International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 7 | Issue 4 | OCT-DEC| 2017 | 263-270
Research Article | Pharmaceutical Sciences | Open Access | UGC Approved | MCI Approved Journal

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SOME NOVEL MANNICH BASES OF 7-AZAISATIN DERIVATIVES

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ABSTRACT

In the field of medicinal chemistry, the synthesis of heterocyclic compounds by different routes while incorporating a variety of known pharmacophores into their molecular systems and evaluating them for possible pharmacological properties. Several of their derivatives and Mannich bases of isatin have been found to be greater interest in view of their disparate biological and pharmacological properties. Keeping this in view it is aimed to synthesis some novel Mannich bases of 7 aza isatin derivatives for evaluation of antimicrobial activity. All the examined compounds showed considerable active against all the tested strains of microorganism.

KEY WORDS

Mannich bases, 7-Aza Isatin, Antibacterial activity, Antifungal activity.

INTRODUCTION

Since the beginning of the search of medicinally important synthetic compounds heterocyclic chemistry always remained the point of attraction because of their diverse biological properties [1-3]. Substitution of heterocyclic compounds on various positions produced medicinally important analogues which are used in the treatment of various diseases. Isatin was first obtained by erdmann [4] and laurent [5] in 1840 as a product of the oxidation of indigo dye by nitricacid and chromic acid Isatin is one of the most important heterocyclic compounds in particular, compounds bearing the Isatin nucleus is known to have unique and were reported to possess antimicrobial [6], analgesic, anti-inflammatory [7], anticancer [8,9], anti-tubercular [10], antimalarial [11], anticonvulsant, anti-depressant activities [10]. so, it's thought worthwhile to synthesis all the compounds and have been screened for antimicrobial activity against two Gram positive bacteria *S. aureus, B. subtilis* and two Gram negative bacteria *E. coli, P. aeruginosa* and also against two fungal strains *C. albicans, A. niger* and comparable with amplicillin and clotrimazole(standards).

MATERIALS AND METHODS

Chemistry

The chemicals and solvents used for the experimental work were laboratory grade only. The melting points were determined by open capillary using Toshniwal melting point apparatus and are uncorrected. Purity of compounds was checked by TLC on Silica Gel precoated plates. IR spectra were recorded in KBr pellets on FTIR Brucker spectrophotometer and frequencies are expressed in cm-1. The 1HNMR spectra were recorded on 400MHz Brucker DPX using CDCl3 Chemical shift values are reported as values in ppm relative to TMS as internal standard, GC/EIMS analyses were performed using an Agilent 6890 gas chromatograph (Agilent Technologies, Palo Alto,CA, USA). Elemental analysis was performed on PerkinElmer series-2400 (PerkinElmer, Inc USA) at Center of Analytical Instrumentation, NIT, Warangal, Telangana, India. The Titled Compounds were coded as PSKa-m.

General procedure for the synthesis of title compounds

a) Synthesis of 1H-pyrrolo [2,3] pyridine-2,3-dione. (II)

Taken 7-aza indole (2.4 mmol), N-bromo succinimide (0.90g, 5.0 mmol) in 20ml of anhydrous dimethyl sulphoxide were stirred at 60°C for 6h and then above 80°C for 20 h under reduced pressure. Poured the reaction mixture into 50ml water followed by extracting with 10ml of dichloromethane three times, the combined extracts were washed three times with distilled water. After removal of the solvent, the residue was purified with dichloromethane. Molecular formula, $C_7H_4N_2O_2$; Molecular weight, 148; R_f value, 0.52 (Chloroform: Ethyl acetate 3:2) The yield of 7-azaIsatin was 82%, m.p.200-203°C FT-IR spectrum (KBr, in cm^{-1}): 3448(N-H str), 1617(C=O str), 1461 (Ar HC=CH str),^{1}H NMR (DMSO-d_6), δppm): 6.8-7.8(m, 4H, Ar-H), 11 (s, 1H, NH), Mass m/z 402 (M+1), Elemental analysis (Calcd/Found)%: C, 20.92/21.0; H, 1.00/0.99; I, 63.15/63.0; N, 6.97/6.90; O, 7.96/7.99.

b) Synthesis of ethyl4-(1,2-dihydro-2-oxopyrrolo [2,3] pyridin-3-ylideneamino) benzoate(III).

Dissolved an appropriate quantity of 7-azaindole-2,3-dione(0.01mol) in alcohol (20ml) and added ethyl p-amino benzoate (0.01mol) and few drops of glacial acetic acid. The reaction mixture was stirred well and refluxed for 3h. Filtered the resultant yellow crystalline solid and washed repeatedly with small quantity of methanol. The product was dried and purified by recrystallization from chloroform. Mol. Formula, $C_{16}H_{13}N_3O_3$; Mol. Wt, 295; R_f value, 0.53 (n-Hexane: EtOAc 3:2), % yield, 78, m.p, 187-189°C. FT-IR spectrum (KBr, in cm^{-1}): 3187(NH str), 1751(Ester C=O str), 2984(Aliphatic CH Str), 3020 (Ar-HC str),^{1}H NMR (DMSO-d_6), δ, ppm): 1.2(t, 3H, CH_3, *J*=7.1Hz), 4.0(s, 2H, NH_2), 4.2(q, 2H,CH_2,*J*=7.1Hz), 6.8-7.7(m, 3H, Ar-H), Mass m/z 295 (M+), Elemental analysis (Calcd/Found)%: C, 65.08/65.0; H, 4.44/4.3; N, 14.23/14.33; O, 16.2/16.5.

c) Synthesis of ethyl 4-(1'- [(substituted amino) 2-oxopyrrolo [2,3-b] pyridin-3-ylidene amino) benzoate (PSKa-m).

In minimum quantity of dimethyl formamide suspended compound of ethyl4-(1,2-dihydro-2-oxopyrrolo [2,3] pyridin-3-ylideneamino) benzoate (0.001mol), and added formaldehyde (1ml, 37%v/v) and various secondary amines(R) (0.001mol) with vigorous stirring. Warmed the solution on a water bath for 2min. and stirred for an hour.Then left at room temperature overnight. By the addition of water, the compounds (PSKa-m) was filtered, washed thoroughly with water, dried and purified by re-crystallization from ethanol. Completion of the reaction was monitored by TLC [ethyl acetate: chloroform (2:3)]. Purification of the compounds may have affected by recrystallization. All the desired compounds

were physically characterized and expressed in Table-1.

Antimicrobial activity

For bacterial growth nutrient agar media was used having composition beef extract, 3g; bacteriological peptones, 5g; agar, 20g, the pH was adjusted to 6.2 ±0.2 at 25 (±2) ° C and for fungal growth malt extract agar (MEA) was used composed of malt extract, 20 g; bacteriological peptone, 5g; agar, 20g, the pH was adjusted to 5.4 ±0.2 at 25 (±2) °C. Media was prepared by dissolving the all ingredients in 1L distilled water and heated upto 60-70° C and was sterilized in an autoclave at 121° C for 15-20 mins. Against the several species the antibacterial and antifungal activity was expressed by the measurement of zone of inhibition by agar diffusion method[14, 15]. At equal distance four holes were made in the sterile agar plates with the help of sterile cork borer in both media i.e. in nutrient agar and in malt extract agar. The synthesized compounds were dissolved in DMSO, 200µg /ml concentration of each compound was filled in the holes. Controlled holes were filled with DMSO solvent. For bacterial isolates plates were placed in a BOD at 37° C ± 2° C and on the other hand fungal isolates were incubated at 28° C ± 2° C for 24-48hrs. Zone of inhibition created by active compounds were measured after 24-48 hrs. Amplicillin was used as standard antibacterial agent while Clotrimazole was used as a standard antifungal agent. The antimicrobial activity of the synthesized compounds is shown in table-3. Ampicillin and clotrimazole(standard) were active at 10 µg /ml on all the Gram (+ve) bacteria with a zone of inhibition for *Bacillus subtilis*, *Staphylococcus aureus,*Gram (-ve) bacteria *Pseudomonas Vulgaris, Escherichia coli* and two fungal strains *C. albicans, A. niger*.

RESULTS AND DISCUSSION

Chemistry:

A series of novel mannich bases of 7- aza isatin derivatives (PSKa-m) were obtained by oxidising 7-azaindole, further refluxing with p-amino ethyl benzoate gives ethyl4-(1,2-dihydro-2-oxopyrrolo [2,3] pyridin-3-ylideneamino) benzoate. Then the titled compounds i,e Mannich bases of (Z)-ethyl 4-(1,2-dihydro-2-oxo pyrrolo[2,3-b] pyridin-3-ylideneamino) benzoate were synthesized by using dimethyl formamide, formaldehyde and various aromatic secondary amines [12,13] illustrated in Scheme-I**.** The chemical structures and purity of synthesized compounds were confirmed by IR, ^{1}H NMR, Mass and the data expressed in Table-2.

SCHEME-I

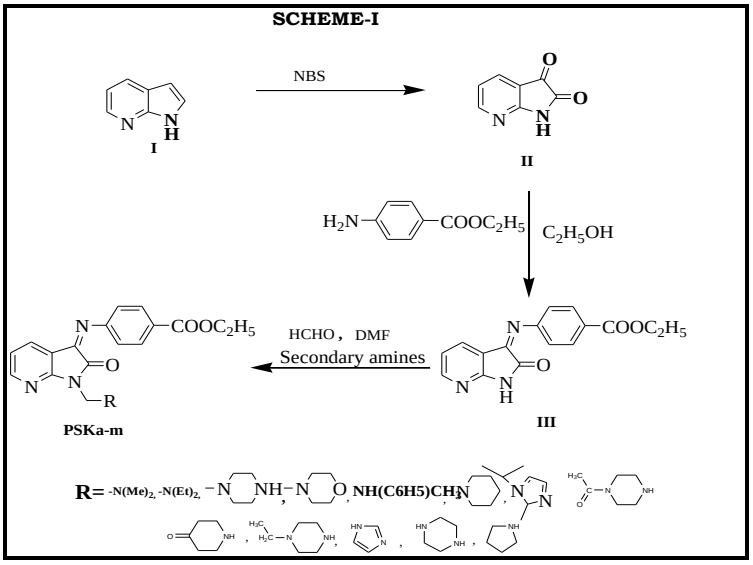
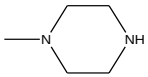
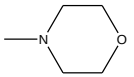
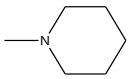
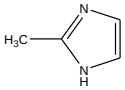
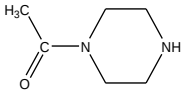
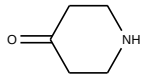
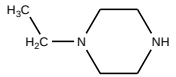
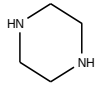


Table-1: Physical data of ethyl 4-(1'- [(substituted amino) 2-oxopyrrolo[2,3-b] pyridin-3-ylideneamino) benzoate (PSKam)

Code	R	MF	MW	% Yield	M.P(ºC)	*R_f	Elemental analysis (Calcd/Found) %
PSKa	-$N(CH_3)_2$	$C_{19}H_{20}N_4O_3$	352	80	180-182	0.56	C, 64.76/64.80; H, 5.72/5.6; N, 15.90/15.8; O, 13.62/14.0
PSKb	$N(C_2H_5)_2$	$C_{21}H_{24}N_4O_3$	380	70	300-301	0.62	C, 66.30/66.80; H, 6.36/6.0; N, 14.73/14.7; O, 12.62/12.4
PSKc		$C_{22}H_{25}N_5O_3$	407	68	240-242	0.61	C, 64.85/64.90; H, 6.18/6.2; N, 17.19/17.2; O, 11.78/12.0
PSKd		$C_{21}H_{22}N_4O_4$	394	60	295-296	0.51	C, 63.95/63.89; H, 5.62/5.5; N, 14.20/14.20; O, 16.23/16.65
PSKe	-$NH(C_6H_5)$ CH_3	$C_{24}H_{22}N_4O_3$	414	65	160-161	0.51	C, 69.55/69.66; H, 5.35/5.55; N, 13.52/13.61; O, 11.58/11.6
PSKf		$C_{21}H_{19}N_5O_3$	392	72	220-222	0.58	C, 69.55/69.8; H, 5.35/5.4; N, 13.52/13.6; O, 11.58/11.6
PSKg		$C_{23}H_{25}N_5O_4$	389	80	145-146	0.70	C, 64.97/65.0; H, 4.92/4.88; N, 17.98/17.99; O, 12.33/12.36
PSKh		$C_{23}H_{25}N_5O_4$	435	70	98-100	0.80	C, 63.44/63.55; H, 5.79/5.88; N, 16.08/16.43; O, 14.70/14.82
PSKi		$C_{22}H_{22}N_4O_4$	406	68	152-153	0.52	C, 65.01/65.0; H, 5.46/5.40; N, 13.78/13.88; O, 15.75/15.88
PSKj		$C_{23}H_{27}N_5O_3$	421	65	224-226	0.48	C, 65.54/65.66; H, 6.46/6.56; N, 16.62/16.50; O, 11.39/11.80
PSKk		$C_{20}H_{17}N_5O_3$	375	75	204-205	0.55	C, 63.99/64.0; H, 4.56/4.6; N, 18.66/18.69; O, 12.79/12.81
PSKl		$C_{21}H_{23}N_5O_3$	393	80	240-243	0.56	C, 64.11/64.15; H, 5.89/5.91; N, 17.80/17.90; O, 12.20/12.20
PSKm		$C_{21}H_{22}N_4O_3$	378	65	220-221	0.61	C, 66.65/66.76; H, 5.86/5.87; N, 14.81/14.83; O, 12.68/12.69

*MF= *Molecular formulae*; MW=*Molecular weight*, M.P =*Melting point*.

Table-2: Spectral data of ethyl 4-(1'-[(substituted amino) 2-oxopyrrolo [2,3-b]pyridin-3-ylideneamino)benzoate (PSKam)

CODE	FT-IR (KBr , cm^{-1})*	^1H NMR ($CDCl_3$, δ, ppm)	MS
PSKa	2936, 1733, 1605, 1271, 1469,3236	δ 8.5 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.69 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.34 (s, 6H), 1.38 (t, *J* = 8.0 Hz, 3H).	352 (M^+)
PSKb	2980, 1729,1608, 1296, 1470,3048	δ 8.88 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.69 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.34 (s, 6H), 1.38 (t, *J* = 8.0 Hz, 3H).	380 (M^+)
PSKc	2932, 1744,1610, 1252, 1472,3263	δ 8.2 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.70 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.50 (s, 8H), 2.32 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	408 (M+1)
PSKd	2906, 1728,1598, 1274, 1469,3187	δ 8.3 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.72 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.67 (t, *J* = 7.1 Hz, 4H), 2.61 (t, *J* = 7.1 Hz, 4H), 1.38 (t, *J* = 8.0 Hz, 3H).	394 (M^+)
PSKe	2924, 1705,1614, 1283, 1447,3033(aromatic CH)	δ 7.9 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 7.27 – 7.20 (m, 2H), 6.88 (tt, *J* = 7.6, 1.6 Hz, 1H), 6.76 (q, *J* = 8.1, 1.5 Hz, 3H), 5.95 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.04 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	414 (M^+)
PSKf	2972,1748,1690, 1229, 1510,3020	δ 8.8 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.69 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 4H), 1.53 – 1.44 (m, 5H), 1.42 – 1.30 (m, 6H).	392 (M^+)
PSKg	2873, 1750, 1679,1267, 1514	δ 8.0 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.21 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.37 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	390 (M+1)
PSKh	2932, 1744,1610, 1252, 1685,3236	δ 8.9 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.70 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.56 (t, *J* = 7.1 Hz, 4H), 2.81 (t, *J* = 7.1 Hz, 4H), 2.06 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	435 (M^+)
PSKi	2898,1732, 1576,1194, 1629,3065	δ 8.6 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.71 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.85 (t, *J* = 7.1 Hz, 4H), 2.52 (t, *J* = 7.1 Hz, 4H), 1.38 (t, *J* = 8.0 Hz, 3H).	406 (M^+)
PSKj	2928, 1774,1685, 1255, 1283,3048	δ 8.3 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.70 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.64 – 2.51 (m, 9H), 2.51 (d, *J* = 8.0 Hz, 1H), 2.48 (d, *J* = 8.0 Hz, 1H), 1.38 (t, *J* = 8.0 Hz, 3H), 1.03 (t, *J* = 8.0 Hz, 3H).	422(M+1)

PSKk	2873, 1750, 1679,1267,1514,3048	δ 8.6 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.71 (s, 1H), 7.39 – 7.34 (m, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.35 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	375 (M^+)
PSKl	2992, 1728,1598, 1274, 1469, 3356(NH)	δ 8.1 (d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.70 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.79 – 2.65 (m, 11H), 1.76 (d, *J* = 5.2, 3.6, 1.8 Hz, 1H), 1.38 (t, *J* = 8.0 Hz, 3H).	393 (M^+)
PSKm	2996, 1748, 1682,1258, 3062	δ 8.2(d, *J* = 7.4, 1.5 Hz, 1H), 8.41 (d, *J* = 7.5, 1.5 Hz, 1H), 8.10 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.39 – 7.34 (m, 2H), 4.69 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.92 – 2.81 (m, 6H), 1.90 – 1.79 (m, 6H), 1.38 (t, *J* = 8.0 Hz, 3H).	378 (M^+)

**Aliphatic CH, ester C=O, C=N, C-O, aromatic HC=CH stretching respectively.*

Antimicrobial screening

All the title compounds were screened for their *in vitro* antimicrobial activity by the Agar diffusion method. To control the sensitivity of the test organisms, the MICs of ampicillin and clotrimazole were determined in parallel experiments. The MIC values were determined as the lowest concentration that totally inhibited visible growth of the microorganisms by adopting serial dilution technique. The MICs of the test compounds PSKa-m and standard drugs is efficiently presented in table 3 and the values are expressed as mean ± standard deviation and statistical analysis was carried out by one-way ANOVA. ***P<0.001, **P<0.01, P<0.05 considered as significant. From the screening, all the compounds showed larger zone of inhibition as compare to standard drug Ampicillin and Clotrimazole. Among all the compounds PSKh, PSKi, PSKm and are more active against the both tested organisms.

Table-3: Antimicrobial activity of ethyl 4-(1'- [(substituted amino) 2-oxopyrrolo [2,3-b] pyridin-3-ylideneamino) benzoate (PSKa-m)

Compound/ Code	Antibacterial Activity				Antifungal Activity	
	S. aureus,	*B. subtilis*	*E. coli*	*P. vulgaris*	*C. albicans*	*A. niger*
Ampicillin	24.1 ± 0.2	22.9 ± 0.03	18.9 ± 0.1	18.4±0.4	*NA*	*NA*
Clotrimazole	*NA*	*NA*	*NA*	*NA*	21.0± 0.3	20.1 ± 0.2
PSKa	7.2 ± 0.3	8.3 ± 0.2	6.5 ± 0.11	5.4 ± 0.3	5.2 ± 0.3	6.2 ± 0.3
PSKb	4.6 ± 0.2	5.6 ± 0.2	3.6 ± 0.2	5.1 ± 0.2	2.9 ± 0.0	2.8 ± 0.2
PSKc	10.5 ± 0.5	12.6 ± 0.4	14.4 ± 0.4	15.1 ± 0.1	10 ± 0	14 ± 1
PSKd	17.1 ± 0.4	18.6 ± 0.6	15.2 ± 0.3	14.1 ± 0.2	15.8 ± 0.3	17.6 ± 0.1
PSKe	18.4 ± 0.2	19.1± 0.3	15.6 ± 0.5	15.1 ± 0.1	9.1± 1.1	13.6 ± 0.2
PSKf	7.2 ± 0.7	7.9 ± 0.05	8.0 ± 0.9	7.8 ± 0.7	4.3 ± 0.2	4.5 ± 0.5
PSKg	12.3 ± 0.5	14.4 ± 0.5	14.1 ± 0.6	14.6± 0.2	8.9 ± 0.1	9.1 ± 0.1
PSKh	23.7 ± 0.5***	22.6 ± 0.5***	19.6 ± 0.5***	17.9± 0.8***	16.6± 0.5***	18.6 ± 0.2***
PSKi	22 ± 1.7***	22.2 ± 0.4***	19.8 ± 0.8***	17.7 ± 0.2***	17.4± 0.4***	18.6 ± 0.2***
PSKj	19.8 ± 0.2	19.8 ± 0.2	16.6 ± 0.2	16.8 ± 0.2	16.1 ± 0.2	15.7 ± 0.2
PSKk	15.1 ± 0.3	16.5 ± 0.1	13.7 ± 0.1	13.2 ± 0.1	8.4 ± 0.4	8.1 ± 0.2
PSKl	21.3 ± 0.4	20 ± 0.5	18.5 ± 0.4	19.1 ± 0.2	12.6 ± 0.6	11.9 ± 1.3
PSKm	22.9 ± 0.1***	21.8 ± 0.1***	18.9 ± 0.0***	16.9 ± 0.0***	18.1 ± 0.7***	19.3 ± 0.7***

Values are expressed as Mean ± SD (n=3). ***P <0.001, **P <0.01, *P <0.05.
All significant differences are considered from control value 0.00; NA=not applicable.

CONCLUSION

With an aim of developing potent antimicrobial agent, a series of novel Mannich bases of 7-Azaisatin derivatives were synthesized from azaindole, molecular structures, purity of compounds confirmed and screened for their *in vitro* antimicrobial activity. The results concluded that compounds containing *N* acetyl piperazine, pyrolidine, piperidinone superior activity against gram +ve, gram-ve bacteria, on fungi strains in other hand compounds containing N ethyl piperazine, pyrolidine shown good results against fungi. It has been very clear from the above findings this progression of novel Mannich bases of 7-Azaisatin derivatives were biologically active, potent and a significant importance in medicinal chemistry.

ACKNOWLEDGMENTS

I gratefully acknowledge the Dr. N.Raghunandan, Principal of Balaji Institute of Pharmaceutical Sciences, Warangal; for providing infra structure facilities to carry out this research work.

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