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Synthesis and Characterization of N-Methyl Indole Derivatives via Desulfitative Displacement by Various Amines and Its Antimicrobial Activity

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ABSTRACT

A modular three step synthetic approach of N-methyl indole derivatives has been carried out by the condensation of N-methyl indole with cyanoacetic acid using acetic anhydride as solvent to yield 3-cyanoacetyl N-methyl indole, which further reacts with carbon disulphide and methyl iodide in basic condition to obtain 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile as a scaffold. Subsequent, the scaffold when reacts with substituted various amine derivatives via desulfitative displacement forms new derivatives of 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile in moderate to good yields. All the novel compounds were evaluated for their antimicrobial activity against Gram+*ve* and Gram-*ve* bacteria and different fungal species which demonstrated well to moderate antimicrobial activity.

Keywords: N-methyl indole, Desulfitative displacement, S-methyl, Anti-microbial agents

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1. INTRODUCTION

It is known from the literature that indole derivatives exhibit varied biological and pharmacological properties[1-3]. Indole and its derivatives have always attracted both synthetic and biological chemist because of it's diverse chemical and pharmacological properties[4]. There are a number of natural products of indole skeleton used as a medicine or employed as a lead molecule for the development of newer and potent molecules. Moreover, Indole is a nonpolar purine analogue that is present in some important biochemical molecules such as tryptophan, serotonin, and melatonin[5]. There are currently many indoles containing drugs in the market[6]. It is found in various natural and synthetic products such as Indolmycin **(1),** Mitomycin **(2),** Indolol **(3)**, Dolasetron **(4)**, Indomethacin **(5)** and Sumatriptan **(6)**, and as shown in figure 1, which used for the treatment of various illnesses[7]

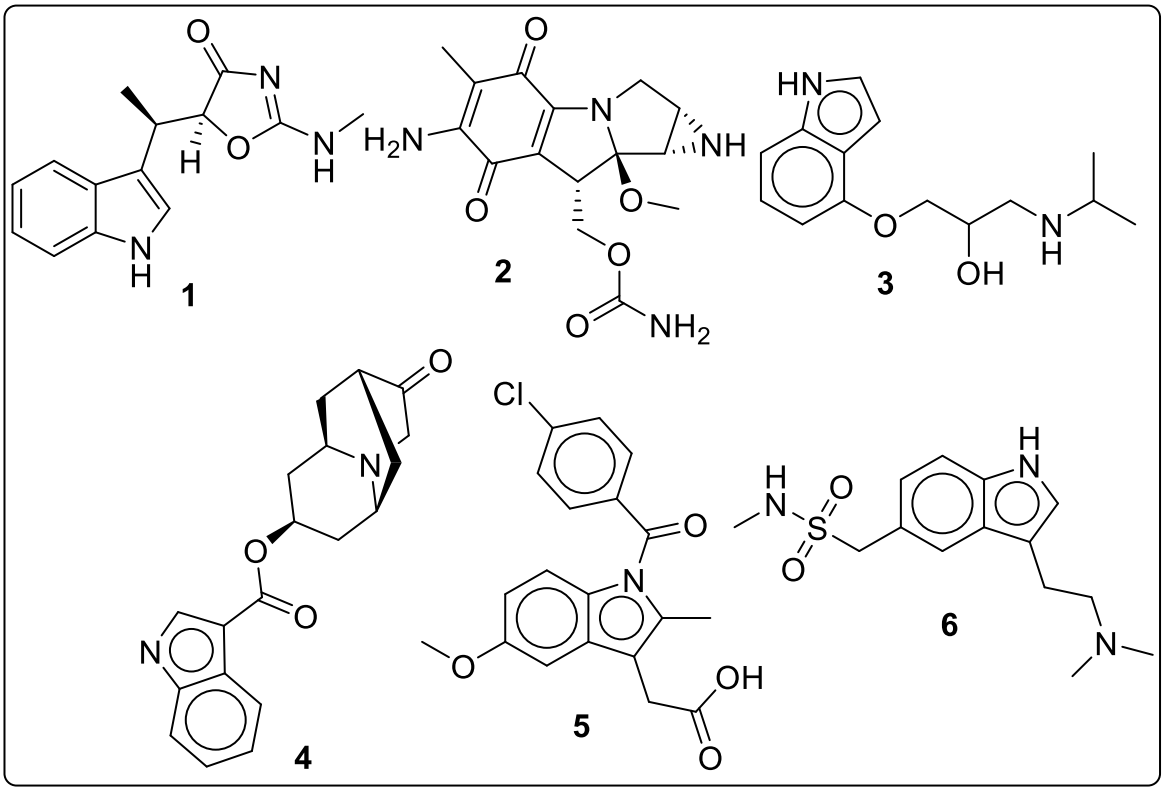

Figure 1. Some of the Indole containing marketed drugs.

Many researchers have synthesized Indole, N-Methyl indole and its fused heterocyclic derivatives. These observations have been guiding for the development of new indole derivatives that possess varied biological activities i.e. antibacterial,[8,9] antifungal,[10,11] antiviral,[12, 13] antitumor,[14] anti-inflammatory,[15, 16] and antihypertensive[17, 18] activities and also as plant growth regulators[19]. Indole ring has attracted the attention of many medicinal chemists as an interesting scaffold in the process of new drug development.[20, 21] Therefore it could be rationally considered as an appropriate core for designing new anti-microbial agents. Some of

the work has been done and more to go. Developments of newer N-Methyl indole have immense possibilities and scope for a research scientist.

We have presented a concise compilation of this work to aid in present knowledge and to help researchers to explore an interesting N-Methyl indole class. In view of the above-mentioned findings and a continuation of our efforts in the synthesis of new biologically active heterocycles.[22-24]

In view of these observations, the synthesis of some new 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile derivatives (KV-1 to KV-15) were carried out. (Reaction scheme).

The increases in drug resistance have become a serious medical problem. Particularly multidrug-resistant species of pathogens is causing a serious problem[25]. Indole type compounds containing 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio) acrylonitrilederivativeshave be very helpful for new drug development. It has been observed that a number of indole derivatives possess effective inhibitory effect against bacteria and fungi[26]. Recently antimicrobial effects of indole-3-carbinol against various human pathogens and its mode of action regarding antifungal activity against fungal pathogens were reported[25]. This investigation might prove our 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile derivatives to be a potent drug. From the literature, it has been found that there is wide scopes of research behind nitrogen-containing heterocyclic compounds are still exist. In nitrogen-containing heterocycle, the indole is most important as far as biological activity is a concern. Addition of another cyano containing organic molecules significantly increased the potentiality of the compounds. Starting reaction of N-methyl indole with cyanoacetic acid to formed 3-cyanoacetyl N-methyl indole, which on further react with carbon disulfide and methyl iodide in basic condition to obtain 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile **(d)**. In last various substituted amine derivatives are interact with compound **d** via desulfitative displacement using methanol as a solvent to obtain title compounds as **KV-1 to KV-15**.Thus, all the 15 compounds which are chemically synthesized are tested for their antibacterial and antifungal activity in this paper.

2. MATERIALS AND METHOD

2. 1. Chemistry

All chemicals were purchased and used without further purification. Reactions were monitored by thin layer chromatography (TLC) on DC 60 F_{254} silica gel-G plates of 0.5 mm thickness, TLC spots were visualized by UV-light irradiation. Melting point was determined using a Buchi B-540 capillary apparatus and are uncorrected. Mass spectra were recorded on a Shimadzu GC-MS-QP-2010 mass spectrometer in ESI (70eV) model using direct inlet probe technique and m/z is reported in atomic units per elementary charge. IR data were recorded on a Shimadzu FT-IR-8400 instrument and are expressed in cm^{-1} (KBr). NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer (400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR) and chemical shifts are referenced to the solvent residual signals with respect to TMS; ^{1}H NMR chemical shifts are designated using the following abbreviations as well as their combinations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, coupling constants in Hz. Elemental analysis of all the synthesized compounds was carried out on Euro EA 3000 elemental analyser and the results are in agreements with the structures assigned.

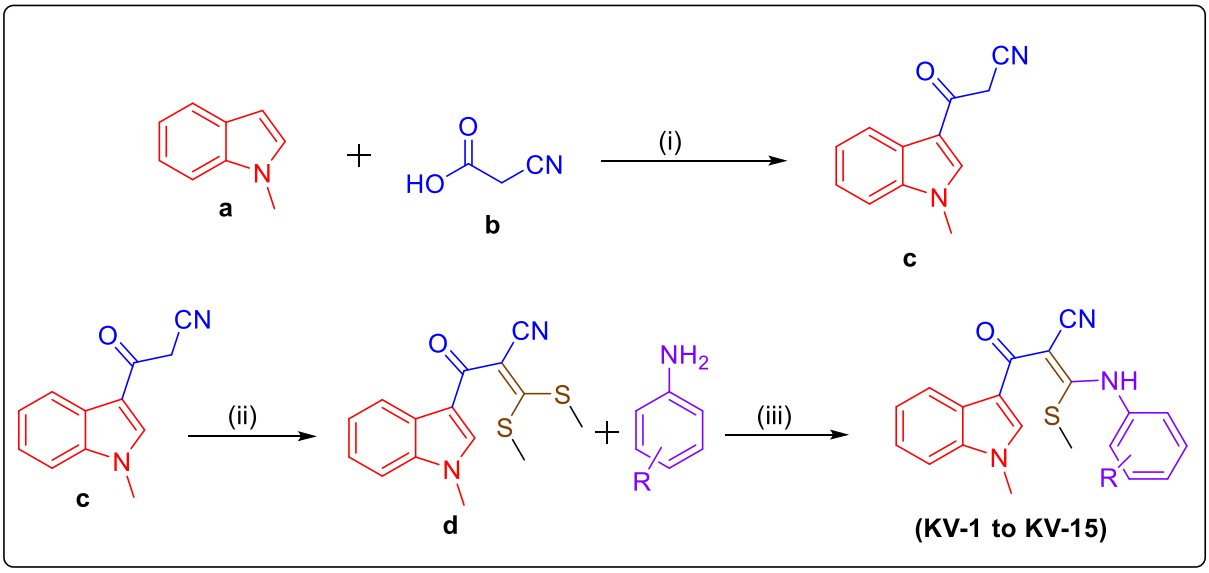

Figure 2. Synthetic Route for the synthesis of KV-1to KV-15. (i) Acetic anhydride, 90 °C, (ii) K_2CO_3, 0 °C, CS_2, CH_3I, (iii) Ethanol, reflux

All over the route of synthesis are shown in **Figure 2**, the first step is condensation of N-methyl indole with cyanoacetic acid using acetic anhydride to formed 3-cyanoacetyl N-methyl indole **(c)** which on further react with carbon disulphide and methyl iodide in basic condition to obtain 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile **(d)**. In last various substituted amine derivatives are interact with compound **d** via desulfitative displacement using methanol as a solvent to obtain 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (**KV-1 to KV-15)**.

2. 2. Synthesis of 3-(1-methyl-1*H*-indol-3-yl)-3-oxopropanenitrile (c)

Take N-methyl indole **(a)** (2.50 gm, 19 mmol), cyanoacetic acid (**b)** (1.62 gm, 19 mmol), and acetic anhydride (20 mL) in 100 mL RBF. Stirr the reaction mass at room temperature to prepare a homogeneous solution. After that the resulting solution was heated at 90 °C temperature for 30 minutes. The progress of reaction was monitored on TLC plate. After completion of reaction, the mixture was allowed to cool at room temperature, the crystal was obtained, filter it through *vaccuo*, and washed with methanol, dried it to obtain 3-(1-methyl-1*H*-indol-3-yl)-3-oxopropanenitrile **(c)** as a solid pure product [**Yield:** 3.0 gm, 79.57%; **mp.** 95 °C; **M.F.** $C_{12}H_{10}N_2O$; **M.W.** 198.08].

2. 3. Synthesis of 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile (d)

Take 3-(1-methyl-1*H*-indol-3-yl)-3-oxopropanenitrile **(c)** (3.0 gm, 15 mmol), potassium carbonate (5.2 gm, 37 mmol), dimethylformamide (50 mL) in 100 mL RBF. Stirred at room temperature for 10 minutes. Then keep RBF on ice bath to take 0 °C temperature, then stirred the reaction mass for 30 minutes followed by dropwise addition of Carbondisulfide (CS_2) (1.3 mL, 22 mmol). Reaction mixture was further stirred for 1 hour followed by dropwise addition of methyl iodide over a period of 20 minutes, and then reaction mixture was stirred for overnight at room temperature. The progress of reaction mass was monitored on TLC plate. After

completion, the reaction mass was poured in ice cold water to obtain solid product, filter it through *vaccuo*, washed it with n-Hexane, dried it to obtain analytically pure 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile **(d)** as a solid with excellent yield. [**Yield:** 4.1 gm, 91 %; **mp.** 89 °C; **M.F.** $C_{15}H_{14}N_2OS_2$; **M.W.** 302.05].

2. 4. General procedure for the synthesis of 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (KV-1 to KV-15)

Take 2-(1-methyl-1*H*-indole-3-carbonyl)-3,3-bis(methylthio)acrylonitrile **(d)** (0.5 gm, 16 mmol), aniline substrate (16 mmol) and methanol (10 mL) in 25 mL RBF. Stirred the reaction mass at 65 °C temperature for 1 hr. The progress of reaction was monitored on TLC plate. After completion, the reaction mixture was cooled at room temperature, to obtain crystalline product, filter it through *vaccuo*, and washed with n-Hexane, dried it to furnished yellow coloured analytically pure solid final compounds as **KV-1 to KV-15**.

Table 2. Physical constant of compounds **KV-1 to KV-15**.

Comp. Code	Substituent R=	Molecular Formula	Molecular Weight	Yield (%)	M.P. (°C)
KV-1	4-OCH_3	$C_{21}H_{19}N_3O_2S$	377	81	175-177
KV-2	-H	$C_{20}H_{17}N_3OS$	347	83	195-197
KV-3	2-Cl	$C_{20}H_{16}ClN_3OS$	381	76	169-171
KV-4	2,4-F_2	$C_{20}H_{15}F_2N_3OS$	383	78	178-180
KV-5	4-Cl	$C_{20}H_{16}ClN_3OS$	381	71	182-184
KV-6	2,4-$(CH_3)_2$	$C_{22}H_{21}N_3OS$	375	63	170-172
KV-7	2-OCH_3	$C_{21}H_{19}N_3O_2S$	377	86	173-175
KV-8	-Py	$C_{19}H_{16}N_4OS$	348	83	163-165
KV-9	4-n-Prop.	$C_{23}H_{23}N_3OS$	389	76	171-173
KV-10	4-tert. butyl	$C_{23}H_{23}N_3OS$	327	80	177-179
KV-11	-Benzyl	$C_{21}H_{19}N_3OS$	361	81	183-185
KV-12	4-Br	$C_{20}H_{16}BrN_3OS$	425	71	175-177
KV-13	2,4,6-$(CH_3)_3$	$C_{23}H_{23}N_3OS$	389	75	197-199
KV-14	4-OH	$C_{20}H_{17}N_3O_2S$	363	69	185-187
KV-15	2,4-Br_2	$C_{20}H_{15}Br_2N_3OS$	502	78	179-181

2. 5. Spectral data for representative compound

3-((4-methoxyphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (KV-1): Yield: 81%; **mp.:** 175-177 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 14.17 (s, 1H), 8.46 (s, 1H), 8.43 – 8.36 (m, 1H), 7.45 – 7.40 (m, 3H), 6.8, (d, *J* = 7.8 Hz, 2H), 6.69, (d, *J* = 8.1 Hz, 2H), 3.91 (s, 3H), 3.87 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 184.40, 172.32, 150.32, 137.90, 135.50, 130.80, 127.52, 125.70, 123.50, 122.94, 122.05, 118.03, 116.01, 115.18, 109.75, 83.04, 55.04, 33.60, 17.40; **IR (KBr, Vmax/ cm^{-1}):** 3308 (-NH str.), 3005 (C-H Str. in aromatic), 2185 (C≡N str.), 1776 (C=O str.), 1676 (C=N str.), 1571, 1369, 1228, 1163, 1085; **Ms:** *m/z* [M^+] 377; **Anal. Cal.** for $C_{21}H_{19}N_3O_2S$: C, 66.82; H, 5.07; N, 11.13; Found: C, 66.77; H, 5.01; N, 11.09 %.

2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)-3-(phenylamino)acrylonitrile (KV-2): Yield: 83%; **mp.:** 195-197 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 14.17 (s, 1H), 8.46 (s, 1H), 8.43 – 8.36 (m, 1H), 7.45 – 7.40 (m, 3H), 7.40 – 7.29 (m, 5H), 3.87 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 184.32, 170.37, 138.33, 136.99, 135.80, 129.56, 127.92, 127.02, 124.76, 123.44, 122.95, 122.65, 122.04, 114.32, 109.84, 85.62, 33.84, 17.46; **IR (KBr, Vmax/ cm^{-1}):** 3309 (-NH str.), 2929 (C-H Str. in aromatic), 2185 (C≡N str.), 1769 (C=O str.), 1681 (C=N str.), 1566, 1357, 1230, 1155, 1126, 1087; **Ms:** *m/z* [M^+] 347; **Anal. Cal.** for $C_{20}H_{17}N_3OS$: C, 69.14; H, 4.93; N, 12.09; Found: C, 69.07; H, 4.88; N, 12.02 %.

3-((2-chlorophenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (KV-3): Yield: 76%; **mp.:** 169-171 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 14.17 (s, 1H), 8.46 (s, 1H), 8.43 – 8.36 (m, 1H), 7.45 – 7.40 (m, 3H), 7.30 – 7.21 (m, 4H), 3.87 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 185.09, 172.55,140.52, 139.23, 138.28, 132.07, 127.04, 126.50, 125.37, 124.60, 123.79, 122.50, 122.01, 121.02, 120.34, 114.09, 109.05, 82.03, 33.90, 17.25; **IR (KBr, Vmax/ cm^{-1}):** 3323 (-NH str.), 2935 (C-H Str. in aromatic), 2189 (C≡N str.), 1784 (C=O str.),1674 (C=N str.),1575, 1396, 1232, 1128, 1085; **Ms:** *m/z* [M^+] 381; **Anal. Cal.** for $C_{20}H_{16}ClN_3OS$: C, 62.90; H, 4.22; N, 11.00; Found: C, 62.86; H, 4.19; N, 10.91 %.

3-((2,4-difluorophenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (KV-4): Yield: 78%; **mp.:** 178-180 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 14.17 (s, 1H), 8.46 (s, 1H), 8.43 – 8.36 (m, 1H), 7.45 – 7.40 (m, 3H), 6.79 (d, *J* = 8.2, 1H), 6.74 (d, *J* = 7.9, 1H), 6.60 (s, 1H), 3.87 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 184.70, ,174.57, 157.58, 155.37, 139.50, 137.02, 126.23, 125.20, 123.09, 122.20, 121.50, 121.07, 120.32, 115.75, 114.03, 109.90, 107.09, 81.09, 33.79, 17.20; **IR (KBr, Vmax/ cm^{-1}):** 3327 (-NH str.), 2935 (C-H Str. in aromatic), 2189 (C≡N str.), 1757(C=O str.), 1697(C=N str.), 1508, 1359, 1228, 1124, 1087; **Ms:** *m/z* [M^+] 383.00; **Anal. Cal.** for $C_{20}H_{15}F_2N_3OS$: C, 62.65; H, 3.94; N, 10.96; Found: C, 62.60; H, 3.89; N, 10.88 %.

3-((4-chlorophenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile (KV-5): Yield: 71%; **mp.:** 182-184 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 14.17 (s, 1H), 8.46 (s, 1H), 8.43 – 8.36 (m, 1H), 7.45 – 7.40 (m, 3H), 7.20 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 7.8 Hz, 2H) 3.87 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 184.37, 171.86, 139.56, 137.70, 135.28, 130.60, 126.70, 125.27, 123.70, 122.60, 121.70, 121.90, 121.50, 117.14, 109.65, 80.28, 33.95,17.36; **IR (KBr, Vmax/ cm^{-1}):** 3379 (-NH str.), 2942 (C-H Str. in

aromatic), 2187 (C≡N str.), 1788 (C=O str.), 1668 (C=N str.), 1545, 1369, 1230, 1129, 1087; **Ms:** *m/z* [M^+] 381.00; **Anal. Cal.** for $C_{20}H_{16}ClN_3OS$: C, 62.90; H, 4.22; N, 11.00; Found: C, 62.84; H, 4.17; N, 10.94 %.

3-((2,4-dimethylphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)-acrylonitrile (KV-6): Yield: 63%; **mp.:** 170-172 °C; **^{1}H NMR**: (400 MHz, $CDCl_3$): δ 13.98 (s, 1H), 8.44 (s, 1H), 8.39 – 8.41 (m, 1H), 7.39 – 7.27 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 7.04 (d, *J* = 8.1 Hz, 1H), 3.87 (s, 3H), 2.35 (s, 3H), 2.33 (s, 3H), 2.23 (s, 3H); **^{13}C NMR:** (100 MHz, $CDCl_3$): δ 184.38, 171.74, 137.53, 136.87, 135.49, 134.57, 133.15, 131.60, 127.81, 127.44, 125.68, 123.24, 122.86, 122.43, 122.20, 114.22, 109.68, 84.35, 33.70, 21.09, 18.18, 17.17; **IR (KBr, Vmax/ cm^{-1}):** 3379 (-NH str.), 2928 (C-H Str. in aromatic), 2187 (C≡N str.), 1790 (C=O str.), 1678 (C=N str.), 1519, 1361, 1261, 1230, 1157, 1087; **Ms:** *m/z* [M^+] 375.00; **Anal. Cal.** for $C_{22}H_{21}N_3OS$: C, 70.37; H, 5.64; N, 11.19; Found: C, 70.31; H, 5.58; N, 11.11 %.

2. 6. Antimicrobial activity

Antibacterial and Antifungal activity was tested by standard agar cup method. All the synthesized compound **(KV-1 to KV-15)** were tested for their *in vitro* antimicrobial activity against Gram *+ve* (*Bacillus megaterium, Micrococcus* spp.), Gram *-ve* (*E. coli, S. typi*) and fungal spps. (*Ganoderma* spp., *A. niger, A. flavus* and *Penicullium* spp.) taking streptomycin, ciprofloxacin, and nystatin as standard drugs. Suspension of 24 to 48 hrs grown fresh bacterial and fungal culture was prepared in N-broth and Potato Dextrose broth respectively. All the bacterial and fungal suspension were equally spreaded on to the sterile Muller Hinton and PDA respectively with the help of sterile swabs. Wells were made in the plates (1 cm) with the help of sterile cork borer. The standard antibiotics were dissolved in sterile distilled water up to 200 µg/mL of final concentration. The culture to be tested was dissolved in DMSO upto the final concentration of 1mg/mL and 0.1 mL of it was loaded in the well. The plate was incubated at 4 ºC for 20 minutes for proper diffusion of chemical and then the plates were incubated in upward position for 24 hrs at 37 ºC for bacterial culture and 48 hrs at 25 ºC for fungal cultures. The control activity against DMSO was also performed. After incubation zone of inhibition was observed and measured.

Table 1. Anti-microbial activity of synthesized compounds.

Code	(i) Antibacterial activity				(ii) Antifungal activity			
	Antibacterial activity (zone in cm), conentration: 1 mg/mL				Antifungal activity (zone in cm), conentration: 1mg/mL			
	Gram +*ve* Bacteria		Gram -*ve* Bacteria					
	B. megaterium	*Micrococcus spp.*	*S. typi.*	*E. coli*	*Penicillium* spp.	*Ganoderma* spp.	*A. niger*	*A. flavus*
KV-1	-	-	1.8	-	1.2	0.9	-	0.5
KV-2	1.3	1.5	1.9	-	2.1	2.5	2.7	2.6

KV-3	2.5	3	2.1	2	2.8	3.2	3.0	3.5
KV-4	2	1.8	1.6	1.1	0.8	1.0	0.5	-
KV-5	1.2	1	-	1.1	0.6	-	0.9	0.6
KV-6	0.9	1.3	1.2	1.2	-	1.1	0.8	0.9
KV-7	2.4	2.8	1.9	2.2	2.5	3.5	2.9	3.4
KV-8	1.2	1.9	1.7	-	1.5	1.9	2	1.8
KV-9	-	1.7	1.2	1.9	0.9	0.5	1.0	-
KV-10	1.5	-	1.2	1	2.1	3	2.5	2.9
KV-11	2.6	2.9	1.8	2	1.0	0.7	0.5	0.8
KV-12	1.2	-	1.7	-	2.1	2.8	3.0	2.9
KV-13	1.6	-	1.8	1.2	1.2	1.5	1.1	0.9
KV-14	1.1	1.2	1.5	-	0.5	0.9	1.0	0.7
KV-15	-	1.6	1.2	-	0.8	0.7	1.1	-
Streptomycin (200 µg/mL)	3	2	2	3.2	-	-	-	-
Ciprofoxacin (200 µg/mL)	3.8	4	4	3	-	-	-	-
Nystatin 200 µg/ml	-	-	-	-	3.2	4	3.5	3.8

3. RESULT AND DISCUSSION

All the synthesized compounds are well purified through column chromatography. We have confirmed the structure of some synthesized compounds by spectroscopic techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectroscopy. The physical constant of the compounds is outlined in **Table 2**. Molecular ion peak was observed in agreement with a molecular weight of the respective compound. The infrared spectra of compounds show characteristic peaks around 2185 cm^{-1}for -C≡N group, and 3300 cm^{-1} is confirmation for –NH group of compounds.

In ^{1}H NMR spectra of the compounds showed characteristic signals of all the aromatic proton between 6.00 to 8.00 δppm in all cases and characteristic singlet signals of all the aliphatic proton between 2.00 to 4.00 δppm and characteristic peak near about 14 δppm for –NH proton in all cases.^{13}C NMR spectra of compounds exhibited chemical shift values of carbonyl carbon near about 155 δppm and chemical shift values of saturated carbon at 33 δppm.

Antimicrobial activity of all the compounds **(KV-1 to KV-15)** was carried out against 4 bacterial strains (*B. megaterium, S. typhi, Micrococcus* spp. and *E. coli*) and 4 fungal strains (*A. niger, A. flavus, Ganoderma* spps. and *Penicillium* spps.) by agar cup method. Zone diameter of inhibition of growth was measured in cm. DMSO was used as a solvent to dissolve the compound. The result indicates that the **KV-3, KV-7** and **KV-11**exhibited potent activity against *E. coli*, *S. typhi*, *Micrococcus* and *B. megaterium* and **KV-1, KV-2, KV-4, KV-8,** and **KV-13** showed moderate activity while others showed no or little activity. The compound **KV-3** showed the highest antimicrobial activity against all the bacterial species and fungal spps.

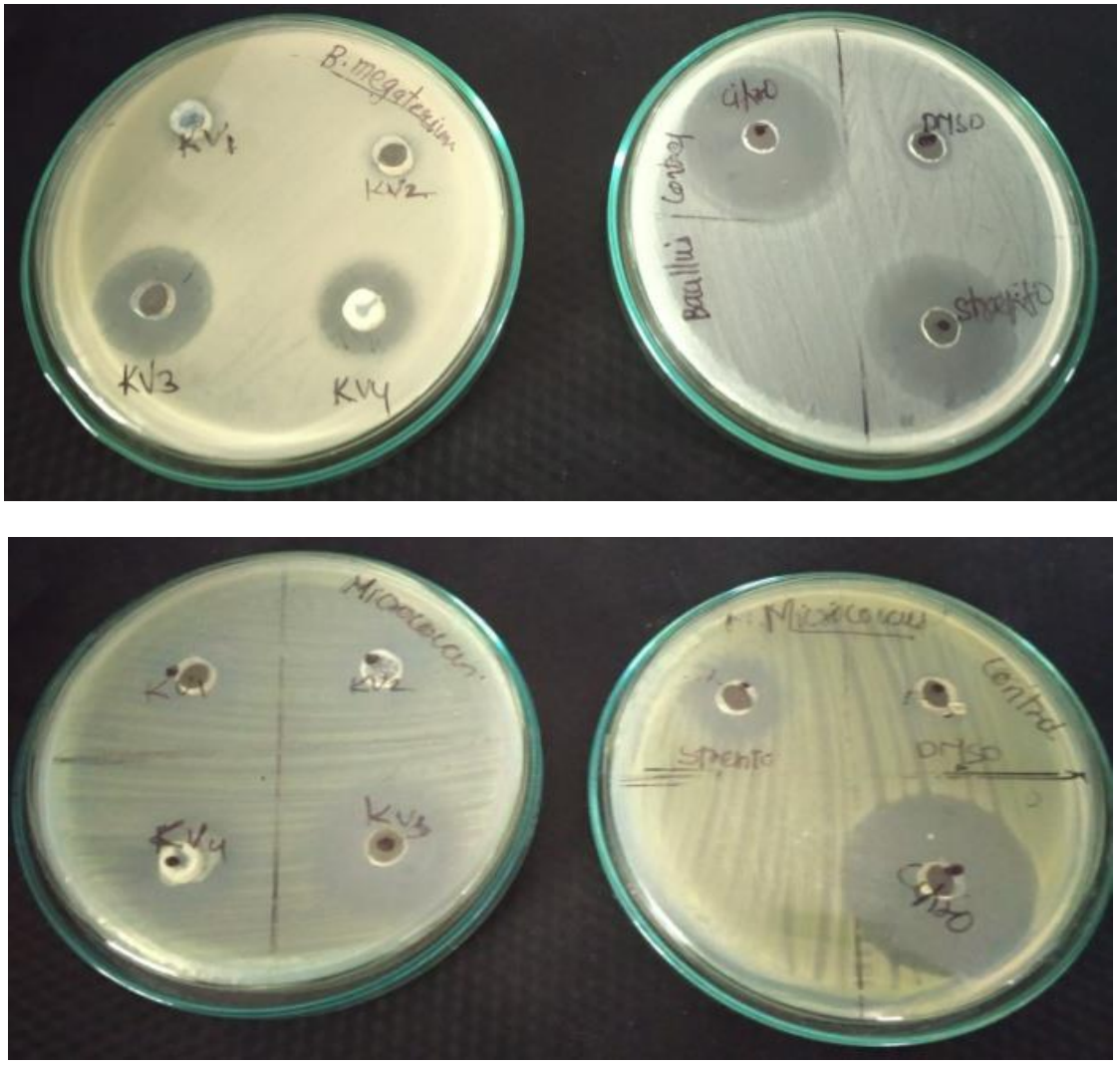

Figure 3. Anti-microbial activity using Agar cup method

4. CONCLUSIONS

The present work indicates a facile and efficient synthesis of some new 3-((substitutedphenyl)amino)-2-(1-methyl-1*H*-indole-3-carbonyl)-3-(methylthio)acrylonitrile derivatives bearing indole moiety via desulfitative displacement by various amines.

The synthetic route is well designed in such a way that reaction required a minimum time for completion with catalyst-free reaction, and easy work up and purification process. The range of yield is moderate to good with maximum purity.

The antibacterial activity of all compounds showed promising activity in comparison to standard drug streptomycin and ciprofloxacin, while the antifungal activity of all compounds showed higher to moderate activity against standard drug Nystatin. This study would be beneficial for further bio-evaluation.

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