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Research Article

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In vitro biological evaluation of indazole-clubbed schiff base derivatives

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ABSTRACT

6-Amino Indazole react with various aromatic aldehyde. Finally the product were characterized by conventional and instrumental methods. Their structures and biological activities were determined.

Keywords: *In vitro* , Indazole, Biological Evaluation, Schiff base.

INTRODUCTION

Azomethines are generally known as Schiff bases to honour Hugo Schiff, who synthesized such compounds. These are the compounds containing characteristic -C=N- group. Several methods have been reported for the preparation of azomethines. Selvam *et.al* [1] have prepared sulfonamide and its derivatives as anti-HIV agents. More *et. al* [2] have marked the biological activity of Schiff bases synthesized from aminothiazoles. Ernst Bayer [3] has reported some metallocomplex Schiff bases derived from *o*-amino phenol. Schiff bases can be synthesized from an aromatic amine and a carbonyl compound by nucleophilic addition forming a hemiaminal, followed by a dehydration to generate an imine [4]. They are well known intermediates for the preparation of azetidinones, thiazolidinones, oxadiazolines and many other derivatives. Azomethines exhibit a wide range of pharmacological activities like antimicrobial [5], antiparasitic [6], anti-inflammatory [7], anticancer [8] *etc*.

Indazole and their derivatives display interesting biological properties and powerful pharmacological activities, such as anti-cancer, and anti-platelet activities, plus serotonin 5-HT3 receptor antagonist [9].

EXPERIMENTAL SECTION

The reagent grade chemicals were obtained from commercial sources and purified by either distillation or recrystallization before use. Purity of synthesized compounds has been checked by thin layer chromatography. Melting points were determined by open capillary method and are uncorrected. IR spectra are recorded on FT-IR Bruker with KBr disc. ^{1}H NMR spectra are recorded in DMSO-d6 on a Bruker DRX-400 MHz using TMS as internal standard. The chemical shift are reported as parts per million (ppm) and mass spectra were determined on Jeol-SX-102(FAB) spectrometer.

Synthetic Procedures

Preperation of 6-amino Indazole

Commercially useful 6-amino indazole is synthesized by nitrating 4-nitro-2-amino toluene in acetic acid to get 6-nitro indazole. Obtained 6-indazole is reacted with hydrogen gas to get 6-amino indazole which is used as agro and pharma intermediates.

Preparation of 4-[(*z*)-(1*h*-indazol-6-ylimino)methyl]-2-methoxyphenol

To a mixture of 6-amino Indazole (0.1 mol.) and substituted aromatic aldehyde (Vanilline, 0.1 mol.) in methanol, catalytic amount of glacial acetic acid added then the resultant mixture was refluxed for (5-6 hours), progress of the reaction was monitored by TLC. After the completion of the reaction, the obtained product was poured into crushed

ice stirred well; solid obtained was recrystallized from suitable solvent. Their physical constant data are given in Table-1 and synthetic scheme in Figure-1.

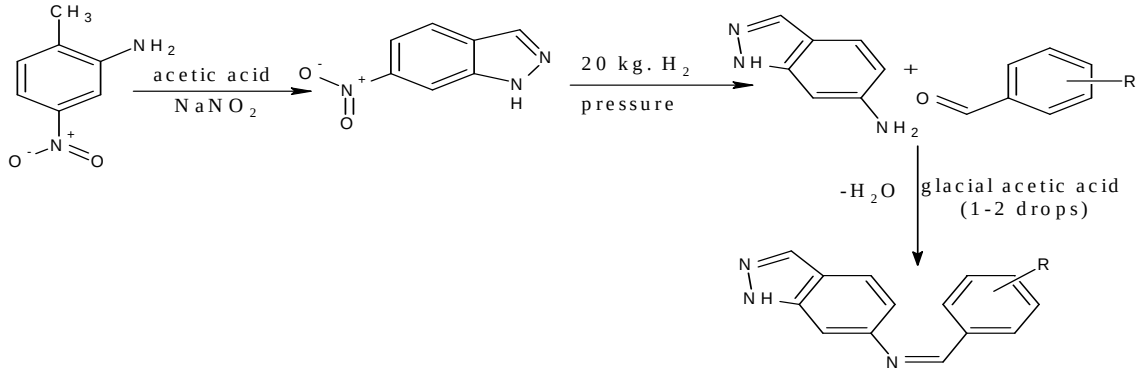

Table-1. Physical constants and elemental analysis of Schiff-base.

Comp. No.	-R	Molecular Formula	M.P °C	Yield %	% of C Found, (calcd.)	% of H Found, (calcd.)	% of N Found, (calcd.)
SP_{VI} -1	3- OCH_3-4- OH-C_6H_3	$C_{15}H_{13}N_3O_2$	175	74	67.42 (67.40)	4.91 (4.90)	15.73 (15.72)
SP_{VI} -2	4-OH-C_6H_4	$C_{14}H_{11}N_3O$	240	72	70.88 (70.87)	4.66 (4.67)	17.73 (17.71)
SP_{VI} -3	4-Cl-C_6H_4	$C_{14}H_{10}Cl_3N_3$	215	77	65.75 (65.76)	3.95 (3.94)	13.88 (13.86)
SP_{VI} -4	2-OH-C_6H_4	$C_{14}H_{11}ON_3$	180	73	70.88 (70.87)	4.68 (4.67)	17.73 (17.71)
SP_{VI} -5	4-NO_2-C_6H_4	$C_{14}H_{10}N_4O_2$	205	75	63.14 (63.15)	3.77 (3.79)	21.05 (21.04)
SP_{VI} -6	2,6-(CH_3)$_2$-C_6H_3	$C_{16}H_{15}N_3$	70	74	77.09 (77.08)	6.07 (6.06)	16.86 (16.85)
SP_{VI} -7	3,4,5-(OCH_3)$_3$-C_6H_2	$C_{17}H_{17}N_3O_3$	70	70	65.57 (65.58)	5.52 (5.50)	13.51 (13.50)
SP_{VI} -8	2,4,5-(OCH_3)$_3$-C_6H_2	$C_{17}H_{17}N_3O_3$	75	80	65.56 (65.58)	5.51 (5.50)	13.52 (13.50)
SP_{VI} -9	3,4-(OCH_3)$_2$-C_6H_3	$C_{16}H_{15}N_3O_2$	70	71	68.32 (68.31)	5.36 (5.37)	14.95 (14.94)
SP_{VI} -10	2-Cl-C_6H_4	$C_{14}H_{10}ClN_3$	190	76	65.77 (65.76)	3.95 (3.94)	13.87 (13.86)
SP_{VI}-11	-C_6H_5	$C_{14}H_{11}N_3$	75	79	76.01 (76.00)	5.03 (5.01)	18.97 (18.99)
SP_{VI} -12	-CH-CH=CH- C_6H_5	$C_{16}H_{13}N_3$	60	75	77.72 (77.71)	5.31 (5.30)	16.98 (16.99)
SP_{VI} -13	-C_4H_2O	$C_{12}H_9N_3O$	290	82	68.26 (68.24)	4.28 (4.29)	19.87 (19.89)
SP_{VI} -14	4-OCH_3-C_6H_4	$C_{15}H_{13}N_3O$	60	80	71.72 (71.70)	5.22 (5.21)	16.73 (16.72)
SP_{VI} -15	2-NO_2-C_6H_4	$C_{14}H_{10}N_4O_2$	56	81	63.14 (63.15)	3.78 (3.79)	21.05 (21.04)

RESULTS AND DISCUSSION

Biological Evaluation

Antibacterial activity

Antibacterial activity was carried out by browth dilution method [10]. The compounds SP_{VI}-1-15 were screened for their antibacterial activity against *Escherichia coli, Staphylocous aureus, Pseudomonas aeruginosa* and *Staphyloccous pyogenes* of concentrations of 1000, 500, 200, 100, 50, 25, 12.5 µg/mL respectively.

Antibacterial activity results showed that, compound SP_{VI}-02 was good active against *E. coli* and moderately active against *S. aureus*. Compound SP_{VI}-04 was moderately active against *E. coli* and *P. aeruginosa.* Compound SP_{VI}-07 was moderately active against *E. coli* and *P. aeruginosa*. Compound SP_{VI}-08 was moderately active against *S. aureus* and *S. Pyogenus.* Compound SP_{VI}09 was good active against *E. coli* and moderately active against *P. aeruginosa*. Compound SP_{VI}-12 was good active against *E. coli* and *P. aeruginosa*. Compound SP_{VI}-13 was good

active against *S. aureus* and moderately active against *S. pyogenus*. Their Antibacterial activity data are given in Table 2.

Antifungal activity

Same compounds were tested for antifungal activity against *C. albicans A. niger* and *A. clavatus* of a concentrations of 1000, 500, 200, 100 µg/mL respectively. The results are recorded in the form of primary and secondary screening. Each synthesized drug was diluted to obtain 1000 µg/mL concentration, as a stock solution.

The data of antifungal activity of this series indicated that, compounds SP_{VI}-15 was good active against *A. niger*, rest of compounds were not showing potential activity against any species. Their Antifungal data are given in Table-2.

Spectra study of 4-[(*z*)-(1*h*-indazol-6-ylimino)methyl]-2-methoxyphenol

IR(KBr. cm^{-1}):1591 cm^{-1}(C=N), 3319 cm^{-1} (-OH, alcohol), 3053 cm^{-1}(C-H, str), 1031 cm^{-1} (C-O-C, Symm. Str.), 1213 cm^{-1} (C-O-C,Asymm. Str.), 1425 cm^{-1} (C=N, Indazole), ^{1}H NMR(ppm) ($CDCl_3$):12.71(s, 1H, N=CH), 7.24-7.41(m, 6H), 3.85-3.94(s, 3H, -OCH_3), MS:268[M+1].

Table-2. Antibacterial and Antifungal activity data

Sr. No.	MINIMAL BACTERICIDAL CONCENTRATIONS (MBC) IN µg / ml				MINIMAL FUNGICIDAL CONCENTRATIONS (FBC) in µg/ml	
	E. coli MTCC 443 µg / ml	*P. aeruginosa* MTCC 1688 µg / ml	*S. aureus* MTCC 96 µg / ml	*S. pyogenus* MTCC 442 µg / ml	*C. albicans* MTCC 227 µg/ml	*A. niger* MTCC 282 µg/ml
SP_{VI}-01	250	250	250	250	>1000	>1000
SP_{VI}-02	62.5	200	100	250	1000	>1000
SP_{VI}-03	200	250	125	200	1000	>1000
SP_{VI}-04	100	125	250	250	1000	1000
SP_{VI}-05	100	200	200	200	500	500
SP_{VI}-06	250	250	500	500	500	1000
SP_{VI}-07	100	100	500	500	1000	1000
SP_{VI}-08	200	200	100	100	1000	>1000
SP_{VI}-09	62.5	100	200	200	>1000	>1000
SP_{VI}-10	200	200	250	250	>1000	500
SP_{VI}-11	250	250	250	200	250	1000
SP_{VI}-12	100	100	200	200	>1000	1000
SP_{VI}-13	200	250	62.5	100	1000	250
SP_{VI}-14	200	250	200	200	1000	500
SP_{VI}-15	250	200	250	250	500	100

CONCLUSION

The Schiff base were synthesized and characterized for their structure elucidation. Various chemical and Spectral data supported the structure thought of Antibacterial and Antifungal studies of these compounds indicated that SP_{VI}-02, SP_{VI}-09, SP_{VI}-12 and SP_{VI}-13 were good active, SP_{VI}-04, SP_{VI}-07 and SP_{VI}-08 were moderately active and compound SP_{VI}-15 was good active against *A. niger*

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