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Synthesis of Some Novel Sydnone Derivatives Containing Coumarine Moiety and Evaluation of Their Antimicrobial and Antitubercular Activities

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ABSTRACT
The family of natural plant metabolites known as coumarin derivatives holds significant importance due to their diverse range of biological actions. Synthetic coumarin derivatives have demonstrated considerable potential in the realms of anticancer, antitumor, and anti-proliferative actions. The objective of this investigation was to produce a new series of sydnone derivatives containing coumarine, namely 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone, through the synthesis of 7-amino-4-methyl-3-substituted phenyl-2H-chromen-2-one 2a-j. The recently produced chemicals were analyzed using infrared (IR), nuclear magnetic resonance (NMR), and elemental analysis. The antibacterial, antifungal, and antitubercular properties of the produced compounds were assessed. The majority of these drugs exhibited favourable to moderate efficacy against the microorganisms that were tested.

Keywords : Nuclear Magnetic Resonance, Infrared, Antibacterial, Antifungal, Antitubercular Properties, Chlorophenyl, Sydnone, Coumarine

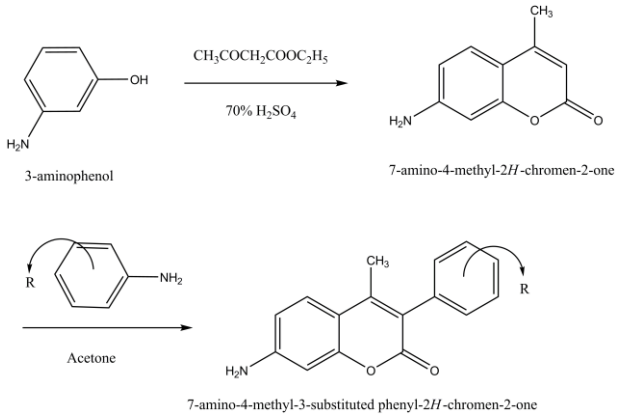
I. INTRODUCTION

Mesoionic compounds are a specific kind of heterocycles that fall within the classification of non-benzenoid aromatics. Mesoionic compounds, which are heterocyclic betaines, possess wide-ranging pharmacological actions and exhibit minimal toxicity, rendering them highly valuable in the field of medicinal chemistry. The anticancer activity of the subject under investigation is particularly noteworthy because to its highly promising outcomes in vivo [1-3]. The literature review revealed that sydnone is the most prominent member of the mesoionic compound family [4-6]. Sydnone derivatives have demonstrated a diverse range of biological activities, including anti-malarial effect [7], anti-inflammatory properties [3], analgesic effects [8], antibacterial activity [9, 10], anti-fungal activity [11], anti-tumor activity [12], and anti-oxidant activity [13].

A diverse range of pharmacological activities has been demonstrated by coumarin and its derivatives, encompassing anti-HIV [14], anti-inflammatory [15], anti-convulsant [16], anti-viral [17], anti-coagulant [18], anti-oxidant [19], anti-bacterial [20], anti-fungal [21], anti-carcinogenic [22], and anti-histamine [23] properties. Promising biological activity have been shown when a mesoionic ring is combined with heterocyclic rings, such as thiazole, triazole [24], and sydnone [25]. Based on the aforementioned facts, a series of novel sydnone derivatives incorporating Coumarine were synthesized and subsequently assessed for their antibacterial and antitubercular properties.

II. METHODS AND MATERIAL

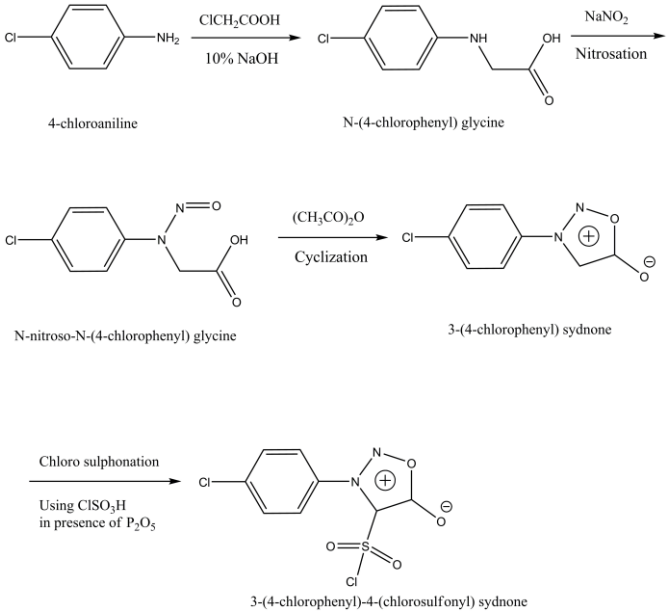
The open capillary method was used to estimate the melting points, are uncorrected. The Thermo Scientific FLASH 2000 in Chandigarh was utilized to conduct elemental analysis. The infrared spectra were acquired using a Shimadzu FTIR spectrometer from Japan, employing a KBr disk. The 1H NMR spectra were obtained using a Bruker Avance II 400 MHz NMR spectrometer at SAIF, Chandigarh. The spectra were recorded in DMSO-d6 with TMS serving as the internal standard. The chemical shifts were calculated and represented in μ ppm. A Bruker Avance II 400 MHz NMR spectrometer at SAIF, Chandigarh was used to record the 13C NMR spectra of the substances. The evaluation of reaction progress and the assessment of synthesized compound purity were conducted using thin-layer chromatography (TLC) on E-Merck precoated 60 F254 plates. The resulting spots were then analyzed using short-wave ultraviolet (UV) light.



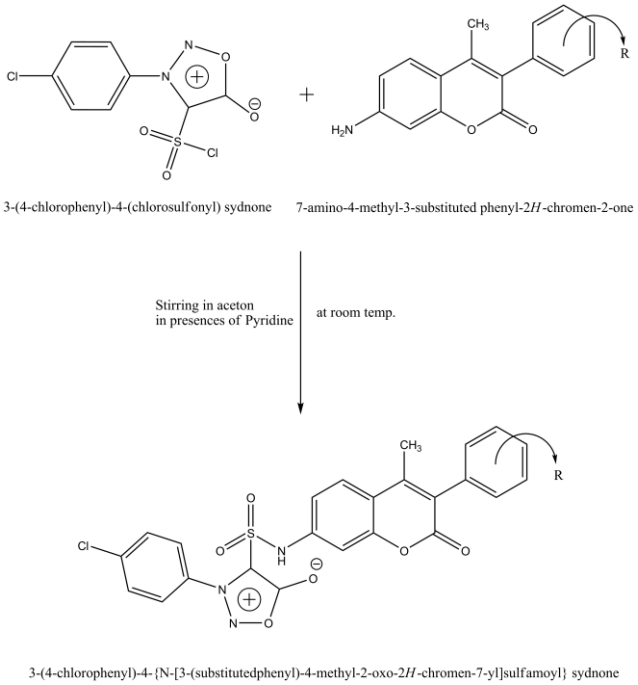
a.R = H; b R = 4-F;c R = 4-OCH_3;d R = 4-Cl; e. R = 3-Cl; f R = 2,3-Cl;

g R = 3-OCH_3; h R = 4-CH_3; i R = 2-NO_2; j R = 3-NO_2

Scheme I. Synthesis of 7-amino-4-methyl-3-substituted phenyl-2*H*-chromen-2-one



Scheme II. Synthesis of 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone



Scheme III. 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone with 7-amino-4-methyl-3-substituted phenyl-2*H*chromen-2-one (2a-j)

Scheme I : Synthesis of 7-amino-4-methyl-3-substituted phenyl-2*H*-chromen-2-one

The following section outlines the synthetic methodologies employed in the production of 7-amino-4-methyl-3-substitutedphenyl-2H-chromen-2-one.

1.1. Preparation of 7-amino-4-methyl-2*H*-chromen-2-one

The experiment involved the careful heating of a combination consisting of 3-aminophenol (0.1 mole) and ethylacetoacetate (0.1 mole) with 70% H2SO³4 (50 ml) for a duration of 0.5 hours. The dark green solution obtained was subsequently chilled and placed onto a mixture of broken ice weighing 250 grams. The crude product underwent filtration, followed by multiple washes with water and subsequent drying at a temperature of 100°C. The recrystallization of anhydrous coumarin from benzene. M.P. 221-223°C.

1.2. Preparation of 7-amino-4-methyl-3-substituted phenyl-2*H*-chromen-2-one

A 0.05 mole substitution of aromatic amine was subjected to diazotization and thereafter introduced into a 60 ml solution of 4-mehyl-7-amino-coumarin, also with a 0.05 mole substitution. The mixture was stirred at room temperature for a duration of several hours. The process of steam distillation was employed to eliminate acetone, while the resulting product was extracted using filtration. It was then washed with water, dried, and refined using neutral alumina. Crystallized using ethanol as a solvent.

SCHEME II: Synthesis of 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone

2.1. Preparation of N-(4-chlorophenyl) glycine

4-chloroaniline A quantity of 1.40 grams (0.011 moles) was introduced into a chilled solution containing 0.95 grams (0.01 moles) of chloroacetic acid and 2 ml of water. The water solution was subsequently neutralized using a 10% sodium hydroxide solution. After being cooled to room temperature in an ice bath, the reaction mixture underwent reflux for duration of 20 minutes. Subsequently, 0.5 grams of sodium hydroxide pellet were introduced into the mixture, and the unreacted aniline was eliminated using extraction with methylene dichloride. The aqueous solution should be acidified using strong hydrochloric acid until complete precipitation is achieved, followed by recrystallization using ethanol. The yield is 80% and the melting point is 145°C.

2.2. Preparation of N– Nitroso-N-(4-chlorophenyl) glycine

A sodium nitrite solution weighing 0.69 gm (0.01 mole) in 5 ml of water was gradually introduced into a suspension containing 1.86 gm (0.01 mole) of N-(4-chlorophenyl) glycine in 40 ml of water. The mixture was subjected to stirring at a temperature range of 0-5°C. Following the completion of the addition process, stirring was maintained for duration of 2 hours and allowed to continue overnight. Subsequently, the reaction mixture was filtered and the nitroso compound was precipitated through the addition of strong hydrochloric acid. The yield is 78% and the melting point is 104°C.

2.3. Preparation of 3-(4-chlorophenyl) sydnone

The N-nitroso-N-(4-chlorophenyl) glycine and acetic anhydride were combined in a weight ratio of 1:5 and subjected to stirring for duration of 10 hours. A gradual pouring of the solution was performed into cold water that had been well agitated. The content's pH was adjusted using a 10% sodium bicarbonate solution and subsequently rinsed with water and dried. A recrystallization process was conducted on the crude sydnones using benzene-petroleum ether. The yield of the sample was 78%, with a melting point range of 140-145°C.

2.4. Preparation of 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone

A volume of 3.5 ml (0.3 mole) of chloro sulphonic acid was gradually added to a mixture containing 2.46 gm (0.1 mole) of 3-(4-chloro phenyl)sydnone and a catalytic amount of P2O5. The mixture was stirred continuously at a temperature of 0-5°C for a duration of 30 minutes. After the addition of all the chlorosulphonic acid, the reaction mixture should be stirred for a duration of 2 hours. Subsequently, it should be allowed to stand at room temperature overnight or alternatively, heated on a water bath for 1 hour to ensure the completion of the reaction. The oily liquid should be allowed to cool before being poured into broken ice while stirring. To achieve a greenish-yellow solid product, it is necessary to disintegrate any clumps of solid material and agitate the mixture for a duration of several minutes. The product should be filtered, washed with cold water, and subsequently dried. The yield is 87%.

Scheme III: Condensation of 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone with 7-amino-4-methyl-3-substituted phenyl-2*H*-chromen-2-one (2a-j)

The compound 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone, with a mole of 0.01 and a mass of 2.56, was dissolved in acetone under ambient conditions. Over a duration of 5 hours, a solution containing 0.01 mole of 7-amino-4-methyl-3-substituted phenyl-2H-chromen-2-one in acetone was incrementally introduced into a solution of 3-(4-chlorophenyl)-4-(chlorosulfonyl) sydnone while maintaining continuous stirring. After 1 hour and 2 hours of stirring, 1.0 ml of pyridine was added to the well-agitated solution during the reaction. The solution was carefully put onto ice while being stirred. The solid was gathered by the process of filtration, rinsed with water, and subsequently dried. The crude product was subjected to recrystallization using ethanol as the solvent.

Compound 2a.The IR spectra, measured in KBr at cm-1, exhibits the following chemical shifts: 3325 (N-H), 2980 (C-H, -CH3 gr.), 2870 (C-H, -CH3 gr.), 1771 (C=O, coumarine), 1750 (C=O, sydnone), 1595 (C=C, Ar.), 1490 (C=C, Ar.), 1315 (S=O), 1180 (S=O), and 820 (C-Cl). The 1H NMR spectra obtained at 400 MHz using CDCl3 were as follows: 2.25 (s, 3H, -CH3), 6.77-7.72 (m, 12H, Ar-H), and 9.40 (s, 1H, -SO2NH-).

Compound 2b. The infrared spectrum (KBr, cm-1) consists of the following peaks: 3320 (N-H), 2920 (C-H, -CH3 gr.), 2860 (C-H, -CH3 gr.), 1747 (C=O coumarine), 1710 (C=O sydnone), 1593 (C=C, Ar.), 1499 (C=C, Ar.), 1300 (S=O), 1190 (S=O), 1094 (C-F), and 835 (C-Cl). The 1H NMR spectra obtained at 400 MHz using CDCl3 were as follows: 2.17 (s, 3H, -CH3), 6.74-7.62 (m, 11H, Ar-H), and 9.30 (s, 1H, -SO2NH-).

Compound 2c. The infrared spectrum (KBr, cm-1) consists of the following peaks: 3321 (N-H), 2950 (C-H, -CH3 gr.), 2855 (C-H, -CH3 gr.), 1770 (C=O, coumarine), 1760 (C=O, sydnone), 1585 (C=C, Ar.), 1495 (C=C, Ar.), 1321 (S=O), 1175 (S=O), 833 (C-Cl), 1252 (C-O-C), and 1009 (C-O-C). The 1H NMR spectra obtained at 400 MHz using CDCl3 were as follows: 2.20 (s, 3H, -CH3), 3.87 (s, 3H, OCH3), 6.69-7.95 (m, 11H, Ar-H), and 9.22 (s, 1H, SO2NH).

Compound 2d. The IR spectrum (KBr, cm-1) corresponds to the following chemical shifts: 3311 (N-H), 2920 (C-H, -CH3 gr.), 2980 (C-H, -CH3 gr.), 1655 (C=O, coumarine), 1755 (C=O, sydnone), 1614 (C=C, Ar.), 1499 (C=C, Ar.), 1152 (S=O), 1320 (S=O), and 752 (C-Cl). The 1H NMR spectra obtained at 400 MHz using CDCl3 were as follows: 2.19 (s, 3H, -CH3), 6.77-7.72 (m, 12H, Ar-H), and 9.40 (s, 1H, -SO2NH-). The values are as follows: 3.80 (s, 3H, OCH3), 6.95-7.99 (m, 11H, Ar-H), and 9.16 (s, 1H, SO2NH).

Compound 2a. IR spectrum (KBr, cm^{-1}): 3325 (N-H), 2980 (C-H, -CH_3 gr.), 2870 (C-H, -CH_3 gr.), 1771 (C=O, coumarine), 1750 (C=O, sydnone), 1595 (C=C, Ar.), 1490 (C=C, Ar.), 1315 (S=O), 1180 (S=O), 820 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.25 (s, 3H, -CH_3), 6.77-7.72 (m, 12H, Ar-H), 9.40 (s, 1H, -SO_2NH-).

Compound 2b. IR spectrum (KBr, cm^{-1}): 3320 (N-H), 2920 (C-H, -CH_3 gr.), 2860 (C-H, -CH_3 gr.),

1747 (C=O coumarine), 1710 (C=O sydnone), 1593 (C=C, Ar.), 1499 (C=C, Ar.), 1300 (S=O), 1190 (S=O), 1094 (C-F), 835 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.17(s, 3H, $-CH_3$), 6.74-7.62 (m, 11H, Ar-H), 9.30 (s, 1H, $-SO_2NH-$).

Compound 2c. IR spectrum (KBr, cm^{-1}): 3321 (N-H), 2950 (C-H, $-CH_3$ gr.), 2855 (C-H, $-CH_3$ gr.), 1770 (C=O, coumarine), 1760 (C=O, sydnone), 1585 (C=C, Ar.), 1495 (C=C, Ar.), 1321 (S=O), 1175 (S=O), 833 (C-Cl), 1252 (C-O-C), 1009 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.20 (s, 3H, $-CH_3$), 3.87 (s, 3H, OCH3), 6.69-7.95 (m, 11H, Ar-H), 9.22 (s, 1H, SO_2NH).

Compound 2d. IR spectrum (KBr, cm^{-1}): 3311 (N-H), 2920 (C-H, $-CH_3$ gr.), 2980 (C-H, $-CH_3$ gr.), 1655 (C=O, coumarine), 1755 (C=O, sydnone), 1614 (C=C, Ar.), 1499 (C=C, Ar.), 1152 (S=O), 1320 (S=O), 752 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.19 (s, 3H, $-CH_3$), 6.77-7.72 (m, 12H, Ar-H), 9.40 (s, 1H, $-SO_2NH-$). 3.80 (s, 3H, OCH3), 6.95-7.99 (m, 11H, Ar-H), 9.16 (s, 1H, SO2NH)

Compound 2e. IR spectrum (KBr, cm^{-1}): 3300 (N-H), 2950 (C-H, $-CH_3$ gr.), 2860 (C-H, $-CH_3$ gr.), 1747 (C=O, coumarine), 1600 (C=O, sydnone), 1489 (C=C, Ar.), 1170 (S=O), 1339 (S=O), 750 (C-Cl), 830 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.25 (s, 3H, $-CH_3$), 7.31-8.08 (m, 11H, Ar-H), 9.46 (s, 1H, $-SO_2NH-$).

Compound 2f. IR spectrum (KBr, cm^{-1}): 3313 (N-H), 2940 (C-H, $-CH_3$ gr.), 2850 (C-H, $-CH_3$ gr.), 1770 (C=O, coumarine), 1700 (C=O, sydnone), 1493 (C=C, Ar.), 1373 (S=O), 1177 (S=O), 755 (C-Cl), 833 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.30 (s, 3H, $-CH_3$), 6.85-8.25 (m, 10H, Ar-H), 9.50 (s, 1H, $-SO_2NH-$).

Compound 2g. IR spectrum (KBr, cm^{-1}): 3320 (N-H), 2922 (C-H, $-CH_3$ gr.), 2855 (C-H, $-CH_3$ gr.), 1720 (C=O, coumarine), 1602 (C=O, sydnone), 1480 (C=C, Ar.), 1373 (C=C, Ar.), 1320 (S=O), 1195 (S=O), 833 (C-Cl), 1250 (C-O-C), 1030 (C-O-C). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.14 (s, 3H, $-CH_3$), 3.79 (s, 3H, $-OCH_3$), 7.03-7.92 (m, 11H, Ar-H), 9.60 (s, 1H, $-SO_2NH-$).

Compound 2h. IR spectrum (KBr, cm^{-1}): 3310 (N-H), 2870 (C-H, $-CH_3$ gr.), 2980 (C-H, $-CH_3$ gr.), 1700 (C=O, coumarine), 1614 (C=O, sydnone), 1499 (C=C, Ar.), 1614 (C=C, Ar.), 1330 (S=O), 1175 (S=O), 825 (C-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.18 (s, 3H, $-CH_3$), 7.19-8.19 (m, 11H, Ar-H), 9.40 (s, 1H, $-SO_2NH-$).

Compound 2i. IR spectrum (KBr, cm^{-1}): 3300 (N-H), 2920 (C-H, $-CH_3$ gr.), 2880 (C-H, $-CH_3$ gr.), 1740 (C=O, coumarine), 1750 (C=O, sydnone), 1493 (C=C, Ar.), 1370 (S=O), 1190 (S=O), 750 (C-Cl), 1342 (NO_2). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.14 (s, 3H, $-CH_3$), 7.03-7.92 (m, 11H, Ar-H), 9.51 (s, 1H, $-SO_2NH-$).

Compound 2j. IR spectrum (KBr, cm^{-1}): 3325 (N-H), 2980 (C-H, $-CH_3$ gr.), 2870 (C-H, $-CH_3$ gr.), 1771 (C=O, coumarine), 1750 (C=O, sydnone), 1595 (C=C, Ar.), 1490 (C=C, Ar.), 1315 (S=O), 1180 (S=O), 820 (C-Cl), 1339 (NO_2).. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.20 (s, 3H, $-CH_3$), 6.67-7.69 (m, 11H, Ar-H), 9.50 (s, 1H, $-SO_2NH-$).

TABLE I. Yields, Melting Points, and Elemental Analysis of Compounds 2a-j

Sr.No.	-R	M.F and M.W	Yield %	M.P °C	Elemental Analysis (%) Found (calcd.)		
					C	H	N
2a	-H	$C_{24}H_{16}O_6N_3ClS$ 509.92	62	221	56.53 (56.58)	3.16 (3.10)	8.24 (8.22)
2b	4-F	$C_{24}H_{15}O_6N_3ClFS$ 527.91	69	140	54.60 (54.53)	2.86 (2.90)	7.96 (7.90)
2c	4-OCH_3	$C_{25}H_{18}O_7N_3ClS$ 539.94	81	250	55.61 (55.67)	3.36 (3.29)	7.78 (7.84)

2d	4-Cl	$C_{24}H_{15}O_6N_3Cl_2S$ 544.36	79	120	52.95 (52.92)	2.78 (2.74)	7.72 (7.68)
2e	3-Cl	$C_{24}H_{15}O_6N_3Cl_2S$ 544.36	74	>300	52.95 (52.90)	2.78 (2.82)	7.72 (7.78)
2f	2,3-Cl	$C_{24}H_{14}O_6N_3Cl_3S$ 578.81	89	220	49.80 (49.78)	2.44 (2.36)	7.26 (7.22)
2g	3-OCH_3	$C_{25}H_{18}O_7N_3ClS$ 539.94	82	175	55.61 (55.56)	3.36 (3.39)	7.78 (7.73)
2h	4-CH_3	$C_{25}H_{18}O_6N_3ClS$ 523.94	86	238	57.31 (57.25)	3.46 (3.40)	8.02 (8.10)
2i	2-NO_2	$C_{24}H_{15}O_8N_4ClS$ 554.92	79	189	51.95 (51.89)	2.72 (2.76)	10.10 (10.04)
2j	3-NO_2	$C_{24}H_{15}O_8N_4ClS$ 554.92	72	129	51.95 (51.98)	2.72 (2.67)	10.10 (10.15)

III.RESULTS AND DISCUSSION

Antimicrobial activity

The majority of the synthesized compounds (2a-j) demonstrated a mild to significant level of antibacterial activity against the organisms that were tested. The Gram-positive bacteria species included S.aureus MTCC 96 and S. pyogenes MTCC 442, whereas the Gram-negative bacteria species included E. coli MTCC 443 and P. aeruginosa MTCC 1688. The typical medications employed were Gentamycin, Ampicillin, chloramphenicol, and ciprofloxacin. . The minimum inhibitory concentration (MIC) was determined. The broth dilution method [26] was used to establish the minimum inhibitory concentration (MIC). The chemicals were concentrated using DMSO as the solvent. Various concentrations (e.g. 1000, 500, 250, 125, and 62.5 µg/mL) of synthesized compounds were generated during primary screening. The active compounds identified during the initial screening were selected for subsequent screening and subsequently diluted to achieve concentrations of 200, 100, 50, 25, 12.5, and 6.250 µg/mL. The nutrient media employed for the growth and dilution of the drug suspension for the test microorganisms was Mueller Hinton broth.The minimum inhibitory concentration (MIC) was determined as the lowest at which the growth of the organism was inhibited. The measurement of the zone of inhibition was conducted using the Kirby-Bauer technique [27]. A volume of 0.01 mL with a concentration of 250 µg/mL was utilized for each test chemical in order to ascertain the zone of inhibition. An incubation period of 24 hours was conducted at a temperature of 37 °C. Table II presents the antibacterial activity of the substances.

Antifungal Activity

An assessment was conducted to determine the antifungal efficacy against C. albicans MTCC 227, A. niger MTCC 282, and A. clavatus MTCC 323. The standard medications employed in the study were gliofulvin and nystatin. Fungal nutrition was conducted using Seborane dextrose broth. An incubation period of 74 hours was conducted at a temperature of 22 °C. Table III displays the antifungal activity of the substances.

Antitubercular activity

Table IV displays the antitubercular activity of the substances.

TABLE II.Antibacterial Activity of Compounds 2a-j

Compounds	Minimum Inhibitory Concentration (μg/ml)			
	Gram-positive		Gram-negative	
	S.aureus ATCC-96	*S.pyogenes* ATCC-443	*E.coli* ATCC-442	*P.aeruginosa* ATCC-441
2a	500	500	50	250
2b	250	500	100	500
2c	250	500	200	500
2d	500	500	100	250
2e	100	200	250	500
2f	500	250	250	62.5
2g	100	250	200	100
2h	100	100	250	250
2i	250	250	500	500
2j	500	500	200	500
Gentamycin	0.25	0.5	0.05	1
Ampicillin	250	100	100	100
Chloramphenicol	50	50	50	50
Ciprofloxacin	50	50	25	25
Norfloxacin	10	10	10	10

TABLE III.Antifungal Activity of Compounds 2a-j

	Compounds	MINIMAL INHIBITION CONCENTRATION FOR FUNGI (μg/ ml)		
		C. albicans MTCC 227	*A. niger MTCC 282*	*A. clavatus MTCC 1323*
1	**2a**	500	500	500
2	**2b**	250	1000	1000
3	**2c**	1000	200	200
4	**2d**	500	1000	1000
5	**2e**	500	1000	1000
6	**2f**	500	1000	1000
7	**2g**	250	1000	1000
8	**2h**	1000	500	500
9	**2i**	1000	>1000	>1000
10	**2j**	500	1000	1000
	NYSTATIN	100	100	100
	GRESEOFULVIN	500	100	100

Table IV: Antitubercular activity (MIC µg/ml) of compounds 2a-j

Compounds	Minimum Inhibitory Concentration (µg/ml)
	M.Tuberculsis(MTCC-96)
2a	100
2b	250
2c	500
2d	250
2e	100
2f	250
2g	500
2h	50
2i	250
2j	12.5
Rifampicin	40

IV. ACKNOWLEDGEMENT

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V. CONCLUSION

Novel coumarin-based sydnone derivatives were synthesized using a standard methodology, followed by a comprehensive evaluation of their antibacterial, antifungal, and antitubercular properties. The recently synthesized medications were effectively characterized using infrared (IR), nuclear magnetic resonance (NMR), and elemental analysis. The approach involved the synthesis of several compounds. Among these compounds, compound 2e, 2g, and 2h exhibited the highest level of activity against S. aureus, whilst compound 2h exhibited the highest level of activity against S. pyogenes. Compounds 2a, 2b, and 2c had the highest level of activity against E. coli, while compound 2f exhibited the highest level of activity against P. aeruginosa. The compounds antifungal activity is illustrated in Table III. The antifungal activity of compounds 2b and 2g against C. albicans was observed to be significant, while compound 2c exhibited favourable antifungal activity against A. niger MTCC 282 and A. clavatus MTCC 1323. The remaining produced compounds showed varying degrees of effectiveness against the tested species, ranging from moderate to poor. The antitubercular action against M. tuberculosis is enhanced by the presence of nitro groups at the 3 positions of the phenyl ring, as observed in compound 2j. Overall,

sydnone compounds derived from coumarin demonstrated exceptional activity.

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