*Research Article*

# Synthesis of novel 5-Bromoisatin based pyrimidine derivatives and their antimicrobial evaluation

**Ramesh Kumar*, Mahesh Kumar**

*Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak-124001 (Haryana) India*

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**Abstract**

**Objective:** In this study, a new series of 5-bromoisatin derivative clubbed with pyrimidine i.e. 3-[4-(2-Amino-6-substituted-phenyl-pyrimidine-4-yl)-phenylamino]-5-bromo-1, 3-dihydro-indol-2-one derivative were synthesized. **Material and Methods:** The reaction of 5-bromoisatin and 4-aminoacetophenone in ethanol yielded Schiff bases (1). These on further reaction with different aromatic aldehyde resulted in synthesis of chalcones (2a-2o) derivatives of 5-bromoisatin. In the subsequent step reaction of chalcones with guanidine hydrochloride yielded pyrimidine derivatives (3a-3o) of 5-bromoisatin derivative. The structures of compounds were confirmed by their physicochemical and spectral means (IR and $^1$HNMR). The synthesized compounds were evaluated *in vitro* for antimicrobial activity by tube dilution method. Minimum inhibitory concentration (MIC) of compounds were determined against *S. aureus*, *B. subtilis* (Gram positive), and *P. aeruginosa*, *E. coli* (Gram negative) bacteria and *C. albican* and *A. niger* fungal strain. **Results:** Although several compounds showed antimicrobial activity, moreover, compound 3g, 3h and 3i showed significant activity. **Conclusion:** Compound substituted with - $NO_2$, -Cl and -Br showed significant antimicrobial activity.

***Keywords*:** 5-Bromoisatin, pyrimidine, antimicrobial, antifungal

## Introduction

Microbial resistance is worldwide threat in contemporary medicine and poses a threat to mankind. As per the report of WHO, in 2016, 490 000 people developed multi-drug resistant TB globally, and drug resistance is starting to complicate the fight against HIV and malaria, as well. Resistance to first-line drugs to treat infections caused by *Staphlylococcus aureus*-a common cause of severe infections in health facilities and the community is widespread. People with MRSA (methicillin-resistant *Staphylococcus aureus*) are estimated to be 64% more likely to die than people with a non-resistant form of the infection. Designing newer antimicrobial agent to counter this resistance is need of hour and has compelled the researcher to develop a new scaffold which can be further optimized as antimicrobial agents. Isatin/substituted isatin is nitrogen containing heterocyclic chemical moiety. In nature, the presence of isatin is reported in plants of the genus *Isatis*, in *Calanthe discolor* LINDL and in *Couroupita guianensis* Aubl. It has also been found in the secretion from the parotid gland of Bufo frogs, and in humans, it is a metabolic derivative of adrenaline (da Silva et al., 2001). In literature, isatin is documented to have a variety of pharmacological action such as antimicrobial (Kumar and Kumar, 2018), anticancer (Ismail et al., 2017), anticonvulsant (Saravanan et al., 2014), antiviral (Abbas et al., 2017), anti HIV (Pawar et al., 2011), antitubercular (Vintonyak et al., 2011) etc. On the other hand, pyrimidine is also nitrogen containing hetrocyclic moiety possessing versatile biological activity and is also a component of deoxyribonucleic acid (DNA) bases; cytosine, thymine, and uracil. The basic skeleton of pyrimidine is also present in vitamin B1 and barbiturates. Pyrimidine derivatives also used as hypnotics, such as veranal (Jubeen et al., 2018). It is reported to have anticancer (Al-Issa., 2013), antimicrobial activity (Holla et al., 2006), antioxidant (Chandrashekaraiah et al., 2014), anti-inflammatory (Rashad et al., 2005), diuretic (Majeed and Shaharyar, 2011), anti-HIV (Kim et al., 1992), antiviral (Hisaki et al., 1999), and antidiabetic (Lee et al., 2005) activities. In view of these facts and in continuation of our previous work, we envisaged to synthesize 5-bromoisatin

***Address for Corresponding Author:***
Ramesh Kumar
Department of Pharmaceutical Sciences,
Maharshi Dayanand University, Rohtak- 124001 (Haryana) India
Email: rkpchem@gmail.com

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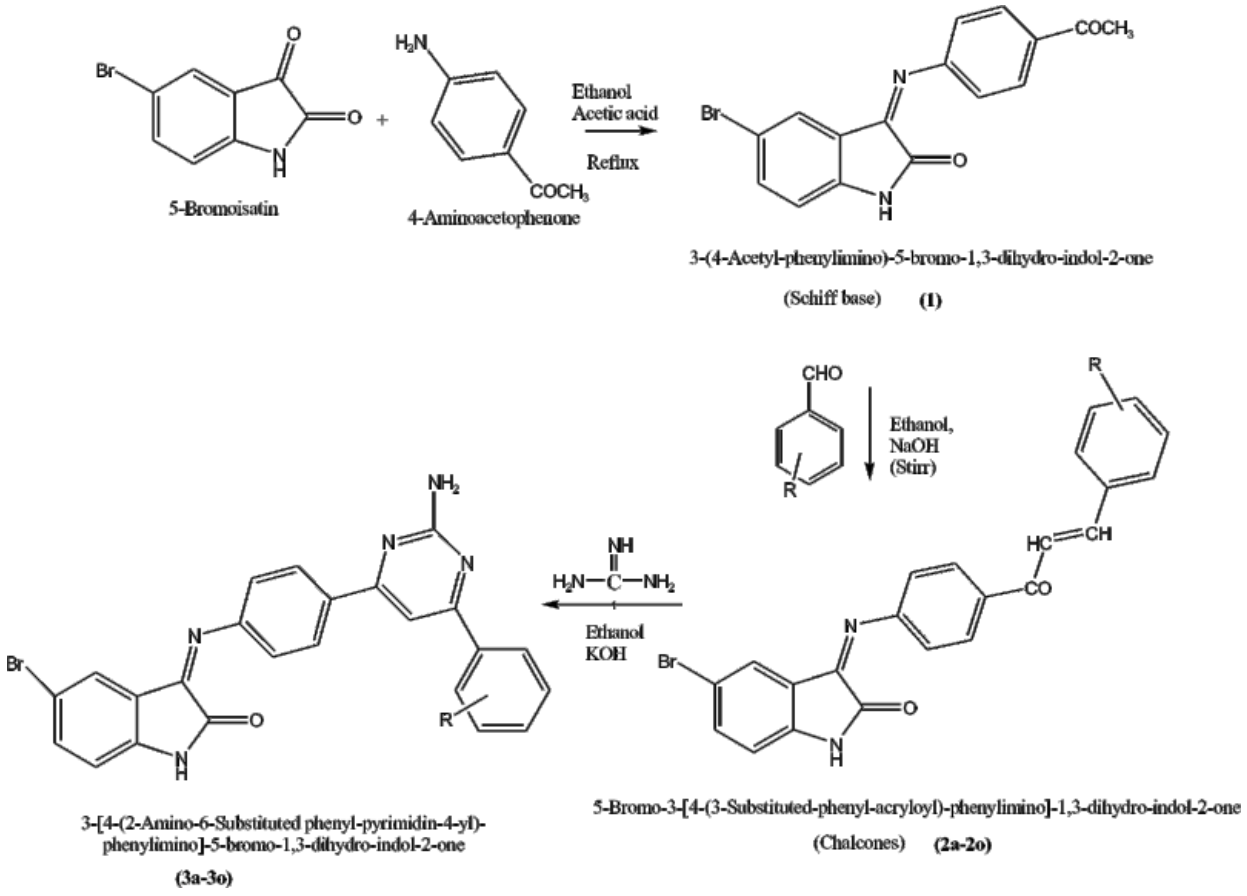
derivative clubbed with pyrimidine unit to get an active motif.

## Material and methods

Chemicals and solvents used in synthesis were of laboratory grade and used as received. Melting points were estimated with melting point apparatus in open capillaries and are uncorrected. The purity of the compounds was ascertained by TLC and the structures of the synthesized compounds were confirmed by IR, $^1$H NMR. Iodine vapours and UV lamp were used for visuliasation of spot. IR spectra were recorded in KBr pellets on FT IR spectrometer. H$^1$NMR were recorded on spectrometer in DMSO using tetramethylsilane as an internal standard. The chemical shifts of the compounds were reported in ppm.

**Synthesis of 3-(4-acetylphenylimino)-5- bromo-1, 3-dihydro indol-2-one (Schiff bases)** (Kumar and Kumar, 2018; Chinnaswamy et al., 2013; Gangarapu et al., 2013)

Equimolar quantity of 5-bromoisatin (0.01mol) and 4-aminoacetophenone (0.01mol) were dissolved in 50 ml ethanol. The content was refluxed in the presence of catalytical amount of glacial acetic acid. The content was put undisturbed overnight. The precipitates of Schiff base-(3-(4-acetylphenylimino)-5- bromo-1, 3-dihydro indol-2-one; 1) obtained were filtered, dried and recrystallized using ethanol.




| Compounds | | -R | Compounds | | -R |
|---|---|---|---|---|---|
| 2a | 3a | -H | 2i | 3i | 2,4-Cl |
| 2b | 3b | 2-$OCH_3$ | 2j | 3j | *p*-$N(CH_3)_2$ |
| 2c | 3c | 4-$OCH_3$ | 2k | 3k | 2-Cl |
| 2d | 3d | 4-OH | 2l | 3l | 2-Br |
| 2e | 3e | 4-Cl | 2m | 3m | 3-$NO_2$ |
| 2f | 3f | 4-Br | 2n | 3n | 3,4-$OCH_3$ |
| 2g | 3g | 2-$NO_2$ | 2o | 3o | 4-OH, 3-$OCH_3$ |
| 2h | 3h | 4-$NO_2$ | --- | ---- | ------- |

**Figure 1.** Scheme shows preparation of Schiff base, chalcone and pyrimidine derivative of 5-bromoisatin

**Synthesis of 5-Bromo-3-[4-(3-Substituted-phenyl-acryloyl)-phenylimino]-1, 3-dihydro-indol-2-one (chalcone derivatives of 5- bromoisatin ) (a-o)** (Furniss et al., 2004; Tomma et al., 2014):

In this step, 0.01 mol of Schiff base (compound 1) and different substituted aromatic aldehydes (0.01mol) were dissolved in 50 ml ethanol. To this 10 ml solution of 10% w/v NaOH was added drop wise. The mixture was then stirred for 2-3 hr till it become thick. The chalcones (5-Bromo-3-[4-(3-substituted-phenyl-acryloyl)-phenylamino]-1, 3-dihydro-indol-2-one) were then filtered and re-crystallized using ethanol. The progress of reaction was monitored using TLC.

**Synthesis of 3-[4-(2-Amino-6-substituted-phenyl-pyrimidin-4-yl)-phenyl imino]-5-bromo-1, 3-dihydro-indol-2-one (Pyrimidine derivatives of 5-Bromoisatin) (3a-3o)** (Kachroo et al., 2014; Trivedi et al. 2008):

A solution of chalcones (a-o) (0.01mol) and guanidine hydrochloride (0.01mol) was prepared in 50 ml ethanol. To this a solution of KOH was added. The content was then refluxed for 10 h on water bath, cooled and then poured in crushed ice. The precipitate obtained were filtered, washed and recrystallized from ethanol.

**Characterization data of synthesized derivatives (5-Bromoisatin derivatives):**

**3a. 3-[4-(2-Amino-6-phenyl-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3416.38 (N-H str, amine), 2949.54 (C-H str, aromatic), 1692 (C=O str.), 1657 (C=N str.). $^1$H NMR (DMSO) (δ-ppm): 8.256 (1H, s, N-H), 6.612-7.774 (8H, m, Ar-H), 4.36 (2H, s, -NH)

**3b. 3-[4-(2-Amino-6-(2-methoxy-phenyl)-pyrimidin-4yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3421.30 (N-H str, amine), 2927.24 (C-H str, aromatic), 1709 (C=O str.), 1662 (C=N str.), 1110.8 (-C-O-$CH_3$, ether). $^1$H NMR (DMSO) δ; 8.012 (1H, s, N-H), 6.74-7.46 (8H, m, Ar-H), 4.21 (2H, s, -NH), 3.87 (3H, s,-$OCH_3$).

**3c. 3-[4-(2-Amino-6-(4-methoxy-phenyl)-pyrimidin-4yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$ ): 3418.70 (N-H str , amine), 2915.14 (C-H str, aromatic),1712 (C=O str.), 1660(C=N str.), 1107.4 (-C-O-$CH_3$, ether).$^1$H NMR (DMSO) δ; 7.82(1H, s, N-H), 6.44-7.6 (8H, m, Ar-H), 4.13 (2H, s, -NH), 3.60 (3H, s,-$OCH_3$).

**3d. 3-[4-(2-Amino-6-(4-hydroxy-phenyl)-pyrimidin-4yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3430.40 (N-H str, amine), 3235.2(O-H str), 2906.7 (C-H str, aromatic), 1715 (C=O str.), 1666(C=N str. aromatic), 1104.5 (-C-O-$CH_3$, ether).$^1$H NMR (DMSO) δ; 8.251(1H, s, N-H), 6.61-7.83 (8H, m, Ar-H), 5.21(1H, s, -OH), 4.211 (2H, s,-$NH_2$).

**3e. 3-[4-(2-Amino-6-(4-chlorophenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3441.45 (N-H str, amine), 2932.47 (C-H str, aromatic), 1716.8 (C=O str.), 1658 (C=N str.). $^1$H NMR (DMSO) δ; 7.68(1H, s, N-H), 6.55-7.78(8H, m, Ar-H), 3.93(2H, s, -NH).

**3f. 3-[4-(2-Amino-6-(4-bromo phenyl)-pyrimidin-4yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3418.60 (N-H str, amine), 2925.24 (C-H str, aromatic), 1708 (C=O str.), 1661 (C=N str.), 1107.8 (-C-O-$CH_3$, ether). $^1$H NMR (DMSO) δ; 7.80(1H, s, N-H), 6.47-7.28 (8H, m, Ar-H), 4.16 (2H, s, -NH), 3.71 (3H, s,-$OCH_3$).

**3g. 3-[4-(2-Amino-6-(2-nitrophenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3392.1 (N-H str, amine), 2881.15 (C-H str, aromatic), 1715.4 (C=O str.), 1635 (C=N str.). $^1$H NMR (DMSO) δ; 7.95(1H, s, N-H), 6.53-7.78 (8H, m, Ar-H), 4.11(2H, s, -$NH_2$).

**3h. 3-[4-(2-Amino-6-(4-nitro-phenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1,3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3389.7 (N-H str , amine), 2877.4 (C-H str, aromatic),1712.5 (C=O str.), 1658 (C=N str.).$^1$H NMR (DMSO) δ; 7.88(1H, s, N-H), 6.59-7.90 (8H, m, ArH), 4.12 (2H, s, -$NH_2$).

**3i. 3-[4-(2-Amino-6-(2, 6-dichloro-phenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3381.2(N-H str, amine), 2877.5(C-H str, aromatic), 1707.2(C=O str.), 1644.3(C=N str.). $^1$H NMR (DMSO) δ; 7.90(1H, s, N-H), 6.59-7.85(8H, m, Ar-H), 4.18 (2H, s, -$NH_2$).

**3j. 3-[4-(2-Amino-6-(4-dimethylamino-phenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3428.6 (N-H str, amine), 2911.5 (C-H str, aromatic), 1726.6 (C=O str.), 1635.6(C=N str.). $^1$H NMR (DMSO) δ; 7.79(1H, s, N-H), 6.69-7.78 (8H, m, Ar-H), 2.86(2H, s, -$NH_2$).

**3k. 3-[4-(2-Amino-6-(2-chlorophenyl)-pyrimidin-4-yl)-phenyl-imino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3390.1 (N-H str , amine), 2878.15 (C-H str, aromatic),1719.8(C=O str.), 1642.5 (C=N str.$^1$H NMR (DMSO) δ; 7.92(1H, s, N-H), 6.54-7.76 (8H, m, Ar-H), 3.95 (2H, s, -NH).

**3l. 3-[4-(2-Amino-6-(2-bromophenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$ ): 3429.4 (N-H str , amine), 2906.7 (C-H str, aromatic),1716.3 (C=O str.), 1644.2 (C=N str.) $^1$H NMR (DMSO) δ; 7.88(1H, s, N-H), 6.58-7.81(8H, m, Ar-H), 4.01 (2H, s, -$NH_2$).

**3m. 3-[4-(2-Amino-6-(3-nitrophenyl)-pyrimidin-4-yl)-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3388.00 (N-H str , amine), 2886.4 (C-H str, aromatic),1714.12 (C=O str.), 1645.5(C=N str.). $^1$H NMR (DMSO) δ; 7.96(1H, s, N-H), 6.51-7.73 (8H, m, Ar-H), 4.21(2H, s, -s, $NH_2$).

**3n. 3-[4-(2-Amino-6-(3, 4-dimethoxyphenyl)-pyrimidin-4-yl]-phenylimino)-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3408.11 (N-H str , amine), 2874.2 (C-H str, aromatic),1718.0 (C=O str.), 1661 (C=N str.), 1116.7(-C-O-$CH_3$, ether). $^1$H NMR (DMSO) δ; 7.82(1H, s, N-H), 6.38-7.51 (8H, m, Ar-H), 4.05 (2H, s, -NH), 3.68(6H, s,-$OCH_3$)

**3o. 3-[4-[2-Amino-6-(4-hydroxy-3-methoxy-phenyl)-pyrimidin-4-yl]-phenylimino]-5-bromo-1, 3-dihydro-indol-2-one** IR (KBr) ($cm^{-1}$): 3411.2 (N-H str , amine), 3241.0 (O-H str), 2880.8 (C-H str, aromatic),1713.0 (C=O str.), 1652.2 (C=N str.), 1123. 2(-C-O-$CH_3$, str, ether). $^1$H NMR (DMSO) δ; 7.92(1H, s, N-H), 6.48-7.35 (8H, m, Ar-H), 4.14 (2H, s, -NH), 3.76 (6H, s,-$OCH_3$).

**Antimicrobial activity**

The antimicrobial activity was performed against Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*); the Gram-negative bacteria (*Escherichia coli* and *P. aeuroginos)* and fungal strains *Candida albicans* and *Aspergillus niger* using the tube dilution method (Cappucino and Sherman, 1999). Double strength nutrient broth- I.P. (bacteria) and sabourand's glucose broth- I.P. (fungi) media were used respectively for the growth of bacteria and fungi. The samples were incubated at 37°C for 24 h (bacteria), at 25°C for 7 d (*A. niger*) and at 37°C for 48 h (*C. albicans*). Ciprofloxacin and fluconazole were standard drugs for antibacterial activity and antifungal activity, respectively. The results were recorded in terms of minimum inhibitory concentration (MIC).

***Determination of MIC***

Minimum inhibitory concentration (MIC) of compounds was determined by two fold serial dilution method. A stock solution (100µg/ml) of the synthesized compounds and standard drugs was prepared in dimethylsulfoxide. Further dilution of each test compound and standard drugs were made in test medium to provide final concentration of 50, 25, 12.5, 6.25, 3.125 and 1.56µg/ml. To all the test tubes 0.1ml of suspension of bacteria in saline was added and tubes were incubated at required temperatures. MIC was that lowest concentration of sample that inhibited the development of turbidity. The observed MIC is presented in table 2.

**Results and discussion**

The title compounds were prepared according to the previously reported procedure. In the first step the reaction of 5-bromoisatin and 4-aminoacetophenone in ethanol yielded Schiff bases (1). These on further reaction with different aromatic aldehyde resulted in synthesis of

**Table 1.** Physicochemical data of synthesized compounds

| Compounds | Molecular Formula | Mol. Wt. | Melting Point ($^oC$) | Rf value | % Yield |
|---|---|---|---|---|---|
| 3a | $C_{24}H_{16}BrN_5O$ | 470.32 | 190-193 | 0.68 | 70.0 |
| 3b | $C_{25}H_{18}BrN_5O_2$ | 500.35 | 212-214 | 0.71 | 68.0 |
| 3c | $C_{25}H_{18}BrN_5O_2$ | 500.35 | 206-209 | 0.76 | 65.0 |
| 3d | $C_{24}H_{16}BrN_5O_2$ | 485.05 | 196-199 | 0.65 | 71.0 |
| 3e | $C_{24}H_{15}BrClN_5O$ | 504.77 | 230-233 | 0.69 | 76.0 |
| 3f | $C_{24}H_{15}Br_2N_5O$ | 549.2 | 224-226 | 0.73 | 71.0 |
| 3g | $C_{24}H_{15}BrN_6O_3$ | 515.32 | 228-230 | 0.77 | 64.0 |
| 3h | $C_{24}H_{15}BrN_6O_3$ | 515.32 | 226-228 | 0.75 | 69.0 |
| 3i | $C_{24}H_{14}BrCl_2N_5O$ | 539.21 | 218-221 | 0.65 | 61.0 |
| 3j | $C_{26}H_{21}BrN_6O$ | 513.39 | 202-205 | 0.78 | 74.0 |
| 3k | $C_{24}H_{15}BrClN_5O$ | 504.77 | 226-229 | 0.67 | 70.0 |
| 3l | $C_{24}H_{15}Br_2N_5O$ | 549.22 | 228-230 | 0.72 | 75.0 |
| 3m | $C_{24}H_{15}BrN_6O_4$ | 515.32 | 222-224 | 0.74 | 68.0 |
| 3n | $C_{26}H_{20}BrN_5O_3$ | 530.37 | 237-239 | 0.60 | 78.0 |
| 3o | $C_{25}H_{18}BrN_5O_3$ | 516.35 | 234-236 | 0.64 | 80.0 |

(Solvent front: chloroform: benzene: acetic acid)

**Table 2.** Antimicrobial activity (μM/ml) of synthesized 5-Bromooisatin derivatives

| Compounds | Minimum Inhibitory Concentration (MIC) | | | | | |
|---|---|---|---|---|---|---|
| | Bacterial strains | | | | Fungal Strains | |
| | Gram Positive | | Gram Negative | | | |
| | *S. aureus* | *B. subtilis* | *P. aeruginosa* | *E. coli* | *C. albicans* | *A. niger* |
| 3a | 1.58 | 1.58 | 1.58 | 1.58 | 1.58 | 1.58 |
| 3b | 1.47 | 1.47 | 1.47 | 1.47 | 1.47 | 1.47 |
| 3c | 1.47 | 1.47 | 1.47 | 1.47 | 1.47 | 1.47 |
| 3d | 1.52 | 1.52 | 1.52 | 1.52 | 1.52 | 1.52 |
| 3e | 0.758 | 0.758 | 0.758 | 0.758 | 1.628 | 1.628 |
| 3f | **0.329** | **0.329** | **0.329** | **0.329** | 1.460 | 1.460 |
| 3g | **0.355** | **0.355** | **0.355** | **0.355** | **0.355** | **0.355** |
| 3h | **0.355** | **0.355** | **0.355** | **0.355** | **0.355** | **0.355** |
| 3i | **0.336** | **0.336** | **0.336** | **0.336** | **0.336** | **0.336** |
| 3j | 1.429 | 1.429 | 1.429 | 1.429 | 1.429 | 1.429 |
| 3k | **0.729** | **0.729** | 1.458 | 1.458 | **0.729** | 1.458 |
| 3l | **0.660** | **0.660** | 1.321 | 1.321 | 1.321 | 1.321 |
| 3m | 1.372 | 1.372 | 1.372 | 1.372 | 1.372 | 1.372 |
| 3n | 1.375 | 1.375 | 1.375 | 1.375 | 1.375 | 1.375 |
| 3o | 1.419 | 1.419 | 1.419 | 1.419 | 1.419 | 1.419 |
| Std | 0.471 | 0.471 | 0.471 | 0.471 | 0.510 | 0.510 |

Standard drugs: Ciprofloxacin (antimicrobial) and Fluconazole (antifungal)

chalcones (2a-2o) derivatives of 5-bromoisatin. In the subsequent step reaction of chalcones with guanidine hydrochloride yielded pyrimidine derivatives (3a-3o) of 5-bromoisatin derivative. The prepared compounds were characterized by their physicochemical (Table 1) and spectral means as discussed in experimental.

The antimicrobial activity of the synthesized compounds was determined by tube dilution method (Cappucino and Sherman, 1999) and the results are given in Table 2. Ciprofloxacin and fluconazole were taken as standard for antibacterial and antifungal activity respectively. The result of antimicrobial activity demonstrate that **compound 3f** ($MIC_{sa}$ = **0.329** μM, $MIC_{bs}$ **0.329** μM, $MIC_{pa}$ **0.329** μM and $MIC_{ec}$ **0.329** μM) and **compound 3g** ($MIC_{sa}$ = **0.355** μM, $MIC_{bs}$ **0.355**μM, $MIC_{pa}$ **0.355** μM and $MIC_{ec}$ **0.355** μM ), **compound 3h** ($MIC_{sa}$ = **0.355** μM, $MIC_{bs}$ **0.355**μM, $MIC_{pa}$ **0.355** μM and $MIC_{ec}$ **0.355** μM), **compound 3i** ($MIC_{sa}$ = **0.336**μM, $MIC_{bs}$ **0. 0.336** μM, $MIC_{pa}$ **0.336** μM and $MIC_{ec}$ **0.336** μM) are active against both gram positive and gram negative strain. **Compound 3j** ($MIC_{sa}$ = 0.791μM, $MIC_{bs}$ 0.791 μM) and **compound 3l** ($MIC_{sa}$ = 0.728μM, $MIC_{bs}$ = 0.728μM) are active against *S. aureus and B. subtilis.* In case of antifungal activity **compound 3j** ($MIC_{ca}$ = 0.355 μM, $MIC_{an}$ = 0.355 μM), **compound 3h** ($MIC_{ca}$ = 0.355 μM, $MIC_{an}$ = 0.355 μM) and **compound 3i** ($MIC_{ca}$ = 0.336μM, $MIC_{na}$ = 0.355 μM) are active against both *C. albican* and *A. niger,* while **compound 3k** ($MIC_{ca}$ = 0.856μM) are active against *A. niger* only.

## Conclusion

In summary we, have synthesized a new series of derivatives of 5-Bromoisatin clubbed with pyrimidine i.e. 3-[4-(2-Amino-6-substituted-phenyl-pyrimidine-4-yl)-phenylamino]-5-bromo-1, 3-dihydro-indol-2-one. Amongst the synthesized compounds several shows antimicrobial activity. Compound **3g** (3-[2-Amino-6-(2-nitrophenyl)-pyrimidin-4-ylimino]-5-bromo-1,3-dihydroindol-2-one), **3h** (3-[2-Amino-6-(4-nitro-phenyl)-pyrimidin-4-ylimino]-5-bromo-1,3-dihydro-indol-2-one) and **3i** (3-[2-amino-6-(2, 6-dichlorophenyl)-pyrimidin-4-ylimino)-5-bromo-1, 3-dihydro-indol-2-one) showed both antibacterial and antifungal activity while compound **3f** (3-[2-Amino-6-(4-bromo phenyl)-pyrimidin-4ylimino]-5-bromo-1, 3-dihydro-indol-2-one) showed only antibacterial activity. Although there could not be established a direct correlation between structure and activity, moreover compound substituted with -$NO_2$, -Cl and -Br showed significant antimicrobial activity.

## Conflicts of Interest

The author declares that there is no conflict of interest.

## References

Abbas SY, El-Bayouki KAM, Basyouni WM, Mostafa EA.

2018. New series of 4 (3H)-quinazolinone derivatives: syntheses and evaluation of antitumor and antiviral activities. Medicinal Chemistry Research, 27:571–582.

Al-Issa SA. 2013. Synthesis and anticancer activity of some fused pyrimidines and related heterocycles. Saudi Pharmaceutical Journal, 21:305–316.

Cappucino JG, Sherman N. 1999. Microbiology-A Laboratory Manual, p263, California: Addison Wesley.

Chandrashekaraiah M, Lingappa M, Gowda VDC, Bhadregowda DG. 2014. Synthesis of some new Pyrimidine-Azitidinone analogues and their antioxidant, *in vitro* antimicrobial, and antitubercular activities. Journal of Chemistry, Article ID 847180, 9 pages.

Chinnaswamy RP, Sundrerajan R. 2013. Synthesis, characterization and *in vitro* antimicrobial activity of some novel 5-substituted Schiff and mannich bases of isatin. Journal of Saudi Chemical Society; 17: 337-344.

da Silva JFM, Garden SJ, Pinto AC. 2001. The Chemistry of Isatins: A Review from 1975 to 1999. Journal of Brazilian Chemical Society, 12(3): 273-324.

Furniss BS, Hannaford AJ, Smith PWG, Tatchell AR. 2004. Vogel's textbook of practical organic chemistry, pp 782, 783, 1034, 5th edn, Delhi: Pearson Education.

Gangarapu K, Manda S, Thumma G, Anreddy RNR. 2013. Synthesis, characterization, and antimicrobial and antioxidant activities of novel bis-isatin carbohydrazone derivatives. Toxicological & Environmental Chemistry, 95:3: 367-378.

Hisaki M, Imabori H, Azuma M, Suzutani T, Iwakura F, Ohta Y, Kawanishi K, Ichigobara Y, Node M, Nishide K, Yoshida I, Ogasawara M. 1999. Synthesis and anti-influenza virus activity of novel pyrimidine derivatives. Antiviral Research, 42 (2):121-37.

Holla BS, Mahalingaa M, Karthikeyana MS, Akberalib PM, Shetty NS. 2006. Synthesis of some novel pyrazolo [3,4-*d*] pyrimidine derivatives as potential antimicrobial agents. Bioorganic & Medicinal Chemistry, 14(6): 2040-2047.

Ismail, Bhaskar K, Thalari G, Bommarapu V, Mulakayal C, Chitta SK, Mulakayala N. 2017. Synthesis of novel spiro-[pyrazolo-[4,3-d]-pyrimidinones and spiro[benzo-[4,5]-thieno[2,3-d]pyrimidine-2,3'-indoline]-2',4(3-*H*)-diones and their evaluation for anticancer activity. Bioorganic & Medicinal Chemistry Letters, 27: 1446–1450.

Jubeena F, Iqbala SZ, Shafiqa N, Khana M, Parveena S, Iqbalb M, Nazir A. 2018. Eco-friendly synthesis of pyrimidines and its derivatives: A review on broad spectrum bioactive moiety with huge therapeutic profile. Synthetic Communications, 48(6): 601–625.

Kachroo M, Panda R, Yadav Y. 2014. Synthesis and biological activities of some new pyrimidine derivatives from chalcones. Der Pharma Chemica, 6(2): 352-359.

Kim HO, Ahn SK, Alves AJ, Beach JW, Jeong LS, Choi BG, Van Roey P, Schinazi RF, Chu CK. 1992. Asymmetric synthesis of 1, 3-dioxolane-pyrimidine nucleosides and their anti-HIV activity. Journal of Medicinal Chemistry, 35 (11):1987-95.

Kumar R, Kumar M. 2018. Synthesis of 3-[4-(2-Amino-6 (substituted phenyl)-pyrimidin-4-yl)-phenylimino]-5-chloro-1, 3-dihydro-indol-2-one derivatives of 5-chloroisatin as potential antimicrobial agents. Journal of Pharmaceutical, Chemical and Biological Sciences, 5(4):399-404.

Lee HW, Kim BY, Ahn JB, Kang SK, Lee JH, Shin JS, Ahn SK, Lee SJ, Yoon SS. 2005. Molecular design, synthesis, and hypoglycemic and hypolipidemic activities of novel pyrimidine derivatives having thiazolidinedione. European Journal of Medicinal Chemistry, 40 (9): 862-874.

Majeed J, Shaharyar M. 2011. Synthesis and *in vivo* diuretic activity of some novel pyrimidine derivatives. Journal of Enzyme Inhibition and Medicinal Chemistry, 26 (6): 819-26.

Pawar VS, Lokwani DK, Bhandari SV, Bothara KG, Chitre TS, Devale TL, Modhave NS, Parikh JK. 2011. Design, docking study and ADME prediction of Isatin derivatives as anti-HIV agents. Medicinal Chemistry Research, 20: 370–380.

Pharmacopoeia of India. 2014. pp. 14, 58, New Delhi: Controller of Publications, Ministry of Health Department, Govt. of India.

Rashad AE, Heikal OA, El-Nezhawy AOH, Abdel-Megeid FME. 2005. Synthesis and Isomerization of Thienotriazolopyrimidine and Thienotetrazolopyrimidine derivatives with potential anti-inflammatory activity. Heteroatom Chemistry, 16(3): 226-234.

Saravanan G, Alagarsamy V, Pandurangan DK. 2014. Anticonvulsant activity of novel 1-(morpholinomethyl)-3-substituted isatin derivatives. Bulletin of Faculty of Pharmacy, Cairo University, 52: 115–124.

Tomma JH, Khazaal MS, Al-Dujaili AH. 2014. Synthesis and characterization of novel Schiff bases containing pyrimidine unit. Arabian Journal of Chemistry, 7: 157-163.

Trivedi AR, Dodiya DK, Ravat NR, Shah VH. 2008.

Synthesis and biological evaluation of some new pyrimidines via a novel chalcone series. ARKIVOC, 11:131-141.

Vintonyak VV, Warburg K, Over B, Hubel K, Rauh D, Waldmann H. 2011. Identification and further development of thiazolidinones spiro-fused to indolin-2-ones as potent and selective inhibitors of Mycobacterium tuberculosis protein tyrosine phosphatase B. Tetrahedron, 67: 671.