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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF NEW 7-AZAISATIN DERIVATIVES.

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Abstract:
The indole and 7-azaindole derivatives both natural and synthetic have various pharmacological activities like antimicrobial, anticonvulsant, antioxidant, antidiabetic, MAO inhibitory and psychotropic activities. So it's a thought worthwhile to synthesis a series of new 7- AzaIsatin derivatives were synthesized by oxidising 7-azaindole followed by refluxing with p-amino ethyl benzoate, further treated with various alkyl halides to give (Z)-ethyl 4-(1substiuted-2-oxopyrrolo[2,3-b] pyridin-3-ylideneamino) benzoate derivatives. The structure and purity of the synthesized compounds was elucidated by spectral analysis (IR Mass, Elemental analysis and 1HNMR). These compounds were also screened for their in vitro antibacterial and antifungal activities by cup-plate method using Ampicillin and Clotimazole as standard drugs.

Key words: *Alkyl Halides, 7-AzaIsatin, Antibacterial activity, Antifungal activity.*

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INTRODUCTION:

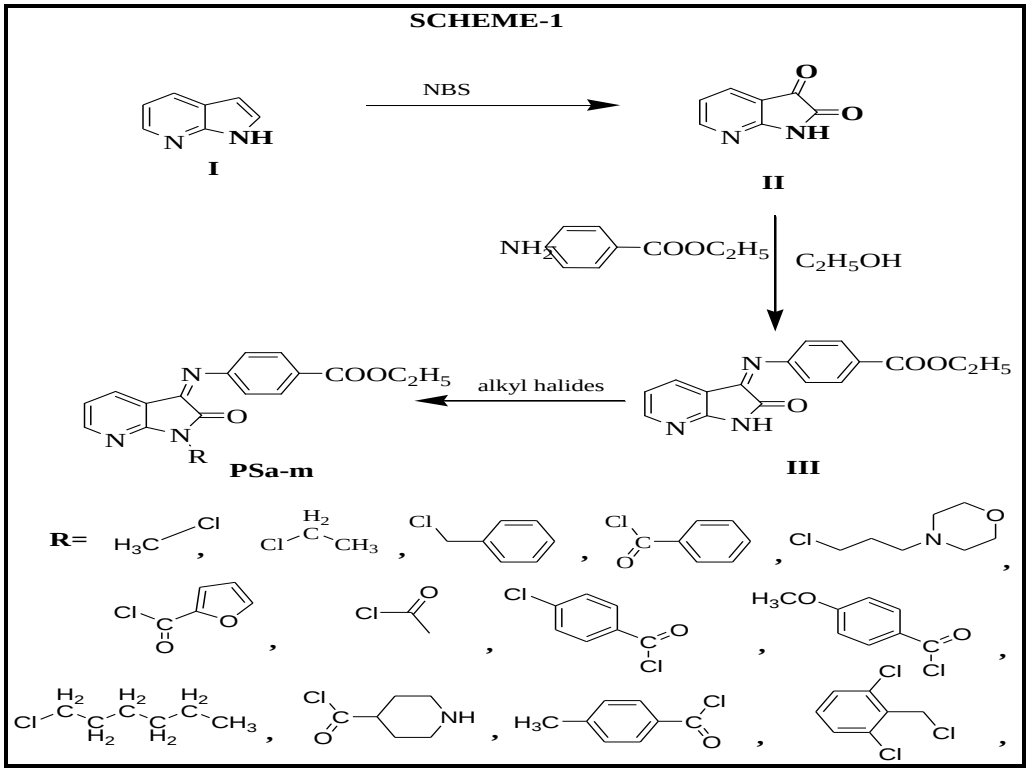
The word derivative is a broad term which involves different kinds of modification in the existing drug molecules and also preparing combination products of different chemical compounds using different approaches Isatin (indoline-2, 3-dione) is a versatile precursor [1]. It is widely distributed in mammalian tissues and body fluids, where Isatin concentrations vary significantly from <0.1 to > 10 μM. Isatin output is increased under conditions of stress. Exogenously administered Isatin is characterized by low toxicity, mutagenicity, and genotoxicity in *vivo* [2]. Due to its numerous biological and pharmacological activities, such as antimicrobial [3-8], antifungal [9], anticancer [10], anti HIV[11] and antihelminthic [12,13]. Some were also examined for their anticonvulsant [14] activities.7-Azaisatin was first obtained by treatment of 7-azaoxindole with nitrous acid to give its 3-oxime, followed by hydrolysis of the oxime [15]. Another route for the preparation of 7-azaisatin from 7-azaindole in five steps with difficulty was reported by Parrick and coworker 16 in 1989. On the other hand, for 7-azaisatins only a few compounds are known, Therefore we wish to prepare a New 7 Aza Isatin derivatives by oxidation of 7 aza indole with NBS which is a convenient method in good to excellent yields for emerging drug targets and required to use these therapeutically potent molecules as drugs in an active area of medicinal chemistry.

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 thermal melting point apparatus and are uncorrected. Purity of compounds was checked by TLC on Silica Gel precoated plates. IR spectra were recorded in KBr on FTIR Brucker spectrophotometer and frequencies are expressed in cm^{-1}. The ^{1}H-NMR 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 and the titled compounds were coded as PSa-m.

SCHEME-1



General procedure for the synthesis of title compounds.

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

Taken 7-azaindole (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) ,yield 82%,FT-IR spectrum (KBr, in cm^{-1}): 3448(N-H str), 1617(C=O str), 1461 (Ar HC=CH str),^{1}H NMR ($CDCl_3$), δppm): 6.8-7.8(m, 4H, Ar-H), 11 (s, 1H, NH), Mass m/z 402 (M+1), Elemental analysis (Calculated/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 ethyl 4-(1,2-dihydro-2-oxopyrrolo[2,3]pyridin-3-ylideneamino)benzoate (III).

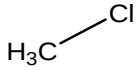
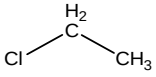
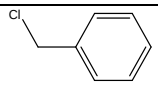
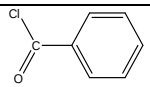
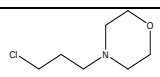
Dissolved an appropriate quantity of 7-azaindole-2, 3-dione (0.01mol) in alcohol (20ml) and added ethyl p-amino benzoate (0.01mol) and few drops of glacial acetic acid. The reaction mixture was stirred well and refluxed for 3h. Filtered the resultant yellow crystalline solid and washed repeatedly with 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 (($CDCl_3$), 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 (Calculated/Found)%: C, 65.08/65.0; H, 4.44/4.3; N, 14.23/14.33; O, 16.2/16.5.

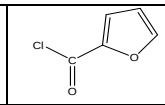
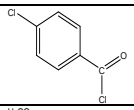
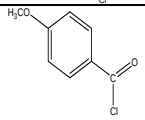
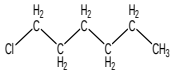
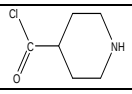
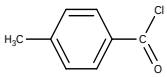
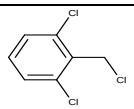
c) Synthesis of ethyl 4-(1'-[(substituted alkyl) 2-oxopyrrolo [2,3-b]pyridin-3 ylideneamino) benzoate (PSa-m).

Taken Potassium hydroxide(6.5g) was added to dimethyl sulphoxide (50ml) in a 250ml conical flask and stirred for 5min. Added 0.03g of Synthesis of ethyl 4-(1,2-dihydro-2-oxopyrrolo[2,3] pyridin-3-ylideneamino)benzoate to the conical flask and stirred an additional 45min. The reaction mixture was placed in an ice bath, and added various alkyhalides (3.55g, 5.05ml) and stirred again for 45min. Water (50ml) was added and the reaction was partitioned with 100ml of ether and repeated three times, taken dryness by rotarory evaporation. Completion of the reaction was monitored by TLC [ethylacetate: chloroform (2:3)]. Purification of the compounds may effected by recrystallization from ethanol. All the compounds (PSa-m) were further physical characterized, and is shown in table-1

RESULTS AND DISCUSSION:

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

Code	R	MF	MW	% Yield	M.P(°C)	R_f	Elemental analysis (Calculated/Found)%
PSa		$C_{17}H_{15}N_3O_3$	309	80	179-180	0.55	C, 66.01/66.10; H, 4.89/4.90; N, 13.58/13.58; O, 15.52/15.55
PSb		$C_{18}H_{17}N_3O_3$	323	70	199-200	0.52	C, 66.86/66.88; H, 5.30/5.33; N, 13.00/13.11; O, 14.84/14.80
PSc		$C_{23}H_{19}N_3O_3$	385	68	171-172	0.51	C, 71.67/72.80; H, 4.97/5.01; N, 10.90/10.91; O, 12.45/12.48
PSd		$C_{23}H_{17}N_3O_4$	399	60	240-242	0.61	C, 69.17/69.22; H, 4.29/4.30; N, 10.52/10.55; O, 16.02/16.11
PSe		$C_{23}H_{26}N_4O_4$	422	65	150-151	0.71	C, 65.39/65.40; H, 6.20/6.23; N, 13.26/13.28; O, 15.15/15.20

PSf		$C_{21}H_{15}N_3O_5$	389	72	230-232	0.68	C, 64.78/64.77; H, 3.88/3.89; N, 10.79/10.80; O, 20.55/20.56
PSg		$C_{18}H_{15}N_3O_4$	337	80	148-150	0.72	C, 64.09/64.10; H, 4.48/4.50; N, 12.46/12.51; O, 18.97/19.00
PSh		$C_{23}H_{16}ClN_3O_4$	433	75	110-111	0.80	C, 63.67/63.68; H, 3.72/3.77; Cl, 8.17; N, 9.69/9.71; O, 14.75/14.77
PSi		$C_{24}H_{19}N_3O_5$	429	69	152-153	0.52	C, 67.13/67.15; H, 4.46/4.50; N, 9.79/9.80; O, 18.63/18.66
PSj		$C_{22}H_{25}N_3O_3$	379	69	214-216	0.48	C, 69.64/69.66; H, 6.64/6.66; N, 11.07/11.11; O, 12.65/12.66
PSk		$C_{22}H_{22}N_4O_4$	406	75	234-235	0.55	C, 65.01/65.11; H, 5.46/5.48; N, 13.78; O, 15.75/15.76
PSl		$C_{24}H_{19}N_3O_4$	413	78	140-143	0.56	C, 69.72/69.77; H, 4.63.4.68; N, 10.16/10.18; O, 15.48/15.49
PSm		$C_{23}H_{17}Cl_2N_3O_3$	454	90	210-211	0.61	C, 60.81/60.83; H, 3.77/3.75; Cl, 15.61/15.60; N, 9.25/9.25; O, 10.57/10.59

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

Chemistry

From the illustrated Scheme-I, a series of New 7-Aza Isatin derivatives PSa-m were prepared by oxidation of 7-azaindole with NBS. The intermediate and the final compounds were characterized by their physico-chemical, IR, ^{1}HNMR, ^{13}CNMR, MS spectral data and elemental analysis. The derivatives showed characteristic NH stretch (between 3300 and 3450cm^{-1}), C=O stretch (between 1730 and 1750cm^{-1}). Ester C=O stretch (1735-1750), N-CH_3 (aliphatic) 2780-2805, 3075-2850 cm-1 for C-H aliphatic and aromatic correspondently,^{1}HNMR spectra of compounds exhibited Aliphatic H proton peak between δ3.7 and 3.9 ppm as singlet, Ar-H between δ 6 and 9 ppm as multiplet corresponding to the protons of the benzene ring. as well as a doublets. The MS spectra of compounds showed M+ and M+1 peak showed. Elemental analysis revealed that variation in experimental values compared with calculated values is within ±0.4% and screened for their *in vitro* antibacterial and antifungal activities. The results of the physical, spectral data of the final compounds are presented in table-2

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

CODE	FT-IR (KBr , cm^{-1})*	^{1}H NMR ($CDCl_3$,δ,ppm)	MS
PSa	2825,1785,1685,1030,3062	δ 8.86 (d, *J* = 7.5, 1.5 Hz, 1H), 8.40 (d, *J* = 7.5, 1.5 Hz, 1H), 8.09 (t, *J* = 7.5 Hz, 1H), 8.06 – 8.01 (m, 2H), 7.35 – 7.29 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.79 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H). 1a	309(M^+)
PSb	2920,1731,1674,1327,3110	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), 4.46 (q, *J* = 8.0 Hz, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.47 (t, *J* = 8.0 Hz, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	323(M^+)
PSc	2919,1683,1590,1116,3064	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 – 7.32 (m, 7H), 7.34 – 7.23 (m, 2H), 5.54 (s, 2H), 4.35 (q, *J* = 8.0	385(M^+)

		Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	
PSd	2924,1641,1588,1292, 1745,3063	δ 9.00 (d, *J* = 7.5, 1.5 Hz, 1H), 8.54 (d, *J* = 7.5, 1.5 Hz, 1H), 8.14 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.73 – 7.65 (m, 3H), 7.54 – 7.40 (m, 7H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	399(M+1)
PSe	1398, 1734, 1580,1163, 1091(C-N-C of morpholine), 3030(CH-Ar),	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), 4.57 (t, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.80 (t, *J* = 7.1 Hz, 4H), 2.63 (t, *J* = 7.1 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 4H), 2.07 (p, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	422(M^+)
PSf	2932,1668.1600,1268,1076 (C-O-C)3030(CH-Ar), 1520	δ 8.98 (d, *J* = 7.5, 1.6 Hz, 1H), 8.51 (d, *J* = 7.5, 1.5 Hz, 1H), 8.14 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.93 (d, *J* = 7.5, 1.6 Hz, 1H), 7.64 (d, *J* = 7.5, 1.5 Hz, 1H), 7.46 – 7.40 (m, 2H), 6.74 (t, *J* = 7.5 Hz, 1H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	389(M+1)
PSg	2828,1770,1670,1525,1025,3030	δ 8.92 (d, *J* = 7.5, 1.5 Hz, 1H), 8.59 (d, *J* = 7.5, 1.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.98 (t, *J* = 7.5 Hz, 1H), 7.46 – 7.40 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 2.74 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	337(M^+)
PSh	1373(CH-aliphatic), 1639,1298,1685,1574,3029, 800(C-Cl)	8.54 (d, *J* = 7.5, 1.5 Hz, 1H), 8.14 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.83 – 7.77 (m, 2H), 7.57 – 7.51 (m, 2H), 7.46 – 7.40 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	433(M^+)
Psi	2991,1725,1670,1025,1525,1120.	δ 9.00 (d, *J* = 7.5, 1.5 Hz, 1H), 8.54 (d, *J* = 7.5, 1.5 Hz, 1H), 8.14 (t, *J* = 7.5 Hz, 1H), 8.07 – 8.01 (m, 2H), 7.90 – 7.84 (m, 2H), 7.46 – 7.40 (m, 2H), 7.11 – 7.06 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.79 (s, 3H), 1.38 (t, *J* = 8.0 Hz, 3H).	429(M+1)
PSj	3123, 1738, 1680, 1342, 1557, 3286.	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), 4.55 (t, *J* = 7.1 Hz, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.83 (p, *J* = 7.1 Hz, 2H), 1.42 – 1.21 (m, 11H), 0.94 – 0.84 (m, 3H).	379(M+1)
PSk	2950,1738,1672,1028,1528, 3310(NH)	δ 8.95 (d, *J* = 7.5, 1.5 Hz, 1H), 8.61 (d, *J* = 7.4, 1.5 Hz, 1H), 8.05 (d, *J* = 1.2 Hz, 1H), 8.03 (d, *J* = 1.2 Hz, 1H), 8.05 – 7.96 (m, 1H), 7.46 – 7.40 (m, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 3.11 (t, *J* = 12.5, 7.1, 5.4 Hz, 2H), 3.06 – 2.90 (m, 3H), 2.16 – 2.07 (m, 3H), 2.09 – 1.97 (m, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	406(M^+)
PSl	2935,1641,1588,1086(C-N),1529,3281	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), 7.41 – 7.31 (m, 6H), 5.71 (s, 2H), 4.35 (q, *J* = 8.0 Hz, 2H), 1.38 (t, *J* = 8.0 Hz, 3H).	413(M^+)
PSm	2832, 1774,1672,1528, 1280,3062,755(C-Cl)	δ 1.29 (3H, t, *J* = 7.1 Hz), 4.28 (2H, q, *J* = 7.1 Hz), 5.36 (2H, s), 7.22-7.30 (3H, 7.26 (d, *J* = 7.6, 5.2 Hz), 7.27 (d, *J* = 8.3, 1.5 Hz)), 7.39 (1H, t, *J* = 8.3 Hz), 7.64 (2H, d, *J* = 8.1, 1.6, 0.4 Hz), 7.86 (1H, d, *J* = 7.6, 1.9 Hz), 8.11 (2H, d, *J* = 8.3, 1.5, 0.4 Hz), 8.43 (1H, d, *J* = 5.2, 1.9 Hz).	454(M^+)

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

Antimicrobial Screening

In the search of new antimicrobial agents, all the twelve synthesized compounds were subjected to antimicrobial screening by estimating the minimum inhibitory concentration (MIC) by adopting serial dilution technique. Test was carried out on four bacterial strains, namely gram-positive bacteria *Staphylococcus aureus (* NCIM 2079), *Bacillus subtilis (*NCIM 2045), gram negative bacteria *Escherichia coli* (NCIM 2345), *Proteus vulgaris* (NCIM 2027) and fungi *Candida albicans* (NCIM 3557), *Aspergillus niger* (NCIM 1058).

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 up to 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 *Proteus vulgaris*, *Escherichia coli* and two fungal strains *C. albicans*, *A. niger*. Values were expressed as mean ± standard deviation and statistical analysis was carried out by one way ANOVA. ***P<0.001, **P<0.01, P<0.05considered as significant.

Table-3: Anti microbial activity of ethyl 4-(1'-[(substituted alkyl) 2-oxopyrrolo [2,3-b]pyridin-3-ylideneamino)benzoate(PSa-m)

Compound/ Code	Antibacterial Activity				Antifungal Activity	
	S. aureus,	***B. subtilis***	***E. coli***	***P. vulagaris***	***C. albicans***	***A. niger***
Ampicillin	24.7± 0.5	22.6± 0.5	19.6± 0.5	18.6 ± 0.5	*NA*	*NA*
Clotrimazole	*NA*	*NA*	*NA*	*NA*	19.8 ± 0.3	21.9 ± 0.07
PSa	6.1 ± 0.1	7.2± 0.5	5.6 ± 1.4	6.1 ± 0.57735	5.6 ± 0.4	8.06 ± 0.1
PSb	8.5 ± 0.5	8.7± 0.1	7.9 ± 0	6.5 ± 1.1	10.9 ± 0.05	13.4 ± 0.4
PSc	26.9 ± 1	26.4± 0.4	26.8 ± 0.2	26.3 ± 0.5	19.6 ± 1.2	23.4 ± 0.5
PSd	18.1± 0.1	20.7± 0.1	17.3 ± 0.6	16.7± 0.2**	20 ± 0**	23.6 ± 0.5**
PSe	20.3 ± 0.4**	23.8±0.05**	22.8 ± 5.3**	19.5 ± 1.5	19.2± 0.6	21.8 ± 1.5
PSf	11.7 ± 2.2	15.7± 0.2	13.9 ± 0.9	15.1 ± 0.5	24.9 ± 1.0***	26.7 ± 1.0***
PSg	28.0 ± 0.05***	27.1± 0.7***	25.3 ± 1.5***	25.5 ± 1.1***	23.8 ± 0.1***	26.8 ± 0.2***
PSh	11.2± 0.5	12.3± 1.9	11.7 ± 0.7	12.9 ± 0.0	15.9± 0.05***	17.9 ± 0.05**
PSi	28.2 ± 0.6***	27.4±0.1***	27.8± 0.2***	27.9 ± 0.1***	22 ± 0	24.2 ± 0.8***
PSj	27.7 ± 0.1***	26.9±0.05***	26.7 ± 0.9***	27.2 ± 0.5***	12.6 ± 0.6	13.9 ± 1.0
PSk	8.5 ± 1.3	10.5± 0.4	6.9 ± 0.1	7.6 ± 1.5	5.2 ± 0.1	5.9 ± 0.05
PSl	24.3 ± 0.5	25.4± 2.2	23 ± 0.05	22.3 ± 0.4	16.2 ± 0.6	17.9 ± 0.1
PSm	15.1± 0.2	18.1± 0.9	15.± 0.2	14.0 ± 1.2	17.2 ± 0.6	20.4 ± 0.4

**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:

The title compounds (PSa-m) were synthesized from azaindole as starting material on oxidation by using N-bromo succinimide and follows in three steps to the desired compounds. In conclusion, we have screened for *in vitro* anti-bacterial activity against the gram positive and gram negative microorganisms. Some of the synthesized compounds PSg, PSi, PSj were highly active against gram positive and gram negative bacteria, comparable with standard drug and for anti-fungal activity against several fungii strains. Some of the compounds PSf, PSg, PSh exhibited very significant antifungal activity, and comparatively potent than standard comparable with standard drugs. These observations may advance a further improvement of our exploration in this field.

REFERENCES:

1. J FM da Silva, SJ Garden, AC Pinto. The Chemistry of Isatins a review from 1975 to 1999. J Braz *Chem Soc*, 2001;12: 273-324.

2. Alexei Medvedev, Olga Buneeva. Isatin an endogenous nonpeptide biofactor A review of its molecular targets, mechanisms of actions, and their biomedical implications. Biofactors, 2018; 44(2): 95-108.

3. WC Sumpter. The chemistry of isatin. Chem Rev, 1944; 34: 393-434.

4. I Pataki, A Adamik, V Glover, G Toth ,G Telegdy. The effects of isatin (indole-2, 3-dione) on pituitary adenylate cyclase-activating polypeptide-induced hyperthermia in rats. BMC Neuroscience, 2002; 3(2): 1471-2202.
5. J Bergman, JO Lindstrom, ULF Tilstam. The structure and properties of some indolic constituents in Couroupita guianensis Aubl. Tetrahedron, 1985; 41(14): 2879-2881.
6. SN Pandey, VS Lakshmi, A Pandey. Biological activity of Mannich bases. Indian J Pharm Sci, 2003; 65(3): 213-222.
7. M D'Ischia, A Palumbo, G Prota. Adrenalin oxidation revisited. New products beyond the adrenochrome stage. Tetrahedron, 1988; 44(20): 6441-6446.
8. RW Daisley, VK Shah. Synthesis and antibacterial activity of some 5-nitro-3-phenyliminoindole-2(3H) ones and their N-Mannich bases. J Pharm Sci, 1984; 73(3): 407408.
9. E Piscopo, MV Diurno, R Gagliardi, M Cucciniello, G Veneruso. Studies on heterocyclic compounds, Indole-2, 3-dione derivatives,variously substituted hydrazones with antimicrobial activity. Bollettino - Societa Italiana di Biologia Sperimentale, 1987; 63 (9): 827-832.
10 MC Liu, TC Lin, AC Sartorelli. Synthesis and antitumor activity of amino derivatives of pyridine-2-carboxaldehyde thiosemicarbazone. J Med Chem, 1992; 35(20): 3672–3677.
11. PN Surendra, P Yogeeswari, DS Ram, G Nath. Synthesis and antimicrobial activity of N-Mannich bases of 3-[N'-sulfadoximino]isatin and its methyl derivative. Boll Chim Farm, 1998; 137(8): 321-324.
12. ME Sarciron, P Audin, I Delabre, C Gabrion, AF Petavy, J Paris. Synthesis of propargylic alcohols and biological effects on Echinococcus multilocularis metacestodes. J Pharm Sci, 1993; 82(6): 605–609.
13. EA El-Sawi, TB Mostafa, BB Mostafa. Studies on the molluscicidal action of some isatin derivatives against Biomphalaria alexandrina in Egypt. J Egypt Soc Parasitol, 1998; 28(2): 481–486.
14. L Tripathi, R Singh, J P Stables. Design & synthesis of N'-[substituted]pyridine-4-carbo hydrazides as potential anticonvulsant agents. Eur J Med Chem, 2011; 46(2): 509-518.
15. H Kagi. About 7-pyroxindole, 7-pyrisatin, and 7, 7'-di-pyr-indigo. Helvetica Chimica acta, 1941; 24 (2): 141E-150E.
16. J Tatsugi, y Izawa. A convenient one-pot synthesis of indane-1, 2, 3-triones by oxidation of indan-1-ones with n-bromosuccinimide-dimethyl sulfoxide reagent. Synthetic communications, 1998; 28(5): 859-864.