5-bromoindole intact and bringing change in the aldehyde portion, we observed that compound **2b** possessed the highest activity among the synthesized compounds (**2a–3b**). Tests with compounds **2a–3b** revealed that BIMs confer higher activity if prepared from benzaldehydes carrying electron-withdrawing substituents (**2m–2p**) than electron-donating ones (**2d–2h**). BIMs having electron-withdrawing substituents at para position of benzaldehyde (**2m**, **2n** and **2p**) were found to be active having MIC value in the range 1–8 μg/mL for Gram-positive strains (except compound **2o**). In the series of compounds **2m–2o**, as the electronegativity of the substituent increases, an increase in antibacterial activity is noted. In case of electron-donating groups, monosubstituted product **2d** was more active than disubstituted products (**2e–2h**). None of the aliphatic aldehydes-and ketones-derived BIMs (**2q–2s** and **3a–3b**) were found to be active. From the observed antimicrobial activities of compounds **1a–3b**, we come to the conclusion that products derived from 5-bromoindole with substituted 4-hydroxy/4-fluorobenzaldehyde (**2b/2m**) are most active in this series, exhibiting MIC of 0.5–2 μg/mL against *S. aureus*, MRSA and VRE. Ciprofloxacin was used as a control drug.

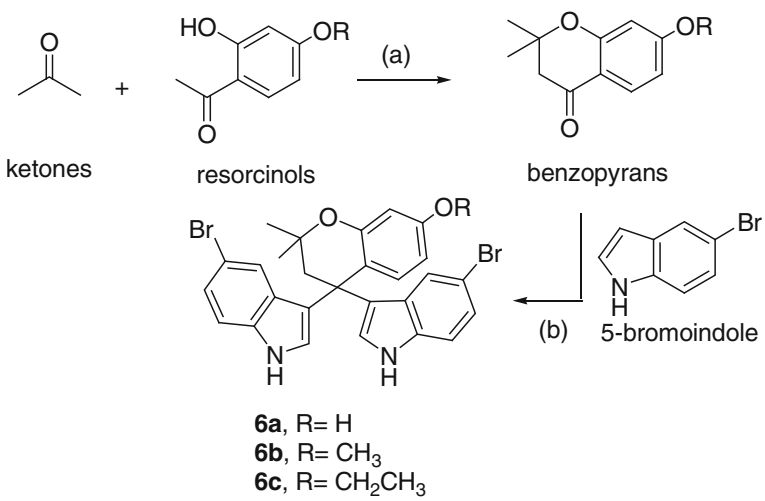
Table 1 Synthesis of bisindolylmethanes using different substituted indoles and carbonyl compounds (ketones and aldehydes)



Scheme 1:

1a, R_1 = phenyl, R_2 = X = H, 96 %
2a-p, R_2 = H, X = Br
2a, R_1 = phenyl, 92 %
2b, R_1 = 4-OH-phenyl, 95 %
2c, R_1 = 3-OH-phenyl, 92 %
2d, R_1 = 4-OMe-phenyl, 91 %
2e, R_1 = 2,3-$(OMe)_2$-phenyl, 91 %
2f, R_1 = 2,4-$(OMe)_2$-phenyl, 87 %
2g, R_1 = 3,4-$(OMe)_2$-phenyl, 89 %
2h, R_1 = 2,5-$(OMe)_2$-phenyl, 88 %
2i, R_1 = 5-bromo-2-methoxy-phenyl, 87 %
2j, R_1 = 4-NMe_2-phenyl, 89 %
2k, R_1 = cyclohexyl, 85 %
2l, R_1 = 2-naphthyl, 86 %
2m, R_1 = 4-F-phenyl, 94 %
2n, R_1 = 4-Cl-phenyl, 94 %
2o, R_1 = 4-Br-phenyl, 93 %
2p, R_1 = 4-NO_2-phenyl, 92 %
2q, R_1 = n-C_3H_7, 89 %
2r, R_1 = n-C_7H_{15}, 86 %
2s, R_1 = n-C_8H_{17}, 81 %
3a, R_1 = CH_3, R_2 = CH_3, 83 %
3b, R_1 = phenyl, R_2 = CH_3, 81 %
4a-b, X = NO_2, R_2 = H
4a, R_1 = 4-OH-phenyl, 92 %
4b, R_1 = 4-F-phenyl, 94 %
5a-b, X = CN, R_2 = H
5a, R_1 = 4-OH-phenyl, 94 %
5b, R_1 = 4-F-phenyl, 95 %

[a] Isolated yield



Scheme 2 Synthesis of hybrid bisindolylmethanes *a* pyrrolidine, benzene, 3h, reflux *b* Fe/Al-pillared clay −425 °C, 90 °C, 30 min

Further to study the effect of 5-substituent at indole, BIM derivatives using 5-nitroindole (**4a** and **4b**) and 5-cyanoindole derivatives (**5a** and **5b**) were synthesized using 4-hydroxybenzadehyde and 4-fluorobenzaldehyde. It was observed that compounds **4a** and **5b** are less active than their halogenated analogue **2b** but as active as compound **2m** as shown in Table 2. Compounds **4b** and **5a** were found to be inactive.

Among the series of synthesized hybrid molecules **6a**–**6c**, compound **6a** was found to be highly active. As we replace the hydroxy group of benzopyran with methoxy (compound **6b**) and ethoxy (compound **6c**) groups, antimicrobial activity decreases.

In a series of synthesized BIM derivatives **1a**–**6c**, some compounds exhibited varied levels of activity against Gram-positive bacteria. Minimum bactericidal concentration (MBC) was determined only for those compounds exhibiting MIC up to 64 μg/mL which we consider as moderately active. The MBC value of active compounds are shown in brackets in Table 2. A compound is considered to exhibit bactericidal activity if the ratio of MBC and MIC <4. All the active compounds were found to be bactericidal in nature. Compound **2b** is found to be equally potent in case of *S. aureus* and more potent in resistant strain (MRSA and VRE) than standard drug molecule ciprofloxacin in terms of MBC values. None of these compounds (**1a**–**6c**) showed antimicrobial activity against Gram-negative bacteria (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853) and fungal strains.

Among potent molecules compound **2m** was selected to study the effect of *N,N′*-disubstitution towards antibacterial over other molecules with comparable activity such as **2b**, **4a** and **5b** due to the absence of free hydroxy group in the former. So we created a library out of an active compound **2m**, where nitrogen of the indole is protected with different substituents like *N*-alkyl (**7a**–**7c**), *N*-benzyl (**7d**–**7h**) and *N*-sulphonyl (**7i**–**7j**) derivatives as shown in Scheme 3. These compounds were further evaluated for antimicrobial activity as shown in Table 3.

Table 3 shows that free –NH moiety of BIMs plays a significant role which is essential for antimicrobial activity. Any kind of substitution on –NH moiety of BIM will decrease its biological activity.

In continuation of our previous work of getting indole-based new chemical entities for antiproliferative potential (Sharma *et al*., 2012), *N,N′*-substituted BIMs were evaluated against various cancer cell lines (Koppikar *et al*., 2010) as shown in Table 4. The synthesized analogues (**7a**-**7j**) were found to be less active than their parent compound **2m** except compound **7e** which shows promising activity (1.1 μmol, IC_{50}) against HeLa cell line.

Experimental section

Chemistry

*General procedure for the synthesis of **1a**–**6c***

*3-((1H-Indol-3-yl)(phenyl)methyl)-1H-indole (**1a**)* It was obtained as pink solid, mp 140–142 °C. IR (KBr) *ν* 3378 (NH), 1602(C=C) cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) *δ* 5. 86 (s, 1H, CH), 6.66 (s, 2H, H-2, 2′), 7.11 (t, $J = 6.9$ Hz, 2H, H-5, 5′), 7.14–7.22 (m, 3H, Ar-2, 2′, ArH-4), 7.28–7.31 (m, 2H, ArH-3, 3′), 7.35–7.42 (m, 6H, H-4, 4′, 6, 6′, 7, 7′), 7.93 (brs, 2H, NH). ^{13}C NMR ($CDCl_3$ 125 MHz) indole [136.9 (C-7′), 128.6 (C-2, 2′), 127.0 (C-3′), 121.2 (C-5), 119.4 (C-6), 118.4 (C-4, 4′), 111.8 (C-7), 110.8 (C-3)] Phenyl [145.3 (C-1), 128.5 (C-2, 2′), 126.3 (C-3, 3′), 123.9 (C-4)], 31.5 (CH). MS: (*m/z*) $[M+Na]^+$ 345. Anal. Calcd. for $C_{23}H_{18}N_2$: C, 85.68; H, 5.63; N, 8.69. Found: C, 85.62; H, 5.60; N, 8.63.

Table 2 Antimicrobial activities of BIM derivatives

Compound	MIC (μg/mL)[a]		
	S. aureus	MRSA	VRE
1a	>256	>256	>256
2a	256	256	256
2b	0.5 (0.5)[b]	1(1)[b]	2(2)[b]
2c	1(1)[b]	2(2)[b]	4(8)[b]
2d	16(32)[b]	32(32)[b]	32(32)[b]
2e	256	256	>256
2f	256	256	>256
2g	128	256	256
2h	128	256	>256
2i	128	256	256
2j	64	128	256
2k	16(32)[b]	32(32)[b]	32(32)[b]
2l	16(16)[b]	32(32)[b]	32(32)[b]
2m	1(1)[b]	1(1)[b]	8(16)[b]
2n	4(4)[b]	8(8)[b]	8(8)[b]
2o	8(16)[b]	32(64)[b]	64(64)[b]
2p	4(4)[b]	8(8)[b]	8(8)[b]
2q	>256	>256	>256
2r	>256	>256	>256
2s	>256	>256	>256
3a	>256	>256	>256
3b	>256	>256	>256
4a	1(1)[b]	1(1)[b]	2(2)[b]
4b	>256	>256	>256
5a	>256	>256	>256
5b	1(1)[b]	1(1)[b]	8(8)[b]
6a	2(2)[b]	2(2)[b]	4(4)[b]
6b	4(4)[b]	4(8)[b]	8(8)[b]
6c	8(8)[b]	32(32)[b]	32(32)[b]
Ciprofloxacin	0.25 (0.5)[b]	16(32)[b]	64(64)[b]

[a] MIC value

[b] MBC value

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(phenyl)methyl)-1H-indole (**2a**)* It was obtained as red solid, mp 245–256 °C. IR (KBr) *v* 3416 (NH), 1607(C=C) cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 5.86 (s, 1H, CH), 6.91 (s, 2H, H-2, 2′), 7.14–7.19 (m, 3H, Ar-2, 2′, ArH-4), 7.20–7.31 (m, 4H, ArH-3, 3′, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}C NMR ($CDCl_3$ 125 MHz) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], Phenyl [145.3 (C-1), 128.5 (C-2, 2′), 126.3 (C-3, 3′), 123.9 (C-4)], 39.5 (CH). MS: (*m/z*) $[M+Na]^+$ 503. Anal. Calcd. for $C_{23}H_{16}Br_2N_2$: C, 57.53; H, 3.36; N, 5.83. Found: C, 57.62; H, 3.30; N, 5.73.

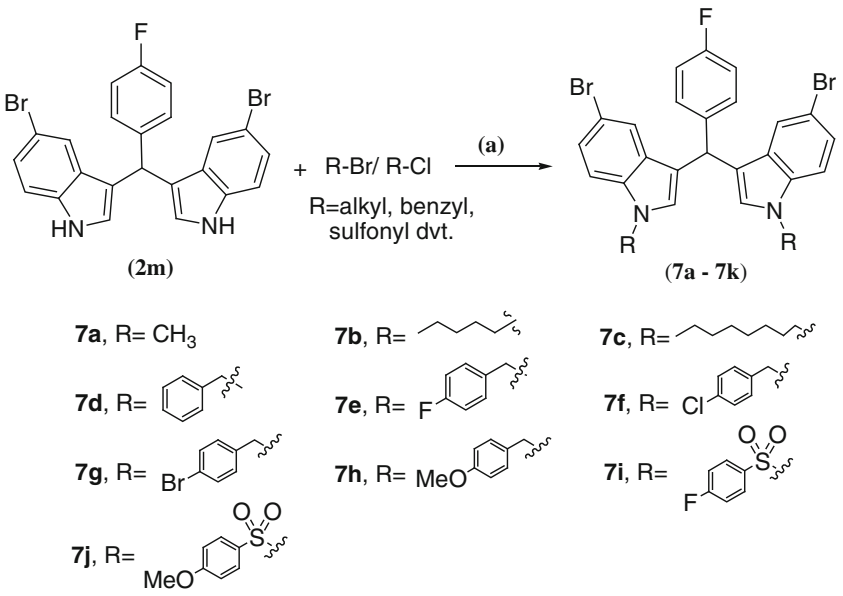
*4-(Bis(5-bromo-1H-indol-3-yl)methyl)phenol (**2b**)* It was obtained as red solid, mp 215–225 °C. IR (KBr) *v* 3402 (OH), 3388 (NH), 1613(C=C) cm^{-1}. ^1H NMR ($CDCl_3$ 500 MHz) δ 5.68 (s, 1H, CH), 6.63 (s, 2H, H-2, 2′), 6.77 (d, $J = 8.5$ Hz, 2H, ArH-3, 3′), 7.13 (d, $J = 8.5$ Hz, 2H, ArH-2, 2′), 7.23 (d, $J = 8.7$ Hz, 2H, H-7,7′), 7.25 (d, $J = 8.7$ Hz, 2H, H-6, 6′),7.47 (s, 2H, H-4, 4′). ^{13}C NMR ($CDCl_3$ 125 MHz) 5-Br-indole [135.4 (C-7′), 128.6 (C-3′), 124.7(C-2), 124.6 (C-6), 122.3 (C-4), 119.2 (C-5), 112.6 (C-7),112.6 (C-3)], 4-OH-Phenyl [154.1 (C-4), 129.6(C-1), 124.9 (C-2,2′), 115.2 (C-3,3′)], 39.0 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 519. Anal. Calcd. for $C_{23}H_{16}Br_2N_2O$: C, 55.67; H, 3.25; N, 5.65. Found C, 55.57; H, 3.35; N, 5.57.

*3-(Bis(5-bromo-1H-indol-3-yl)methyl)phenol (**2c**)* It was obtained as red solid, mp 210–220 °C. IR (KBr) *v* 3479 (OH), 3378 (NH), 1611 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$ 500 MHz) δ 5.68 (s, 1H, CH), 6.53 (s, 1H, ArH-2), 6.57 (d, $J = 8.5$ Hz, 2H, ArH-4), 6.61 (d, $J = 8.5$ Hz, 2H, ArH-6), 6.67 (s, 2H, H-2, 2′), 6.9 (m, 1H, ArH-5), 7.23 (d, $J = 8.7$ Hz, 2H, H-7,7′), 7.25 (d, $J = 8.7$ Hz, 2H, H-6, 6′),7.47 (s, 2H, H-4, 4′). ^{13}C NMR ($CDCl_3$ 125 MHz) 5-Br-indole [135.3 (C-7′), 128.7 (C-3′), 124.5(C-2), 124.2 (C-6), 122.1 (C-4), 119.3 (C-5), 112.7 (C-7),112.6 (C-3)], 3-OH-Phenyl [154.1 (C-3), 139.6(C-1), 130.2 (C-5), 123.1 (C-6), 114.9 (C-2), 112.9 (C-4)], 39.0 (CH). ESI MS: (*m/z*) $(M+Na)^+$ 519. Anal. Calcd. for $C_{23}H_{16}Br_2N_2O$: C, 55.67; H, 3.25; N, 5.65. Found C, 55.61; H, 3.30; N, 5.61.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(4-methoxyphenyl)methyl)-1H-indole (**2d**)* It was obtained as red solid, mp 276–286 °C. IR (KBr) *v* 3318 (NH), 1603 (C=C), 1303 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, -OCH_3), 5.34 (s, CH), 6.62 (s, 2H, H-2, 2′), 6.50 (d, $J = 8.3$ Hz, 2H, ArH-3, 3′), 6.70 (d, $J = 8.3$ Hz, 2H, ArH-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}C NMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.3 (C-7′), 128.7 (C-3′), 124.7(C-2), 124.5 (C-6), 122.1 (C-4), 119.3 (C-5), 112.7 (C-7), 112.6 (C-3)], 4-OCH_3-Phenyl [157.1 (C-4),130.1 (C-1) 129.6 (C-2,2′), 115.2 (C-3,3′), 55.3 (OCH_3)], 38.9 (CH). ESI MS: (*m/z*) $[M+Na]^+$533.3. Anal. Calcd. for $C_{24}H_{18}Br_2N_2O$: C, 56.50; H, 3.56; N, 5.49. Found C, 55.57; H, 3.55; N, 5.54.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(2,3-dimethoxyphenyl)methyl)-1H-indole (**2e**)* It was obtained as red solid, mp 285–295 °C. IR (KBr) *v* 3328 (NH), 1613 (C=C), 1317 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, -OCH_3), 3.78 (s, -OCH_3), 5.34 (s, 1H, CH), 6.47–6.59 (m, 3H, ArH-4, 5, 6), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.2 (C-7′), 128.7 (C-3′), 124.7(C-2), 124.5 (C-6), 122.0 (C-4), 119.6 (C-5), 112.3 (C-7),112.

Scheme 3 Synthesis of N-substituted bisindolylmethanes of an active compound **2m** a KOH, DMSO, rt 3 h



0 (C-3)], 2,3-$(OMe)_2$-Phenyl [150.1 (C-2), 149.4 (C-3), 124.3 (C-1), 122.4 (C-6), 122.1(C-5), 112.5 (C-4), 56.5 (OCH_3 at C-2), 56.3 (OCH_3 at C-3)], 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 563. Ana.l Calcd. for $C_{25}H_{20}Br_2N_2O_2$: C, 55.58; H, 3.73; N, 5.19. Found C, 55.60; H, 3.75; N, 5.14.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(2,4-dimethoxyphenyl) methyl)-1H-indole (**2f**)* It was obtained as red solid, mp 295–305 °C. IR (KBr) *v* 3313 (NH), 1611 (C=C), 1307 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, 2x-OCH_3), 5.34 (s, 1H, CH), 6.16 (s, 1H, ArH-3), 6.20 (d, $J = 8.5$ Hz, 1H, ArH-5), 6.80 (d, $J = 8.5$, 1H, ArH-6), 6.92 (s, 2H, H-2, 2′), 7.21-7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.2 (C-7′), 128.7 (C-3′), 124.7 (C-2), 124.5 (C-6), 122.0 (C-4), 119.3 (C-5), 112.7 (C-7), 112.6 (C-3)], 2,4-$(OMe)_2$-Phenyl [159.4 (C-2), 157.2 (C-4), 131.2 (C-6), 115.7 (C-1), 110.3 (C-5), 101.1 (C-3), 56.4 (OCH_3 at C-2), 56.3 (OCH_3 at C-4)], 39.0 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 563. Anal. Calcd. for $C_{25}H_{20}Br_2N_2O_2$: C, 55.58; H, 3.73; N, 5.19. Found C, 55.56; H, 3.75; N, 5.14.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(3,4-dimethoxyphenyl) methyl)-1H-indole (**2g**)* It was obtained as red solid, mp 285–295 °C. IR (KBr) *v* 3321 (NH), 1622 (C=C), 1303 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, 2x-OCH_3), 5.34 (s, 1H, CH), 6.46 (s, 1H, ArH-2), 6.50 (m, 2H, ArH-5, 6), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.7 (C-3′), 124.7 (C-2), 124.5 (C-6), 122.1 (C-4), 119.3 (C-5), 112.7 (C-7),112.6 (C-3)], 3,4-$(OMe)_2$-Phenyl [149.4 (C-3), 146.2 (C-4), 129.7 (C-1), 122.4 (C-6), 115.2 (C-5), 114.3 (C-2), 56.3 (OCH_3 at C-3 and C-4)], 39.1 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 563. Anal. Calcd. for $C_{25}H_{20}Br_2N_2O_2$: C, 55.58; H, 3.73; N, 5.19. Found C, 55.61; H, 3.71; N, 5.17.

Table 3 Antimicrobial activities *N,N′*-substituted BIM derivatives

Compound	MIC (μg/mL)[a]		
	S. aureus	MRSA	VRE
7a	4 (4)[b]	8 (8)[b]	8 (8)[b]
7b–7j	>128	>128	>128
Ciprofloxacin	0.25 (0.5)[b]	16 (32)[b]	64 (64)[b]

[a] MIC value

[b] MBC value

Table 4 Cytotoxic effects of compounds **2m** and **7a–7j** on PC-3, HeLa and A-549 human cancer cells

Compound	IC_{50} μmol[a]		
	PC-3	HeLa	A-549
2m	3.9 ± 0.010	2.7 ± 0.173	4.5 ± 0.061
7a	38.9 ± 0.361	25.4 ± 0.111	29.4 ± 0.144
7b	40.3 ± 0.100	27.2 ± 0.165	32.5 ± 0.035
7c	44.9 ± 0.200	32.4 ± 0.177	38.7 ± 0.026
7d	43.1 ± 0.100	28.3 ± 0.176	28.2 ± 0.187
7e	36.5 ± 0.110	1.1 ± 0.090	8.7 ± 0.008
7f	38.5 ± 0.020	18.5 ± 0.180	22.8 ± 0.173
7g	43.7 ± 0.044	49 ± 0.430	24.7 ± 0.046
7h	43.5 ± 0.165	48.5 ± 0.265	36.4 ± 0.090
7i	>100	>100	>100
7j	>100	>100	>100

[a] IC50 values are indicated as the mean +SD of three independent experiments

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(2,5-dimethoxyphenyl) methyl)-1H-indole (**2h**)* It was obtained as red solid, mp 275–285 °C. IR (KBr) *v* 3348 (NH), 1606 (C=C), 1309 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, 2x-OCH_3), 5.34 (s, 1H, CH), 6.41–6.58 (m, 3H, ArH-3, 4, 6), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.1 (C-7′), 128.7 (C-3′), 124.7 (C-2), 124.5 (C-6), 122.1 (C-4), 119.3 (C-5), 112.7 (C-7),112.6 (C-3)], 2,5-$(OMe)_2$-Phenyl [150.1 (C-5), 149.2 (C-2), 124.7 (C-1), 115.4 (C-3), 113.0 (C-6), 112.0 (C-4), 56.5 (OCH_3 at C-2), 56.5 (OCH_3 at C-5], 39.0 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 563. Anal. Calcd. for $C_{25}H_{20}Br_2N_2O_2$: C, 55.58; H, 3.73; N, 5.19. Found C, 55.54; H, 3.75; N, 5.16.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(5-bromo-2-methoxyphenyl)methyl)-1H-indole (**2i**)* It was obtained as red solid, mp 260–270 °C. IR (KBr) *v* 3337 (NH), 1603 (C=C), 1307 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 3.73 (s, -OCH_3), 5.34 (s, 1H, CH), 6.54 (d, $J = 8.5$ Hz, 1H, ArH-3), 7.12–7.14 (m, 2H, ArH-4, 6), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.1 (C-7′), 128.7 (C-3′), 124.7 (C-2), 124.5 (C-6), 122.1 (C-4), 119.3 (C-5), 112.7 (C-7),112.6 (C-3)], 5-Br-2-MeO-Phenyl [157.1 (C-2), 134.2 (C-6), 129.7 (C-4), 125.4 (C-1), 116.0 (C-3), 115.1 (C-5), 56.5 (OCH_3)], 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 612. Anal. Calcd. for $C_{24}H_{17}Br_3N_2O$: C, 48.93; H, 2.91; N, 4.76. Found C, 48.97; H, 2.85; N, 4.77.

*4-(Bis(5-bromo-1H-indol-3-yl)methyl)-N,N-dimethylbenzenamine (**2j**)* It was obtained as red solid, mp 240–250 °C. IR (KBr) *v* 3318 (NH), 1603 (C=C), cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 2.87 (s, 2xCH_3), 5.34 (s, 1H, CH), 6.47 (d, $J = 8.5$ Hz, 2H, ArH-2), 6.87 (d, $J = 8.5$ Hz, 2H, ArH-2), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.99 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.4 (C-7′), 128.6 (C-3′), 124.7 (C-2), 124.6 (C-6), 122.3 (C-4), 119.2 (C-5), 112.6 (C-7),112.6 (C-3)], 4-NMe_2-phenyl [146.4 (C-4), 130.2 (C-2,2′), 127.4 (C-1),114.7 (C-3, 3′), 40.5 (2xCH_3)], 40.1 (CH). ESI *MS:* (*m/z*) $[M+Na]^+$ 546. Anal. Calcd. for $C_{25}H_{21}Br_2N_3$ C, 57.38; H, 4.05; N, 8.03. Found C, 57.35; H, 4.03; N, 8.07.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(cyclohexyl)methyl)-1H-indole (**2k**)* It was obtained as red solid, mp 195–205 °C. IR (KBr) *v* 3378 (NH), 1623 (C=C), 1317 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 400 MHz) δ 1.23–1.54 (m, 10H, 5xCH_2, cyclohexyl), 2.12-2.14 (m, 1H, CH, cyclohexyl), 3.86 (d, $J = 3.2$ Hz, 1H, CH), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], cyclohexyl [41.3 (C-1), 30 (C-2, 2′), 28.4 (C-3, 3′), 26.2 (C-4)], 37.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 509. Anal. Calcd. for $C_{23}H_{22}Br_2N_2$: C, 56.81; H, 4.56; N, 5.76. Found C, 56.86; H, 4.53; N, 5.78.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(naphthalen-2-yl)methyl)-1H-indole (**2l**)* It was obtained as red solid; mp 170–180 °C. IR (KBr) *v* 3378 (NH), 1611 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 5.34 (s, 1H, CH), 6.72 (s, 2H, H-2, 2′), 7.18–7.67 (m, 11H, H-6, 6′, 7, 7′, 7 × ArH napthyl), 7.69 (s, 2H, H-4, 4′), 7.99 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.1 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.7 (C-6), 122.1 (C-4), 119.7 (C-5), 112.5 (C-7), 112.3 (C-3)], napthyl [135.2 (C-1), 133.9 (C-2′), 131.7 (C-6′), 128.2 (C-8), 127.7 (C-6), 127.5 (C-3), 127.3 (C-7), 127.1 (C-2), 126.7 (C-4), 125.4 (C-5)], 37.6 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 557. Anal. Calcd. for $C_{27}H_{18}Br_2N_2$: C, 61.16; H, 3.42; N, 5.28. Found C, 61.18; H, 3.53; N, 5.17.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-1H-indole (**2m**)* It was obtained as red solid, mp 140–150 °C. IR (KBr) *v* 3318 (NH), 1603 (C=C), 1107 (C–F) cm^{-1}.^1H NMR ($CDCl_3$ 400 MHz) δ 5.71 (s, 1H, CH), 6.49 (s, 2H, H-2, 2′), 6.98 (t, $J = 8$ Hz, 2H, ArH-3,3′), 7.17–7.23 (m, 6H, H-6,6′,7, 7′, ArH-2,2′), 7.42(s, 2H, H-4,4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.6 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 521. Anal. Calcd. for $C_{23}H_{15}Br_2FN_2$: C, 55.45; H, 3.03; N, 5.62. Found C, 55.64; H, 3.02; N, 5.68.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(4-chlorophenyl)methyl)-1H-indole (**2n**)* It was obtained as red solid, mp 170-180 °C. IR (KBr) *v* 3318 (NH), 1603 (C=C), 713 (C–Cl) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 5.71 (s, 1H, CH), 6.60 (s, 2H, H-2, 2′), 7.17–7.28 (m, 8H, H-6,6′,7,7′, ArH 2,2′, 3,3′), 7.44 (s, 2H, H-4,4′), 8.10 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.06 (C-4), 118.5(C-5), 112.7 (C-7), 112.7 (C-3)], 4-Cl-Phenyl [141.6 (C-1), 132.2 (C-4), 129.8 (C-2, 2′), 125.1 (C-3, 3′)] 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 537. Anal. Calcd. for $C_{23}H_{15}Br_2ClN_2$: C, 53.68; H, 2.94; N, 5.44. Found C, 53.64; H, 2.92; N, 5.38.

*5-Bromo-3-((5-bromo-1H-indol-3-yl)(4-bromophenyl)methyl)-1H-indole (**2o**)* It was obtained as red solid, mp 180–190 °C. IR (KBr) *v* 3318 (NH), 1603 (C=C), 589 (C–Br) cm^{-1}. ^1H NMR ($CDCl_3$ 200 MHz) δ 5.70 (s, 1H, CH), 6.60 (s, 2H, H-2, 2′), 7.13–7.28 (m, 8H, H-6, 6′, 7, 7′, ArH-2,

2′, 3, 3′), 7.45 (s, 2H, H-4, 4′), 8.10 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.3 (C-7′), 128.0 (C-3′), 124.8 (C-2), 122.2 (C-6), 122.1 (C-4), 118.7 (C-5), 112.7 (C-7), 112.5 (C-3)], 4-Br-Phenyl [137.5 (C-1),131.2 (C-4), 130.8 (C-2, 2′), 126.1 (C-3, 3′)], 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 582. Anal. Calcd. for $C_{23}H_{15}Br_3N_2$: C, 49.41; H, 2.70; N, 5.01. Found C, 49.43; H, 2.72; N, 5.08.

5-Bromo-3-((5-bromo-1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole ***(2p)*** It was obtained as red solid, mp 280–290 °C. IR (KBr) *v* 3328 (NH), 1623 (C=C), 1547, 1372 (NO_2) cm^{-1}. 3402, 3047, 2915, 1520, 1454, 1349, 1043, 743 cm^{-1}. ^{1}H NMR ($CDCl_3$ 200 MHz) δ 5.77 (s, 1H, CH), 6.95 (s, 2H, H-2,2′), 7.17-7.39 (m, 6H, H-6, 6′, 7, 7′, ArH-2, 2′), 7.67 (s, 2H, H-4,4′),7.87 (d, $J = 6$ Hz, 2H, ArH-3,3′), 8.10 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.3 (C-7′), 128.0 (C-3′), 124.8 (C-2), 122.2 (C-6), 122.1 (C-4), 118.7 (C-5), 112.7 (C-7), 112.5 (C-3)], 4-NO_2-Phenyl [145.5 (C-4),143.2 (C-1), 130.8 (C-2, 2′), 121.1 (C-3, 3′)], 39.3 (CH). ESI MS: (*m/z*) $[M+Na]^+$ 548. Anal. Calcd. for $C_{23}H_{15}Br_2N_3O_2$: C, 52.60; H, 2.88; N, 8.00. Found C, 52.43; H, 2.72; N, 8.08.

5-Bromo-3-(1-(5-bromo-1H-indol-3-yl)butyl)-1H-indole ***(2q)*** It was obtained as yellowish oil. IR (KBr) *v* 3348 (NH), 1623 (C=C) cm^{-1}. ^{1}H NMR ($CDCl_3$ 200 MHz) δ 0.95 (t, $J = 7.2$, 7.4, 3H, CH_3), 1.22–1.44 (m, 2H, CH_2) 2.05–2.15 (m, 2H, CH_2), 4.34 (t, $J = 7.3$ Hz, 7.5 Hz, CH), 6.82 (s, 2H, H-2,2′), 7.16–7.26 (m, 4H, H-6,6′,7,7′), 7.65 (s, 2H, H-4,4′), 8.19 (s, 2NH). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole[135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], 37.5 (CH-alkyl), 33.7, 21.3 (2xCH_2-alkyl), 14.1 (CH_3-alkyl). ESI MS: *m/z* $(M+Na)^+$469. Anal. Calcd. for $C_{20}H_{18}Br_2N_2$: C, 53.84; H, 4.07; N, 6.28. Found C, 53.87; H, 4.03; N, 6.21.

5-Bromo-3-(1-(5-bromo-1H-indol-3-yl)octyl)-1H-indole ***(2r)*** it was obtained as yellowish oil. IR (KBr) *v* 3317 (NH), 1603 (C=C) cm^{-1}. ^{1}H NMR ($CDCl_3$ 200 MHz) δ 0.83–0.86 (m, 3H, CH_3), 1.23-1.34 (m, 10H, 5xCH_2), 2.10–2.30 (m, 2H, CH_2), 4.32(t, $J = 7.5$ Hz, 1H, CH), 6.92 (s, 2H, H-2, 2′), 7.21–7.26 (m, 4H, H-6,6′,7,7′), 7.65 (s, 2H, H-4,4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], 35.2 (CH-alkyl), 33.9, 31.8, 29.6, 29.3, 28.2, 22.6 (6xCH_2-alkyl), 14.1(CH_3-alkyl). ESI MS: (*m/z*) $[M+Na]^+$ 525. Anal. Calcd. for $C_{24}H_{26}Br_2N_2$: C, 57.39; H, 5.22; N, 5.58. Found C, 57.36; H, 5.23; N, 5.56.

5-Bromo-3-(1-(5-bromo-1H-indol-3-yl)nonyl)-1H-indole ***(2s)*** It was obtained as yellowish oil. IR (KBr) *v* 3373 (NH), 1613 (C=C) cm^{-1}.^{1}H NMR ($CDCl_3$ 200 MHz) δ 0.83–0.86 (m, 3H, CH_3), 1.23-1.34 (m, 12H, 6xCH_2), 2.10–2.30 (m, 2H, CH_2), 4.32(t, $J = 7.5$ Hz, 1H, CH), 6.92(s, 2H, H-2), 7.21–7.26 (m, 4H, H-6,6′,7,7′), 7.65 (s, 2H, H-4,4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$ 50 MHz) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], 35.2 (CH-alkyl), 33.9, 31.8, 29.6, 29.3, 28.2, 22.8, 22.6 (7xCH_2-alkyl), 14.1(CH_3-alkyl). ESI MS: (*m/z*) $[M+Na]^+$ 539. Anal. Calcd. for $C_{25}H_{28}Br_2N_2$ C, 58.16; H, 5.47; N, 5.43. Found C, 58.18; H, 5.37; N, 5.40.

5-Bromo-3-(2-(5-bromo-1H-indol-3-yl)propan-2-yl)-1H-indole ***(3a)*** It was obtained as yellowish oil. IR (KBr) *v* 3358 (NH), 1617 (C=C) cm^{-1}.^{1}H NMR (200 MHz, $CDCl_3$). δ 1.23 (s, 6H, 2x CH_3), 6.91 (s, 2H, H-2, 2′), 7.20–7.26 (m, 4H, H-6, 6′, 7, 7′), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], 44.1 (C), 30.2 (2xCH_3). ESI MS: (*m/z*) $[M+Na]^+$ 455. Anal. Calcd. for $C_{19}H_{16}Br_2N_2$ C, 52.81; H, 3.73; N, 6.48. Found C, 52.86; H, 3.71; N, 6.56.

5-Bromo-3-(1-(5-bromo-1H-indol-3-yl)-1-phenylethyl)-1H-indole ***(3b)*** It was obtained as yellowish oil. IR (KBr) *v* 3378 (NH), 1627 (C=C) cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$). δ 1.90 (s, 3H, CH_3), 6.71 (s, 2H, H-2, 2′), 7.10–7.30 (m, 4H, H-6, 6′, 7, 7′, ArH-2, 2′, 3, 3′, 4), 7.65 (s, 2H, H-4, 4′), 7.98 (s, 2NH). ^{13}CNMR ($CDCl_3$) 5-Br-indole [135.2 (C-7′), 128.6 (C-3′), 124.6 (C-2), 122.6 (C-6), 122.0 (C-4), 119.6 (C-5), 112.5 (C-7), 112.3 (C-3)], Phenyl [140.8 (C-1), 128.7 (C-3, 3′), 127.8 (C-2, 2′), 126.1 (C-4)], 49.1 (C), 14.9 (CH_3). ESI MS: (*m/z*) $[M+Na]^+$ 517. Anal. Calcd. for $C_{19}H_{16}Br_2N_2$ C, 58.33; H, 3.67; N, 5.67. Found C, 58.46; H, 3.71; N, 5.56.

4-(Bis(5-nitro-1H-indol-3-yl)methyl)phenol) ***(4a)*** It was obtained as yellow solid, yield 92 %, mp 235–245 °C. IR (KBr) *v* 3472 (OH), 3348 (NH), 1537, 1385 (NO) cm^{-1}. ^{1}HNMR (CD_3OD 400 MHz) δ 5.82 (s, 1H, CH), 6.66 (d, $J = 8.4$ Hz, 2H, ArH-3, 3′), 6.80 (s, 2H, H-2, 2′), 7.07 (d, $J = 8.4$ Hz, 2H, ArH-2, 2′), 7.36 (d, $J = 8.4$ Hz, 2H, H-7, 7′), 7.92-7.89 (d, $J = 8.4$ Hz, 2H, H-6, 6′), 8.14 (s, 2H, H-4, 4′). ^{13}C NMR (DMSO-d_6 100 MHz) 5-NO_2-indole [140.0 (C-7′), 139.7, (C-5), 127.3 (C-2), 125.7(C-3′), 121.0 (C-3), 116.4 (C-4), 116.1 (C-6), 111.9 (C-7)], 4-OH-Phenyl [155.6, (C-4), 133.9 (C-1), 129.0 (C-2,2′), 115.1 (C-3,3′)], 37.5 (CH) HRMS (-ESI): Calc. $[M-H]^-$ 427.1042. Found $[M-H]^-$ 427.1053. Anal. Calc.for $C_{23}H_{15}N_4O_5$: C, 64.48; H, 3.76; N, 13.08. Found C, 64.43; H, 3.82; N, 13.12.

*3-((4-Fluorophenyl)(5-nitro-1H-indol-3-yl) methyl)-5-nitro-1H-indole (**4b**)* It was obtained as yellowish green solid, yield 94 %, mp 240–250 °C. IR (KBr) *v* 3317 (NH), 1543, 1378 (NO), 1123 (C–F) cm^{-1}. ^{1}HNMR (DMSO-d_6 + $CDCl_3$ 400 MHz) δ 5.87 (s, 1H, CH), 6.77 (s, 2H, H-2, 2′), 6.93 (t, J = 8.0 Hz, 2H, ArH-3, 3′), 7.22 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.94 (d, J = 8.8 Hz, 2H, H-6, 6′), 8.16 (s, 2H, H-4, 4′), 10.97 (s, 2H, 2NH). ^{13}C NMR (DMSO-d_6 100 MHz) 5-NO_2-indole [140.0 (C-7′), 139.7 (C-5), 127.5 (C-5), 125.7(C-3′), 121.0 (C-3), 116.6 (C-4), 116.1 (C-6), 112.1 (C-7)], 4-F-Phenyl [159.6, (C-4), 133.2 (C-1), 129.9 (C-2,2′), 115.2 (C-3,3′)], 37.6 (CH). HRMS (+ESI): Calc. [M+H]431.1156 $^+$. Found $[M+H]^+$ 431.1159. Anal. Calc. for $C_{23}H_{16}FN_4O_4$: C, 64.19; H, 3.51; N, 13.02. Found C, 64.13; H, 3.41; N, 13.01.

*4-(Bis(5-cyano-1H-indol-3-yl)methyl)phenol (**5a**)* It was obtained as dark red colour solid, yield: 94 %, mp 240–250 °C. IR (KBr) *v* 3472 (OH), 3348 (NH), 2210 (CN) cm^{-1}. ^{1}HNMR (DMSO-d_6 500 MHz): δ 5.89 (s, 1H, CH), 6.68 (d, J = 8.2 Hz, 2H, ArH-3, 3′), 7.07 (s, 2H), 7.16 (d, J = 8.3 Hz, 2H, ArH-2, 2′), 7.41 (d, J = 8.4 Hz, 2H, H-6, 6′), 7.54 (d, J = 8.4 Hz, 2H, H-7, 7′), 7.76 (s, 2H, H-4,4′), 11.39 (s, NH), 11.40 (s, NH). ^{13}C NMR (DMSO-d_6 125 MHz) 5-CN-indole [138.2 (C-7′), 129.0 (C-3′), 126.0 (C-4), 124.5 (C-6), 123.5 (C-2), 120.7 (C-3), 100.2 (C-5)], 4-OH-Phenyl [155.6, (C-4), 134.0 (C-1), 129.0 (C-2,2′), 119.3 (C-3,3′)], 37.7 (CH). HRMS (+ESI): Calc. $[M+H]^+$389.1402.Found $[M+H]^+$ 389.1397. Anal. Calc. for $C_{25}H_{17}N_4O$: C, 77.30; H, 4.15; N, 14.42. Found C, 77.23; H, 4.11; N, 14.51.

*3-((4-Fluorophenyl)(5-cyano-1H-indol-3-yl) methyl)-5-cyano-1H-indole (**5b**)* It was obtained as pink colour solid, yield 95 %, mp 245–255 °C. IR (KBr) *v* 3363 (NH), 2210 (CN), 973 (C–F) cm^{-1}. ^{1}HNMR (CD_3OD 400 MHz) δ 5.86 (s, 1H, CH), 6.76 (s, 2H, H-2, 2′), 6.94 (t, J = 8.8 Hz, 2H, ArH-3, 3′), 7.27–7.21 (m, 4H, 6, 6′, ArH-2,2 ‘), 7.40 (d, J = 8.4 Hz, 2H, H-7, 7′), 7.53 (s, 2H, H-4, 4′). ^{13}C NMR ($CDCl_3$ 100 MHz) 5-CN-indole [138.2 (C-7′), 129.0 (C-3′), 126.0 (C-4), 124.5 (C-6), 123.5 (C-2), 120.7 (C-3), 100.2 (C-5)], 4-F-Phenyl [159.6, (C-4), 133.2 (C-1), 129.9 (C-2,2′), 115.2 (C-3,3′)], 37.6 (CH). HRMS (+ESI): Calc. $[M+H]^+$ 391.1359. Found $[M+H]^+$ 391.1342. Anal. Calc. for $C_{25}H_{16}FN_4$: C, 76.91; H, 3.87; N, 14.35. Found. C, 76.89; H, 3.85; N, 14.31.

*4,4-Bis(5-bromo-1H-indol-3-yl)-2,2-dimethyl chroman-7-ol (**6a**)* It was obtained as colourless solid, yield 67 %, mp 145–155 °C. IR (KBr) *v* 3472 (OH), 3371 (NH) cm^{-1}. ^{1}H NMR ($CDCl_3$ 400 MHz) δ 1.23–1.27 (m, 6H, 2xCH_3), 2.04 (s, 2H, CH_2 of Benzopyran), 6.40 (d, J = 8.4 Hz, 1H, ArH-3), 6.93 (s, 1H, ArH-5), 6.99 (s, 2H, H-2, 2′), 7.06 (d, J = 8.4, 1H,ArH-2), 7.18 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.21 (d, J = 8.8 Hz, 2H, H-6, 6′), 7.42 (s, 2H, H-4, 4′), 8.05 (s, 2NH). ^{13}C NMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.2 (C-7′), 128.4 (C-3′), 124.9 (C-2), 122.9 (C-6), 121.9 (C-4), 118.4 (C-5), 112.6 (C-7), 110.4(C-3)] Benzopyran [143.7 (C-4), 132.9 (C-2), 127.4 (C-3), 117.3(C-5)], 34.0 (CH_2), 28.9 (2xCH_3). HRMS (+ESI) Calc. $[M+H]^+$ 564.9949. Found $[M+H]^+$ 564.9957. Anal. Calc. for $C_{27}H_{21}Br_2N_2O_2$: C, 57.27; H, 3.92; N, 4.95. Found C, 57.26; H, 3.93; N, 4.96.

*5-Bromo-3-(4-(5-bromo-1H-indol-3-yl)-7-methoxy-2,2-dimethylchroman-4-yl)-1H-indole (**6b**)* It was obtained as light yellow solid, yield 64 %, mp 165–175 °C. IR (KBr) *v* 3371 (NH), 1210 (C–O) cm^{-1}. ^{1}H NMR ($CDCl_3$ 400 MHz) δ 1.22-1.27 (m, 6H, 2xCH_3), 2.03 (s, 2H, CH_2), 3.73 (s, 3H, OCH_3), 6.41 (d, J = 8.4 Hz, 1H, ArH-3), 6.91 (s, 1H, ArH-5), 6.95 (s, 2H, H-2, 2′), 7.07 (d, J = 8.4, 1H,ArH-2), 7.18 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.23 (d, J = 8.8 Hz, 2H, H-6, 6′), 7.42 (s, 2H, H-4, 4′), 8.03 (s, 2NH). ^{13}C NMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.1 (C-7′), 128.7 (C-3′), 125.0 (C-2), 122.9 (C-6), 121.7 (C-4), 118.5 (C-5), 112.6 (C-7), 110.4(C-3)] Benzopyran [158.7 (C-4), 132.9 (C-2), 123.4 (C-3), 111.3(C-5), 55.9 (OCH_3)], 34.0 (CH_2), 28.9 (2xCH_3). HRMS (+ESI). Calc. $[M+H]^+$ 579.0106. Found $[M+H]^+$ 579.0113. Anal Calc. for $C_{28}H_{23}Br_2N_2O_2$: C, 57.95; H, 4.17; N, 4.83. Found C, 57.96; H, 4.17; N, 4.86.

*5-Bromo-3-(4-(5-bromo-1H-indol-3-yl)-7-ethoxy-2,2-dimethylchroman-4-yl)-1H-indole (**6c**)* It was obtained as colourless solid, yield 64 %, mp 170–180 °C. IR (KBr) *v* 3348 (NH), 1210 (C–O) cm^{-1}^{1}H NMR ($CDCl_3$ 400 MHz): δ 1.23–126 (s, 6H, 2xCH_3), 1.30 (m, 3H, CH_3, ethoxy), 2.07 (s, 2H, CH_2), 3.98 (m, 2H, CH_2, ethoxy), 6.41 (d, J = 8.4 Hz, 1H, ArH-3), 6.91 (s, 1H, ArH-5), 6.95 (s, 2H, H-2, 2′), 7.07 (d, J = 8.4, 1H,ArH-2), 7.18 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.23 (d, J = 8.8 Hz, 2H, H-6, 6′), 7.42 (s, 2H, H-4, 4′), 8.03 (s, 2NH). ^{13}C NMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.1 (C-7′), 128.7 (C-3′), 125.0 (C-2), 122.9 (C-6), 121.7 (C-4), 118.5 (C-5), 112.6 (C-7), 110.4(C-3)] Benzopyran [158.7 (C-4), 132.9 (C-2), 123.4 (C-3), 111.3(C-5), 64.9 (OCH_2), 14.1 (CH_3)], 34.0 (CH_2), 28.9 (2xCH_3). HRMS (+ESI): Calc. $[M+H]^+$ 593.0262. Found $[M+H]^+$ 593.0267. Anal. Calc. for $C_{29}H_{25}Br_2N_2O_2$: C, 58.60; H, 4.41; N, 4.71. Found C, 57.56; H, 4.37; N, 4.76.

*General procedure for the synthesis of **7a–7j***

A mixture of compound 2m (1equiv.) and KOH (2 equiv.) in DMSO (10 mL) was stirred at room temperature for 15 min. After that addition of alkyl/benzyl/sulphonyl(2 equiv.) was made into reaction mixture. After completion

of the reaction, the mixture was extracted with ethyl acetate (3 × 25 mL) and water. The combined organic layer was dried with anhydrous sodium sulphate, concentrated in vacuo and purified by column chromatography (ethyl acetate:petroleum ether = 0.5:9.5) to afford the pure product.

*5-Bromo-3-((5-bromo-1-methyl-1H-indol-3-yl)(4 fluorophenyl)methyl)-1-methyl-1H-indole (**7a**)* It was obtained as red solid, yield 84 %, mp175–185 °C. IR (KBr) *v*1179 (C–F) cm^{-1}. ^{1}HNMR ($CDCl_3$ 400 MHz) *δ* 3.49 (s, 6H, 2x-NCH_3), 5.53 (s, 1H, CH), 6.28 (s, 2H, H-2,2′), 6.79 (t, J = 8.8 Hz, 2H, Ar H-3,3′), 6.98 (d, J = 8.8 Hz, 2H, Ar H-2,2′), 7.02-7.11 (m, 4H, H-6, 6′, 7, 7′), 7.25 (s, 2H, H-4,4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)],4-F-Phenyl [159.6 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 39.3 (CH)], 42.1 (2xNMe). HRMS (+ESI): Calc. $[M+H]^+$524.9800. Found $[M+H]^+$ 524.9806. Anal. Calc. for $C_{25}H_{18}Br_2FN_2$: C, 57.06; H, 3.64; N, 5.32 found C, 57.13; H, 3.61; N, 5.11.

*5-Bromo-3-((5-bromo-1-pentyl-1H-indol-3-yl)(4-fluorophenyl)methyl)-1-pentyl-1H-indole (**7b**)* It was obtained as colourless solid, yield 72 %, mp 195–205 °C. IR (KBr) ν 1179 (C–F) cm^{-1}. ^{1}H NMR ($CDCl_3$ 400 MHz) δ 0.85 (t, J = 8 Hz, 6H, CH_3), 1.21–1.31 (m, 8H, 4xCH_2), 1.72–1.76 (m, 4H, 2xCH_2), 3.98 (t, J = 8 Hz, 4H, 2xCH_2), 5.71 (s, 1H, CH), 6.49 (s, 2H, H-2, 2′), 6.98 (t, J = 8 Hz, 2H, ArH-3, 3′), 7.17–7.23 (m, 6H, H-6, 6′, 7, 7′, ArH-2, 2′), 7.42(s, 2H, H-4,4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.4 (C-7′), 128.9 (C-3′), 124.3 (C-2), 122.3 (C-6), 117.2, (C-4), 115.4, (C-5), 112.1 (C-7), 110.9 (C-3)],4-F-Phenyl [159.6 (C-4),129.8 (C-1), 128.3 (C-2, 2′), 115 (C-3, 3′)], 39.1 (CH), 46.4, 29.8, 28.9, 22.2, (4xCH_2), 13.9 (CH_3). HRMS (+ESI): Calc. $[M+H]^+$ 637.1052. Found $[M+H]^+$ 637.1058. Anal. Calc. for $C_{33}H_{34}Br_2FN_2$: C, 62.08; H, 5.53; N, 4.39. Found C, 62.13; H, 5.61; N, 6.57.

*5-Bromo-3-((5-bromo-1-octyl-1H-indol-3-yl)(4-fluorophenyl) methyl)-1-octyl-1H-indole (**7c**)* It was obtained as colourless solid, yield 68 %, mp 210–220 °C. IR (KBr) ν 1123 (C–F) cm^{-1}. ^{1}H NMR ($CDCl_3$ 400 MHz) δ 0.85 (t, J = 8 Hz,3H, CH_3), 1.21–1.31 (m, 20H, 10xCH_2), 1.72–1.76 (m, 4H, 2xCH_2), 3.98 (t, J = 8 Hz, 4H, 2xCH_2), 5.74 (s, 1H, CH), 6.48 (s, 2H, H-2, 2′), 6.98 (t, J = 8 Hz, 2H, ArH-H-3, 3′), 7.16–7.22 (m, 6H, H-6, 6′, 7, 7′, ArH-2, 2′), 7.43 (s, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 129.1 (C-3′), 124.5 (C-2), 122.3 (C-6), 1119.1, (C-4), 115.4, (C-5), 112.1 (C-7), 110.9 (C-3)], 4-F-Phenyl [159.6 (C-4),129.1 (C-1), 128.7 (C-2, 2′), 115 (C-3, 3′)], 39.4 (CH), 46.7, 29.9, 29.8, 28.9,2 6.3, 23.5 22.2, (7xCH_2), 13.9 (CH_3). HRMS (+ESI): Calc. $[M+H]^+$ 721.1991. Found $[M+H]^+$721.1998. Anal. Calc. for $C_{39}H_{46}Br_2FN_2$: C, 64.82; H, 6.56; N, 3.88. Found C, 64.87; H, 6.61; N, 3.84.

*1-Benzyl-3-((1-benzyl-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole (**7d**)* It was obtained as red solid, yield 78 %, mp 140–150 °C. IR (KBr) ν 1570 (C=C), 1139 (C–F) cm^{-1}. ^{1}HNMR ($CDCl_3$ 400 MHz) δ 5.13(s, 4H, 2xCH_2), 5.70 (s, 1H, CH), 6.52 (s, 2H, H-2, 2′), 6.92–6.94 (m, 4H, ArH-3, 3′, 2, 2′), 7.01 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.11–7.23(m, 12H, H-6, 6′, 2x5H of phenyl), 7.40 (s, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.6 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 2xbenzyl [136.3 (C-1), 129.1 (C-2, 2′), 128.7(C-3, 3′), (C-4), 49.5(CH_2)], 39.7(CH). HRMS (+ESI). Calc. $[M+H]^+$ 677.0426. Found $[M+H]^+$ 677.0428. Anal. Calc. for $C_{37}H_{26}Br_2FN_2$: C, 65.50; H, 4.01; N, 4.13. Found C, 65.24; H, 4.07; N, 4.15.

*1-(4-Fluorobenzyl)-3-((1-(4-fluorobenzyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole (**7e**)* It was obtained as red solid, yield 84 %, mp 120–130 °C. IR (KBr) ν 1570 (C=C), 1129 (C–F) cm^{-1}. ^{1}HNMR ($CDCl_3$ 400 MHz) δ 4.98 (s, 4H, 2XCH_2), 5.57 (s, 1H, CH), 6.38 (s, 2H, H-2, 2′), 6.79–6.87 (m, 8H, H-7, 7′, ArH-3, 3′ of 4-F-Phenyl, 2x ArH-3, 3′ of 4-F-benzyl), 6.98–7.09 (m, 8H, H-6, 6′, ArH-2, 2′ of 4-F-Phenyl, 2x ArH-2, 2′ of 4-F-benzyl), 7.29 (s, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.6 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 4-F-Phenyl [159.6 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 2x 4-F-benzyl [159.5 (C-4), 131.1 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′), 49.3(CH_2)], 39.6(CH). HRMS (+ESI) Calc. $[M+H]^+$713.0238. Found $[M+H]^+$ 713.0234. Anal. Calc. for $C_{37}H_{24}Br_2F_3N_2$: C, 62.20; H, 3.53; N, 3.92. Found C, 62.24; H, 3.57; N, 3.85.

*1-(4-Chlorobenzyl)-3-((1-(4-chlorobenzyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole (**7f**)* It was obtained as red solid, yield 73 %, mp 135–145 °C. IR (KBr) ν 1571 (C=C), 721 (C–Cl) cm^{-1}. ^{1}HNMR ($CDCl_3$ 400 MHz) δ 4.99(s, 4H, 2xCH_2), 5.58 (s, 1H, CH), 6.38 (s, 2H, H-2, 2′), 6.75 (d, J = 8.4 Hz, 4H, 2xArH-3, 3′ of 4-Cl-benzyl), 6.82 (t, J = 8.8 Hz, 2H, ArH-3, 3′of 4-F-phenyl), 6.86 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.02–7.09 (m, 8H, H-6, 6′, ArH-2, 2′ of 4-F-phenyl, 2xArH-2,2′ of 4-Cl-benzyl), 7.27 (s, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4),

118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.3 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 2x 4-Cl-Benzyl [141.6 (C-1), 130.2 (C-4), 129.8 (C-2, 2′), 125.1 (C-3, 3′), 49.7 (CH_2)], 39.3 (CH). HRMS (+ESI). Calc. $[M+H]^+$ 744.9647. Found $[M+H]^+$ 744.9646. Anal. Calc. for $C_{37}H_{24}Br_2Cl_2FN_2$: C, 59.47; H, 3.37; N, 3.75. Found C, 59.24; H, 3.27; N, 3.85.

1-(4-Bromobenzyl)-3-((1-(4-bromobenzyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole ***(7g)*** It was obtained as yellow solid, yield 83 %, mp 185–195 °C. IR (KBr) ν 1531 (C=C), 533 (C–Br) cm^{-1}. ^1H NMR ($CDCl_3$ + DMSO-d_6 400 MHz,). δ 5.06 (s, 4H, 2xCH_2), 5.62 (s, 1H, CH), 6.56 (s, 2H, H-2, 2′), 6.76 (d, J = 8 Hz, 4H, 2xArH-3, 3′ of 4-Br-benzyl), 6.86 (t, J = 8.4 Hz, 2H, ArH-3, 3′of 4-F-phenyl), 6.96 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.12–7.23 (m, 8H, H-6, 6′, ArH-2, 2′ of 4-F-phenyl, 2xArH-2,2′ of 4-Br-benzyl, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.3 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 2x 4-Br-Benzyl [137.5 (C-1),129.2 (C-4), 130.8 (C-2, 2′), 126.1 (C-3, 3′), 49.4 (CH_2)], 39.3 (CH). HRMS (+ESI): Calc. $[M+H]^+$ 834.8616. Found $[M+H]^+$ 834.8607. Anal. Calc. for $C_{37}H_{24}Br_4FN_2$ C, 53.14; H, 3.01; 2.27; N, 3.35. Found C, 53.24; H, 3.07; N, 3.25.

1-(4-Methoxybenzyl)-3-((1-(4-methoxybenzyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole ***(7h)*** It was obtained as red colour solid, yield 80 %, mp 225–235 °C. IR (KBr) ν 1578 (C=C), 1210 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$ 400 MHz) δ 3.79 (s, 6H, 2x-OCH_3), 5.07 (s, 4H, 2xCH_2), 5.67 (s, 1H, CH), 6.58 (s, 2H, H-2, 2′), 6.72 (d, J = 8 Hz, 4H, 2xArH-3, 3′ of 4-MeO-benzyl), 6.78 (t, J = 8.4 Hz, 2H, ArH-3, 3′of 4-F-phenyl) 6.89 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.12–7.19 (m, 6H, H-6, 6′, ArH-2, 2′ of 4-F-phenyl, 2xArH-2,2′ of 4-MeO-benzyl), 7.31 (s, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [135.3 (C-7′), 128.4 (C-3′), 124.8 (C-2), 122.1 (C-6), 122.07 (C-4), 118.5 (C-5), 112.7 (C-7), 112.7 (C-3)], 4-F-Phenyl [159.3 (C-4), 133.2 (C-1), 130.8 (C-2, 2′), 115.1 (C-3, 3′)], 2x 4-MeO-Benzyl [157.1(C-4),130.1 (C-1) 129.6 (C-2,2′), 115.2 (C-3,3′), 55.3 (OCH_3),49.4 (CH_2)], 39.3 (CH). HRMS (+ESI) Calc. $[M+H]^+$ 737.0638. Found $[M+H]^+$ 737.0641. Anal. calc. for $C_{39}H_{30}Br_2FN_2O_2$: C, 63.43; H, 4.23; N, 3.79. Found C, 63.34; H, 4.27; N, 3.75.

1-(4-Fluorobenzenesulphonyl)-3-((1-(4-fluorobenzenesulphonyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole) ***(7i)*** It was obtained as red solid, yield 84 %, mp 65–75 °C. IR (KBr) ν 1348, 1170 (Sulphonyl), 1121 (C–F) cm^{-1}. ^1H NMR ($CDCl_3$ 400 MHz,) δ 5.45 (s, 1H, CH), 6.85 (s, 2H, H-2, 2′), 7.05-7.25 (m, 10H, H-7, 7′, ArH-2, 2′, 3, 3′ of 4-F-Phenyl, 2x ArH-3, 3′ of 4-F-bezenesulphonyl), 7.45 (d, J = 4 Hz, 2H, H-6, 6′), 7.71–7.74 (m, 4H, 2xArH-2,2′ of 4-F-bezenesulphonyl), 7.85 (s, 1H, H-4), 7.88 (s, 1H, H-4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [134.9, (C-7′), 129.4 (C-3′), 123.8, (C-2), 122.6, (C-6), 117.2, (C-4), 117.1 (C-5), 115.4 (C-7)], 4-F-Phenyl [161.1 (C-4), 133.4 (C-1), 129.7 (C-2, 2′), 115.4 (C-3, 3′)], 2x 4-F-benzenesulphonyl [166.9 (C-4), 134.8 (C-1), 131.3 (C-2, 2′), 116.0 (C-3, 3′)], 38.7 (CH). HRMS (+ESI): Calc. $[M+H]^+$ 812.9163. Found $[M+H]^+$ 812.9169. Anal. Calc. for $C_{35}H_{20}Br_2F_3N_2O_4S_2$: C, 51.61; H, 2.60; N, 3.44. Found C, 51.67; H, 2.63; N, 3.47.

1-(4-Methoxybenzenesulphonyl)-3-((1-(4-methoxybenzenesulphonyl)-5-bromo-1H-indol-3-yl)(4-fluorophenyl)methyl)-5-bromo-1H-indole ***(7j)*** It was obtained as yellow colour solid, yield 82 %, mp 85–95 °C. IR (KBr) ν 1353, 1172 (Sulphonyl), 1121 (C–F) cm^{-1}. ^1H NMR ($CDCl_3$ 400 MHz) δ 3.65(s, 2x-OCH_3, 6H), 5.27 (s, 1H, CH), 6.66 (s, 2H, H-2, 2′), 6.73 (d, J = 9.2 Hz, 4H, 2x ArH-3, 3′ of 4-MeO-bezenesulphonyl), 6.85 (t, J = 8.4 Hz, 2H, ArH-3, 3′ of F-Phenyl), 6.91-6.94 (m, 2H, ArH-2, 2′of 4-MeO-bezenesulphonyl), 7.06–7.08 (m, 2H, ArH-2, 2′), 7.23 (d, J = 8.8 Hz, 2H, H-7, 7′), 7.44 (d, J = 8.8 Hz, 2H, H-6, 6′), 7.68 (d, J = 8.8 Hz, 2H, H-4, 4′). ^{13}CNMR ($CDCl_3$ 100 MHz) 5-Br-indole [134.9, (C-7′), 129.4 (C-3′), 123.8, (C-2), 122.6, (C-6), 117.2, (C-4), 117.1 (C-5), 115.4 (C-7)], 4-F-Phenyl [161.1, (C-4), 133.4 (C-1), 129.7, (C-2, 2′), 115.4, (C-3, 3′)], 2x 4-MeO-benzenesulphonyl [165.7, (C-4), 130.2 (C-1), 129.3 (C-2, 2′), 116.0 (C-3, 3′)], 38.7 (CH). HRMS (+ESI): Calc. $[M+H]^+$ 836.9563. Found $[M+H]^+$836.9564 Anal. Calc. for $C_{37}H_{26}Br_2FN_2O_6S_2$ C, 53.00; H, 3.25; N, 3.34 found C, 52.87; H, 4.13; N, 4.97.

Biology

Antibacterial assay

antibacterial assayAntibacterial activity assay of the compounds was performed using microdilution method (Clinical and Laboratory Standard Institute, 2009) against three Gram-positive strains (*S. aureus* ATCC 29213, Methicillin-resistant *S. aureus* and Vancomycin-resistant *Enterococcus faecalis*) and two Gram-negative strains (*Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853). Bacterial suspensions were prepared in sterile normal saline from 24-h-grown culture. The MIC was determined in Muller–Hinton Broth (MHB; BD Biosciences, USA). Two-fold serial dilutions of compounds were prepared in MHB in µl volume in a 96-well U-bottom microtitre plate (Tarson, Mumbai, India). The final concentrations of the

compounds ranged from 0.5 to 256 μg/mL. The turbidity of bacterial suspensions was adjusted to 0.5 McFarland standard ($\sim 1.5 \times 10^8$ CFU mL^{-1}), which was further diluted in of 5×10^6 CFU mL^{-1}. The plates were incubated at 37 °C for 24 h and were read visually. The minimum concentration of the sample showing no turbidity was recorded as MIC. The MBC was determined by plating 20 μl sample on MHA plate.

Cell viability assay

PC-3, HeLa cells (3×10^3 cells/well) and A-549 were plated into a 96-well tissue culture plate with appropriate medium and left overnight to adhere. The next morning the media were changed and 200 μL serum containing fresh media were added to each well. Serially diluted compounds (100, 10, 1 and 0.1 μM) were added in wells in triplicate so that the final concentration of DMSO solvent was 0.5 %. A vehicle DMSO group was kept as a negative control and staurosporine was used as positive control. After 48-h incubation MTT solution (5 mg/mL) was added to each well and the cells were further incubated at 37 °C for 4 h. The formazan crystals formed were dissolved by addition of DMSO. After 15 min of incubation at room temperature, the amount of coloured formazan derivatives was determined by measuring optical density using microplate reader at 570 nmol. The percentage viability was determined according to the protocol described (Koppikar et al., 2010).

Conclusions

In conclusion, we have designed the compounds which showed moderate to excellent antibacterial activity against Gram-positive bacteria and also in some resistant strains like MRSA and VRE, but showed no activity on Gram-negative bacteria and fungal strains. Compounds **2b**, **2m**, **4a** and **5b** were found to be the most potent inhibitors, exhibiting MIC as well as MBC values equal to or less than that of ciprofloxacin (0.5–2 μg/mL) against *S. aureus*, MRSA and VRE. Compound **2b** was the most potent, exhibiting MIC of 0.5, 1 and 2 μg/mL against Gram-positive bacteria and some resistant strains like MRSA and VRE. During SAR study it was observed that substitution at *N*,*N*′ position (**7a**–**7j**) of **2m** diminishes its antibacterial activity though in vitro antitumor activity against a panel of prostate, cervical and lung cell lines was found to be in micromolar range. Compound **7e** was showing promising antiproliferative activity against HeLa cell line.

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