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Coumarin Based Imino-Chalcone Hybrid Motifs & Their Bioassays-Design, Synthesis and Its Study

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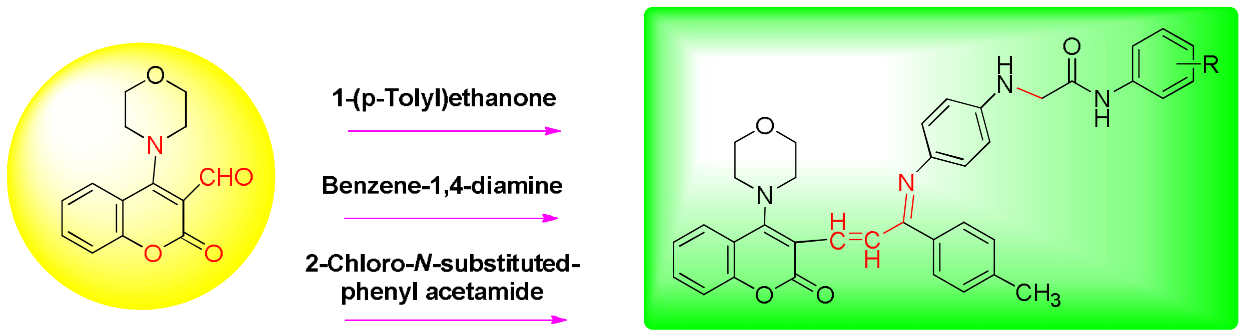
Graphical Abstract:



4-Morpholino-2-oxo-2*H*-chromene-3-carbaldehyde

2-((4-((*Z*)-(3-(4-Morpholino-2-oxo-2*H*-chromen-3-yl)-1-(*p*-tolyl)allylidene)amino)phenyl)amino)-*N*-substituted phenyl acetamide

Abstract: The work highlights a five step synthesis of a series of novel 2-((4-((Z)-(3-(4-morpholino-2-oxo-2H-chromen-3-yl)-1-(p-tolyl) allylidene) amino) phenyl) amino)-N-substituted phenyl acetamides (6a-j), from 4-hydroxy-2H-chromen-2-one, morpholine, 1-(p-tolyl) ethanone, benzene-1,4-diamine and 2-chloro-N-phenyl acetamide.IR, ^{1}HNMR,^{13}CNMR and mass-spectrophotometry were used for the confirmation of the newly designed compounds. Broth dilution technique was used for the evaluation of the in vitro antibacterial and antifungal strains of the newly synthesized compounds. Potent activity against the specific microbial strains is being observed by some of the newly synthesized compounds.

Key words:4-Hydroxy-2H-chromen-2-one, Vilsmeier–Haack reaction, N-aryl acetamide, Antimicrobial activity.

I. INTRODUCTION

The need for a more supportable and appropriate medication is continually testing and spurring. Various medications encasing basic heterocyclic or mixtures of different heterocyclic platforms have been utilized as a part of the present days [1]. Heterocyclic compounds are imperative and they indicate assorted pharmacological activities. They are cyclic compounds containing carbon, nitrogen, sulfur and oxygen as heteroatom. The SAR of such particles uncovers that the heterocyclic ring can be supplanted by some other moiety with comparable lipophilicity and electron distribution with no loss in its biological activity [2]. Antimicrobial operators diminish or thoroughly hinder the development and duplication of microorganisms. They are supportive in the treatment of various irresistible sicknesses like intestinal sickness, tuberculosis, meningitis, pneumonia, AIDS, etc [3].

Coumarin (otherwise called 2H-Chromen-2-one, or 1, 2-benzopyrone), is a natural compound, which has a place with the benzopyran heterocyclic compound [4]. Coumarins and their subsidiaries normally exist in microbial metabolites and animals. They are extensively obtained in high contents from different plants. Coumarin is perceived as an enchantment moiety since they assume an imperative part in synthetic organic chemistry, agrarian and normal products [5].

Coumarin derivates are potential bioactive specialists because of their expansive scope of organic exercises, for example, anti-oxidant[6, 7], antimalarial [8], antitumor [9-13], anticancer [14-16], against alzheimer [17], antipyretic [18], calming [19, 20], antimicrobial [21-24], pain relieving [25, 26], antihistamic operators [27], diuretic [28], upper [29, 30] and so forth. Chalcones are outstanding precursors of the bioflavonoid (flavonoids) and additionally is of lavanoids backbone. Chalcones derivatives have extensive variety of natural activities due to α, β-unsaturated ketone skeleton. The presence of different substituent's into the two aryl rings is likewise a subject of premium since it prompts enhanced structure-action relationship (SAR) [31, 32]. Thus, we are accounted for some novel warfarin-schiff bases annelated antimicrobial specialists which appeared in Figure 1.

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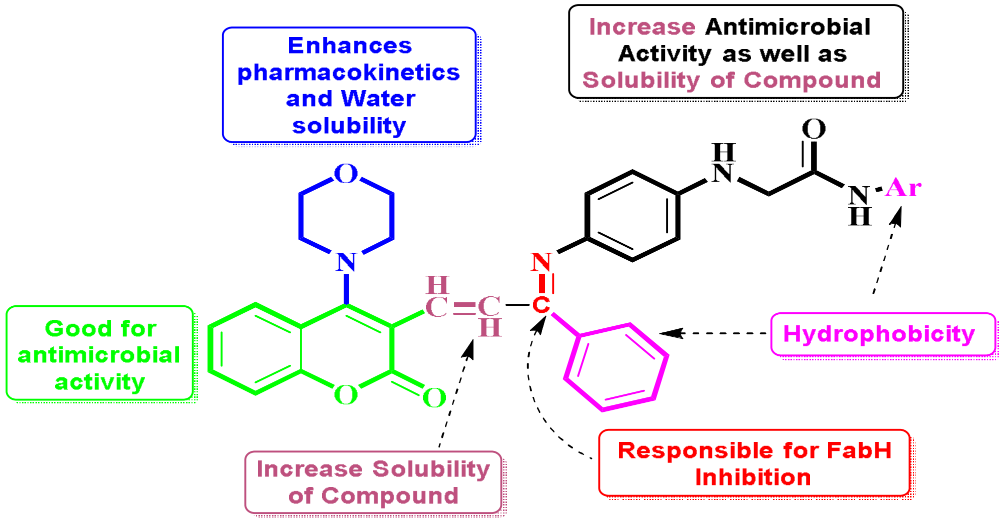
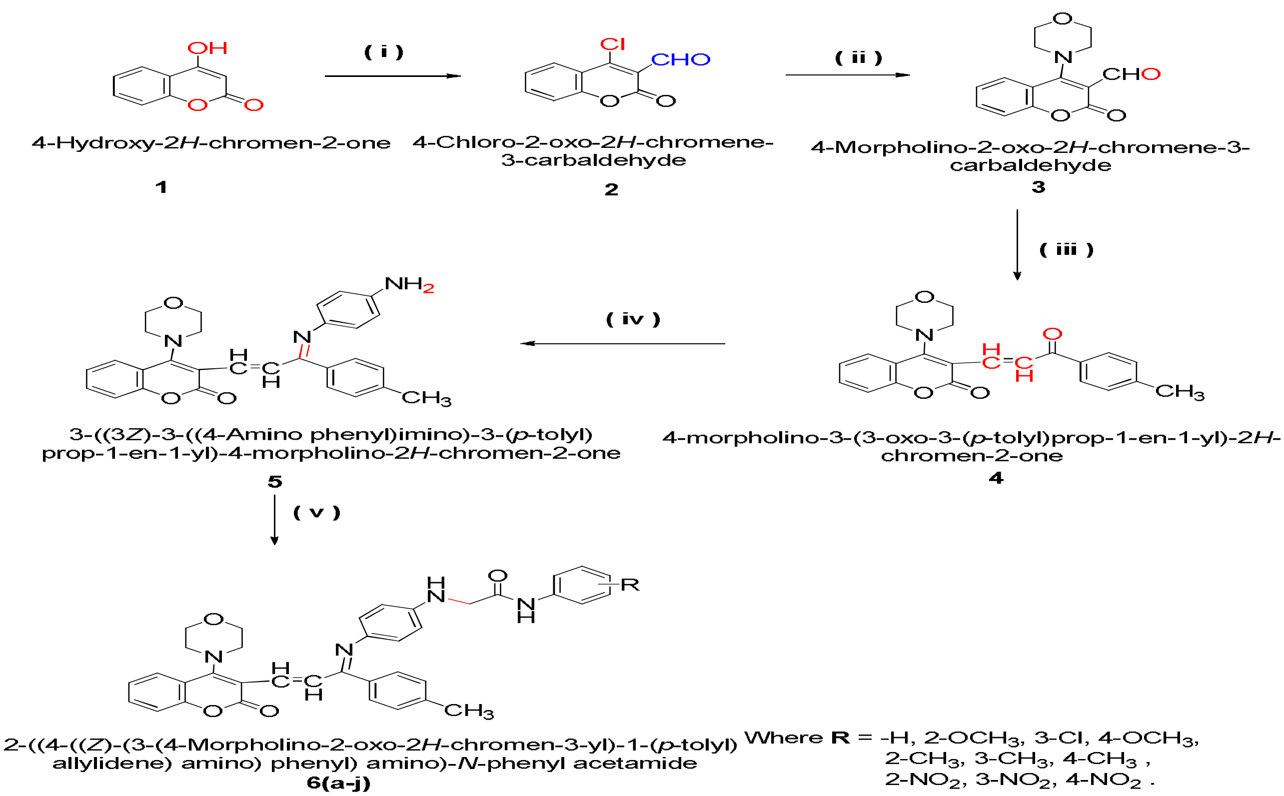


Figure 1. Structural features of warfarin-like Schiff bases 6a-j for antimicrobial activities.

Natural organic compounds containing imine (or azomethine) group gives a decent extension in the research area. Imine groups are available in a few compounds like natural, synthetic and naturally derived organic compounds. Fundamentally, imine (otherwise called azomethine or Schiff's base) is a nitrogen analogue of an aldehyde or ketone in which the carbonyl group has been supplanted by an imine (or azomethine) gathering. More often than not, imines are formed by the condensation of primary amines and active carbonyl groups, under particular conditions (corrosive, base catalysis or with warm). The greater part of compounds containing an imine group have extensive variety of organic activities, for example, antifungal, antibacterial, anti malarial, hostile to proliferative, calming, antiviral, and antipyretic properties. The imine assemble display in such compounds demonstrated strong organic activities. Imine groups are critical compounds which have wide scope of modern utilize [33].

II. CHEMISTRY



Scheme 1. Synthetic pathway for compounds 6a-j.

1) *Reagentsand conditions:(i)* DMF/$POCl_3$ (0-5°C), 60-70°C, 5-6h; **(ii)** Morpholine, Dichloromethane, TEA, 0-5°C, 2h; **(iii)** 1-(p-tolyl) ethanone, ethanol, Piperidine reflux, 2h; **(iv)** benzene-1,4-diamine, ethanol, reflux, 5h; **(v)** 2-chloro-*N*-phenyl acetamide, THF, reflux, 7h.

III. RESULTS AND DISCUSSION

A. *In vitro* antibacterial activity

In the present work, iminoylchalcone motif has been created by the condensation of 4-substituted coumarin and substituted N-acetamido through consecutive steps. Fictionalization has been done on phenyl core of 2-chloro-N-phenyl acetamide ring to get different compounds. The observations indicates that the test compounds (6a-j) showed intriguing antibacterial action (Table 1), however with a level of variations. The chloro group containing last compound i.e. 6c indicated great activity against particular bacterial strain. The last subordinates containing electron pulling back nitro group i.e. 6h and 6j showed unrivaled hindrance profile for the chosen bacterial strains. Then again huge deviation of action has been seen against Gram-negative strains where the unsubstituted phenyl ring containing coumarin mixes i.e. 6a showed higher hindrance against the bacterial strain P. aeruginosa. Rest of alternate compounds showed moderate to poor movement. Ciprofloxacin and Chloramphenicol were utilized as standard control drugs for antibacterial movement.

B. *In vitro antifungal activity*

Antifungal action information (Table 2) uncovered that the recently synthesized compound 6a demonstrated temperate restraint against the contagious strain A. clavatus, and other recently combined compounds 6b, 6c, 6i, and 6j indicated great restraint against C. albicans, A. niger and A. clavatus. Rest of the other compounds showed up with moderate to poor movement profile. Nystatin and Greseofulvin were utilized as standard control drugs for antifungal movement.

Table 1. In vitro antibacterial activity of newly synthesized compounds 6a-j.

		MINIMAL INHIBITORY CONCENTRATION (µg/ml)			
Compound	R	E.coli MTCC 442	P.aeruginosa MTCC 441	S.aureus MTCC 96	S.pyogenus MTCC 443
6a	-H	50	100	100	100
6b	2-OCH_3	25	50	100	62.5
6c	3-Cl	50	50	100	50
6d	4- OCH_3	50	62.5	125	50
6e	2-CH_3	200	250	500	500
6f	3-CH_3	100	62.5	500	500
6g	4-CH_3	125	200	250	100
6h	2-NO_2	100	25	100	50
6i	3- NO_2	62.5	50	100	50
6j	4-NO_2	100	62.5	62.5	50
Ciprofloxacin	-	25	25	50	50
Chloramphenicol	-	50	50	50	50

S. aureus Staphylococcus aureus, E. coli Escherichia coli, P. aeruginosa Pseudomonas aeruginosa, S.pyogenus Streptococcus pyogenes.

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Table 2.In vitro antifungal activity of newly synthesized compounds 6a-j.

Compound	R	MINIMAL FUNGICIDAL CONCENTRATION (µg/ml) C.albicans MTCC 227	A.niger MTCC 282	A.clavatus MTCC 1323
6a	-H	100	500	250
6b	2- OCH_3	250	250	500
6c	3-Cl	100	500	100
6d	4- OCH_3	500	100	250
6e	2-CH_3	1000	>1000	>1000
6f	3-CH_3	500	1000	1000
6g	4-CH_3	500	1000	1000
6h	2-NO_2	250	100	250
6i	3- NO_2	500	250	250
6j	4-NO_2	250	500	500
Nystatin	-	100	100	100
Greseofulvin	-	500	100	100

A. niger Aspergillus niger, A. clavatus Aspergillus clavatus, C. albicans Candida albicans.

IV. EXPERIMENTAL

A. *Material and methods*

All the chemicals and solvents used for the synthesis work were acquired from commercial sources of analytical grade, and used without further purification. Melting points were determined by using open capillary tubes and are uncorrected. TLC was checked on E-Merck pre-coated 60 F254 plates and the spots were rendered visible by exposing to UV light or iodine. IR spectra were 136 Volume 51 recorded on SHIMADZU HYPER IR. NMR spectra were recorded on 400 MHz BRUKER AVANCE instrument using TMS as internal standard (Chemical Shift in δ, ppm) and DMSO-d_6 as a solvent. Spectra were taken with a resonant frequency of 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. The splitting patterns are designated as follows; **s**, singlet; **d**, doublet; **dd**, doublet of doublets; **t**, triplate and**m**, multiplet. Elemental analysis was done on "Haraeus Rapid Analyser". The mass spectra were recorded on JOEL SX-102 (EI) model with 60 eV ionizing energy.

Table 3. Characterization of newly synthesized compounds 6a-j.

Compound	-R	Molecular Formula	M.P. ^{0}C	Yield %	Elemental Analysis	% C	% H	% N
6a	-H	$C_{36}H_{32}N_4O_4$	290	78	R	74.23	5.72	9.36
					F	74.28	5.77	9.40
6b	2-OCH_3	$C_{37}H_{34}N_4O_5$	299	72	R	72.30	5.58	9.11
					F	73.34	5.62	9.16
6c	3-Cl	$C_{36}H_{31}ClN_4O_4$	289	70	R	69.84	5.05	9.05
					F	69.89	5.10	9.09
6d	4-OCH_3	$C_{37}H_{34}N_4O_5$	296	72	R	72.30	5.58	9.11
					F	72.32	5.60	9.13
6e	2-CH_3	$C_{37}H_{34}N_4O_4$	295	73	R	74.23	5.72	9.36

					F	74.27	5.77	9.41
6f	3-CH_3	$C_{37}H_{34}N_4O_4$	292	76	R	74.23	5.72	9.36
					F	74.19	5.68	9.31
6g	4-CH_3	$C_{37}H_{34}N_4O_4$	276	70	R	74.23	5.72	9.36
					F	74.25	5.74	9.38
6h	2-NO_2	$C_{36}H_{31}N_5O_6$	277	73	R	68.67	4.96	11.12
					F	68.72	5.00	11.17
6i	3-NO_2	$C_{36}H_{31}N_5O_6$	290	75	R	68.67	4.96	11.12
					F	68.62	4.91	11.08
6j	4-NO_2	$C_{36}H_{31}N_5O_6$	288	77	R	68.67	4.96	11.12
					F	68.65	4.98	11.15

B. Synthesis of 4-chloro-2-oxo-2H-chromene- 3-carbaldehyde (2)

Phosphorous oxychloride (0.18 mol) was added dropwise to a stirring mixture of 4-hydroxy-2*H*-chromen-2-one (0.6 mol) in DMF (46.2 mL) at 0°C, producing a semisolid mass. A clear solution has appeared after stirring for 1 hour at room temperature. Then the temperature was gradually raised up to 60°C and further stirred for 5-6 hours at 60°C. Progress of the reaction was monitored by TLC using ethyl acetate: hexane (6:4) as eluent. After the completion of reaction, it was added to a beaker having crushed ice with stirring. The separated solid mass was filtered off and washed thoroughly with water and then aqueous Na_2CO_3(10%). The yellow solid product was obtained and purified by recrystallization from acetone to get the title product. Yield: 85%

C. Synthesis of 4-morpholino-2-oxo-2H-chromene-3-carbaldehyde (3)

To an ice-cold solution of 4-chloro-2-oxo-2*H*-chromene- 3-carbaldehyde (0.002mol) in dichloromethane (10 mL), a solution of morpholine (0.004 mol) in dichloromethane (5 mL) was added drop wise at 0-5 °C during 30 min. The mixture was further stirred at room temperature for 2 hours. After the completion of the reaction mixture was washed with 3x10 mL of water in order to remove unreacted morpholine and its salt. The organic phase was dried over sodium sulphate and the solvent was evaporated under reduced pressure. Progress of the reaction was monitored by TLC using chloroform: methanol (9:1) as eluent. The precipitated solid was collected by filtration, and recrystallized from acetone to get a yellow solid product. Yield: 80%

D. Synthesis of 4-morpholino-3-(3-oxo-3-(p-tolyl) prop-1-en-1-yl)-2H-chromen-2-one (4)

A solution of 4-morpholino-2-oxo-2H-chromene-3-carbaldehyde (0.01 mol) in 10 ml ethanol was added to 1-(p-tolyl) ethanone (0.01 mol) in 10 ml ethanol containing 4-5 drops of piperidine. The reaction mixture was refluxed for 2 hours at 60-70°C. Progress of the reaction was monitored by TLC using chloroform: methanol (9:1) as eluent. The yellow compound which separated out was filtered and washed with water. The crude product was purified by recrystallization from ethanol to get the title solid product. Yield: 75%.

E. Synthesis of 3-((3Z)-3-((4-aminophenyl) imino)-3-(p-tolyl) prop-1-en-1-yl)-4-morpholino-2H-chromen-2-one (5)

A solution of (0.002 mol) in 10 ml ethanol was added to the mixture of (0.002 mol) in 10 ml ethanol containing acetic acid (0.5 mL). The reaction mixture was refluxed for 5 hours. Progress of the reaction was monitored by TLC using ethyl acetate: hexane (4:6) as eluent. After the completion of reaction, the residue was poured into crushed ice to give a solid. The separated solid was filtered off and recrystallized from methanol to get the title compound. Yield: 75%

F. General procedure for the synthesis of compounds (6a-j)

A mixture of 3-((3Z)-3-((4-aminophenyl) imino)-3-(p-tolyl) prop-1-en-1-yl)-4-morpholino-2*H*-chromen-2-one (0.0014 mol) and K_2CO_3 (0.0021 mol) in tetrahydrofuran (10 ml) was stirred for 40 minutes at room temperature. Then the solution of 2-chloro-*N*-phenyl acetamide (0.0014 mol) in tetrahydrofuran (5 ml), and small catalytic amount of tri ethyl amine was added to this reaction mixture and refluxed for 7 hours. Progress of the reaction was monitored by TLC using ethyl acetate: hexane (6:4) as eluent. After the completion of reaction, the excess solvent was removed in vacuum, and the left solid was treated with crushed ice to afford a solid product. The solid obtained was filtered, washed with water, and recrystallized from absolute alcohol, to get the title compound. Yield: 78%

Similarly, other final compounds (6a-j) were prepared by various substituted aryl acetamide, and their physical and chemical analysis data are discussed in Table 3.

1) *4.6.1. 2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-(p-tolyl) allylidene) amino) phenyl) amino)-N-phenyl acetamide (6a):*Yield 78%,.IR (νmax cm^{-1}): 1024 (C-N stretching in aromatic), 1040 (C-N-C stretching in morpholine), 1170 (C-O-C stretching in morpholine), 1270 (C=N stretching in schiff base), 1380 (C-C stretching in aromatic), 1636 (C=C stretching in aromatic), 1745 (C=O, lactone stretching in coumarin), 2903 (-CH_2 stretching in alkane), 3025 (CH=CH stretching in aromatic), 3405 (-CONH stretching in amide), 3420 (C-NH stretching in amine), ^{1}H NMR (400 MHz, DMSO-d_6) δppm: 3.176 (t, 4H, *J*= 3.8 Hz), 3.760 (t, 4H, *J*= 3.8 Hz), 3.985 (s, 2H), 5.942 (s, 1H), 6.503-7.632 (m, 20H), 8.907 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 121.46, 123.72, 125.11, 128.60, 128.97, 129.31, 129.92, 130.36, 131.80, 132.16, 132.29, 137.76, 147.45, 164.14, 167.97, 171.17. ESIMS (m/z): 584.24 (M+). mp 290°C. Ana. Calcd for $C_{36}H_{32}N_4O_4$ (584.66): C, 74.23; H, 5.72; N, 9.36; found: C, 74.28; H, 5.77; N, 9.40.
2) *N-(2-Methoxyphenyl)-2-((4-((Z)-(3-(4-morpholino-2–oxo-2H-chromen-3-yl)-1phenyl allylidene) amino) phenyl) amino) acetamide (6b):* Yield 72%, IR (νmax cm^{-1}): 1029 (C-N stretching in aromatic), 1104 (C-N-C stretching in morpholine), 1201 (C-O-C stretching in morpholine), 1255 (C=N stretching in schiff base), 1280 (-OCH_3 stretching in aromatic), 1370 (C-C stretching in aromatic), 1629 (C=C stretching in aromatic), 1720 (C=O, lactone stretching in coumarin), 2870 (-CH_2 stretching in alkane), 3022 (CH=CH stretching in aromatic), 3380 (-CONH stretching in amide), 3480 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δppm: 3.152 (t, 4H, *J= 3.6 Hz*), 3.764 (t, 4H, *J= 3.8 Hz*), 3.807 (s, 3H), 3.964 (s, 2H), 5.875 (s, 1H), 6.538-7.628 (m, 19H), 9.128 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) : 44.54, 48.54, 66.10, 96.01, 112.61, 117.93, 117.98, 121.50, 125.02, 125.11, 127.95, 128.60, 128.97, 129.92, 130.00, 130.36, 131.80, 132.16, 132.29, 137.76, 147.45, 147.91, 164.14, 167.72, 171.17.ESIMS (m/z): 614.32 (M+).mp 299°C. Anal. Calcd for $C_{37}H_{34}N_4O_5$(614.69): C, 72.30; H, 5.58; N, 9.11; found: C, 73.34; H, 5.62; N, 9.16.
3) *N-(3-Chlorophenyl)-2-((4-((Z)-(3-(4-morpholino-2-oxo-2H–chromen-3–yl)1-phenyl allylidene) amino) phenyl) amino) acetamide (6c):*Yield 70%, IR (KBr ,νmax cm^{-1}): 740 (-Cl stretching in aromatic), 1023 (C-N stretching in aromatic), 1090 (C-N-C stretching in morpholine), 1210 (C-O-C stretching in morpholine), 1265 (C=N stretching in schiff base), 1420 (C-C stretching in aromatic), 1675 (C=C stretching in aromatic), 1740 (C=O, lactone stretching in coumarin), 2895 (-CH_2 stretching in alkane), 3035 (CH=CH stretching in aromatic), 3308 (-CONH stretching in amide), 3365 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δppm: 3.475 (t, 4H, *J= 4.2 Hz*), 3.774 (t, 4H, *J= 4.0 Hz*), 4.037 (s, 2H), 5.929 (s, 1H), 6.409-7.696 (m, 19H), 8.532 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 120.45, 124.84, 125.11, 127.95, 128.60, 128.97, 129.90, 129.92, 130.36, 131.80, 132.16, 132.29, 134.34, 139.54, 147.45, 156.43, 164.14, 167.97, 171.17. ESIMS (m/z): 618.20 (M+). mp 289°C. Anal. Calcd for $C_{36}H_{31}ClN_4O_4$ (619.11): C, 69.84; H, 5.05; N, 9.05; found: C, 69.89; H, 5.10; N, 9.09.
4) *N-(4-Methoxyphenyl)-2-((4-((Z)-(3-(4-morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino) acetamide (6d):*Yield 72%, IR (νmax cm^{-1}): 1200 (C-N stretching in aromatic), 1206 (C-N-C stretching in morpholine), 1209 (C-O-C stretching in morpholine), 1280 (C=N stretching in schiff base), 1300 (-OCH_3 stretching in aromatic), 1460 (C-C stretching in aromatic), 1670 (C=C stretching in aromatic), 1739 (C=O, lactone stretching in coumarin), 2910 (-CH_2 stretching in alkane), 3045 (CH=CH stretching in aromatic), 3470 (-CONH stretching in amide), 3490 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δppm: 3.483 (t, 4H, *J*= 3.8 Hz), 3.771 (t, 4H, *J= 4.0 Hz*), 3.778 (s, 3H), 4.030 (s, 2H), 5.837 (s, 1H), 6.517-7.692 (m, 19H), 9.740 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 44.54, 48.54, 56.04, 66.10, 96.01, 114.58, 117.93, 117.98, 122.00, 125.11, 128.60, 128.97, 129.92, 130.36, 131.29, 131.80, 132.16, 132.29, 147.45, 156.43, 164.14, 167.97, 171.17. ESIMS (m/z): 614.25 (M+). mp 296°C. Anal. Calcd for $C_{37}H_{34}N_4O_5$(614.69): C,72.30; H, 5.58; N,9.11; found: C, 72.32; H, 5.60; N, 9.13.
5) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino)-N-(o-tolyl) acetamide (6e):*Yield73%, IR (νmax cm^{-1}): 1029 (C-N stretching in aromatic), 1040 (C-N-C stretching in morpholine), 1173 (C-O-C stretching in morpholine), 1270 (C=N stretching in schiff base), 1444 (C-C stretching in aromatic), 1635 (C=C stretching in aromatic), 1743 (C=O, lactone stretching in coumarin), 2870 (CH_3 stretching in aromatic), 2890 (-CH_2 stretching in alkane), 3030 (CH=CH stretching in aromatic), 3304 (-CONH stretching in amide), 3380 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.115 (s, 3H), 3.061 (t, 4H, *J*= 4.2 Hz), 3.754 (t, 4H, *J*= 3.8 Hz), 4.033 (s, 2H), 6.076 (s, 1H), 6.444-7.613 (m, 19H), 9.021 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 17.35, 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 121.46, 123.72, 125.11, 128.60, 128.97, 129.31, 129.92, 130.36, 131.80, 132.16, 132.29, 137.76, 147.45, 194.14, 167.97, 171.17. ESIMS (m/z): 598.26 (M+). mp 295°C. Anal. Calcd for $C_{37}H_{34}N_4O_4$ (598.69): C, 74.23; H, 5.72; N, 9.36; found: C, 74.27; H, 5.77; N, 9.41.
6) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino)-N-(m-tolyl) acetamideone (6f):*Yield 76%, IR (νmax cm^{-1}): 1021 (C-N stretching in aromatic), 1029 (C-N-C stretching in morpholine), 1030 (C-O-C

stretching in morpholine), 1275 (C=N stretching in schiff base), 1442 (C-C stretching in aromatic), 1660 (C=C stretching in aromatic), 1747 (C=O, lactone stretching in coumarin), 2800 (CH_3 stretching in aromatic), 2930 (-CH_2 stretching in alkane), 3075 (CH=CH stretching in aromatic), 3403 (-CONH stretching in amide), 3321 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.313 (s, 3H), 3.354 (t, 4H, *J*= 3.6 Hz), 3.769 (t, 4H, *J*= 3.8 Hz), 4.010 (s, 2H), 5.900 (s, 1H), 6.530-7.629 (m, 19H), 9.822 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.21, 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 120.29, 125.11, 126.50, 127.95, 128.60, 128.94, 128.97, 129.92, 130.36, 131.80, 132.16, 132.29, 138.32, 139.50, 147.45, 164.14, 167.97, 171.17. ESIMS (m/z): 598.56 (M+).mp 292°C.Anal. Calcd for $C_{37}H_{34}N_4O_4$ (598.69): C, 74.23; H, 5.72; N, 9.36; found: C, 74.19; H, 5.68; N, 9.31.

7) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino)-N-(p-tolyl) acetamide (6g):*Yield 70%, IR (νmax cm^{-1}): 1023 (C-N stretching in aromatic), 1045 (C-N-C stretching in morpholine), 1130 (C-O-C stretching in morpholine), 1310 (C=N stretching in schiff base), 1406 (C-C stretching in aromatic), 1671 (C=C stretching in aromatic), 1737 (C=O, lactone stretching in coumarin), 2840 (CH_3 stretching in aromatic), 2911 (-CH_2 stretching in alkane), 3055 (CH=CH stretching in aromatic), 3470 (-CONH stretching in amide), 3333 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.306 (s, 3H), 3.338 (t, 4H, *J*= 4.4 Hz), 3.774 (t, 4H, *J*= 4.8 Hz), 3.807 (s, 2H), 5.760 (s, 1H), 6.478-7.641 (m, 19H), 9.816 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.13, 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 119.33, 125.11, 127.95, 128.60, 128.97, 129.75, 129.92, 130.36, 131.80, 132.16, 132.29, 133.31, 147.45, 164.14, 167.97, 171.17. ESIMS (m/z): 598.13 (M+). mp 276°C. Anal. Calcd for $C_{37}H_{34}N_4O_4$ (598.69): C,74.23; H, 5.72; N, 9.36; found: C, 74.25; H, 5.74; N, 9.38.
8) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino)-N-(2-nitrophenyl) acetamide (6h):* Yield 73%, IR (νmax cm^{-1}): 1100 (C-N stretching in aromatic), 1140 (C-N-C stretching in morpholine), 1210 (C-O-C stretching in morpholine), 1330 (C=N stretching in Schiff base), 1430 (C-C stretching in aromatic), 1515 (-NO_2 stretching in aromatic), 1675 (C=C stretching in aromatic), 1735 (C=O, lactone stretching in coumarin), 2914 (-CH_2 stretching in alkane), 3045 (CH=CH stretching in aromatic), 3433 (-CONH stretching in amide), 3490 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.305 (t, 4H, *J*= 4.6 Hz), 3.764 (t, 4H, *J*= 4.0 Hz), 4.103 (s, 2H), 5.902 (s, 1H), 6.488-7.681 (m, 19H), 8.239 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 44.54, 48.54, 66.10, 96.01, 117.36, 117.93, 117.98, 124.07, 125.11, 128.60, 128.97, 129.92, 130.36, 131.80, 132.16, 132.29, 133.67, 136.51, 147.45, 164.14, 167.97, 171.17. ESIMS (m/z): 630.39 (M+). mp 277°C. Anal. Calcd for $C_{36}H_{31}N_5O_6$ (629.66): C, 68.67; H, 4.96; N, 11.12; found: C, 68.72; H, 5.00; N, 11.17.
9) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino)-N-(3-nitrophenyl) acetamide (6i):*Yield 75%, IR (νmax cm^{-1}): 1109 (C-N stretching in aromatic), 1140 (C-N-C stretching in morpholine), 1240 (C-O-C stretching in morpholine), 1320 (C=N stretching in schiff base), 1460 (C-C stretching in aromatic), 1540 (-NO_2stretching in aromatic), 1677 (C=C stretching in aromatic), 1746 (C=O, lactone stretching in coumarin), 2933 (-CH_2 stretching in alkane), 3025 (CH=CH stretching in aromatic), 3400 (-CONH stretching in amide), 3440 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.251(t, 4H, *J*= 4.2 Hz), 3.761 (t, 4H, *J*= 4.4 Hz), 3.971 (s, 2H), 6.159 (s, 1H), 6.484-8.250 (m, 19H), 9.100 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 44.54, 48.54, 66.10, 96.01, 115.89, 117.93, 117.98, 120.28, 125.11, 127.95, 128.60, 128.97, 129.27, 129.92, 130.36, 131.80, 132.16, 132.29, 139.64, 147.45, 148.70, 164.14, 167.97, 171.17. ESIMS (m/z): 630.43 (M+). mp 290°C. Anal. Calcd for $C_{36}H_{31}N_5O_6$ (629.66): C, 72.30; H, 4.96; N, 11.12; found: C, 68.62; H, 4.91; N, 11.08.
10) *2-((4-((Z)-(3-(4-Morpholino-2-oxo-2H-chromen-3-yl)-1-phenyl allylidene) amino) phenyl) amino) -N-(4-nitrophenyl) acetamide (6j):*Yield 77%, IR (νmax cm^{-1}): 1120 (C-N stretching in aromatic), 1190 (C-N-C stretching in morpholine), 1230 (C-O-C stretching in morpholine), 1340 (C=N stretching in schiff base), 1455 (C-C stretching in aromatic), 1560 (-NO_2 stretching in aromatic), 1674 (C=C stretching in aromatic), 1749 (C=O, lactone stretching in coumarin), 2936 (-CH_2 stretching in alkane), 3060 (CH=CH stretching in aromatic), 3390 (-CONH stretching in amide), 3447 (C-NH stretching in amine); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.421 (t, 4H, *J*= 3.8 Hz), 3.769 (t, 4H, *J*= 3.6 Hz), 4.073 (s, 2H), 5.899 (s, 1H), 6.460-8.236 (m, 19H), 9.733 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 44.54, 48.54, 66.10, 96.01, 117.93, 117.98, 120.66, 125.11, 125.54, 128.60, 128.97, 129.92, 130.36, 131.80, 132.16, 132.29, 144.14, 145.42, 147.45, 164.14, 167.97,171.17.ESIMS (m/z): 630.23 (M+). mp 288°C. Anal. Calcd for $C_{36}H_{31}N_5O_6$ (629.66): C, 68.67; H, 4.96; N, 11.12; found: C, 68.65; H, 4.98; N, 11.15.

V. CONCLUSION

This article highlights the synthesis and examination of biological activities of some 2-((4-((Z)-(3-(4-morpholino-2-oxo-2H-chromen-3-yl)-1-(p-tolyl) allylidene) amino) phenyl) amino)-N-phenyl substituted acetamides which were further screened against wide range of pathogenic bacteria and fungi. IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis were used to confirm the structures of the newly synthesized compounds. At MICs value of 62.5-500 µg/ml some analogues were found to be potentially active against all microorganisms which were highlighted by the results obtained by bioassays. Analogues with coumarin constituent displayed good activity and can be highlighted as new active leads that provide a powerful incentive for further research in this area. The MIC values of these novel compounds indicates that the halogen atom and alkyl or alkoxy substitution presence gave rise to a better pharmacological as well as antifungal strains in comparison to the other synthesized compounds. The structural variations such as nitro group at -o & -p position to the aromatic phenyl nucleus of acetamide annelated to coumarin residue resulted in an increase in activity due to the crowding effect of nitro group. The chemical structure of the tested compounds in the study done showed higher potency with the chlorine and nitro like electron withdrawing groups. Out of 10 screened compounds 6b, 6c, 6d, 6h, 6i and 6j exhibited good in vitro antibacterial and antifungal activities in comparison to others.

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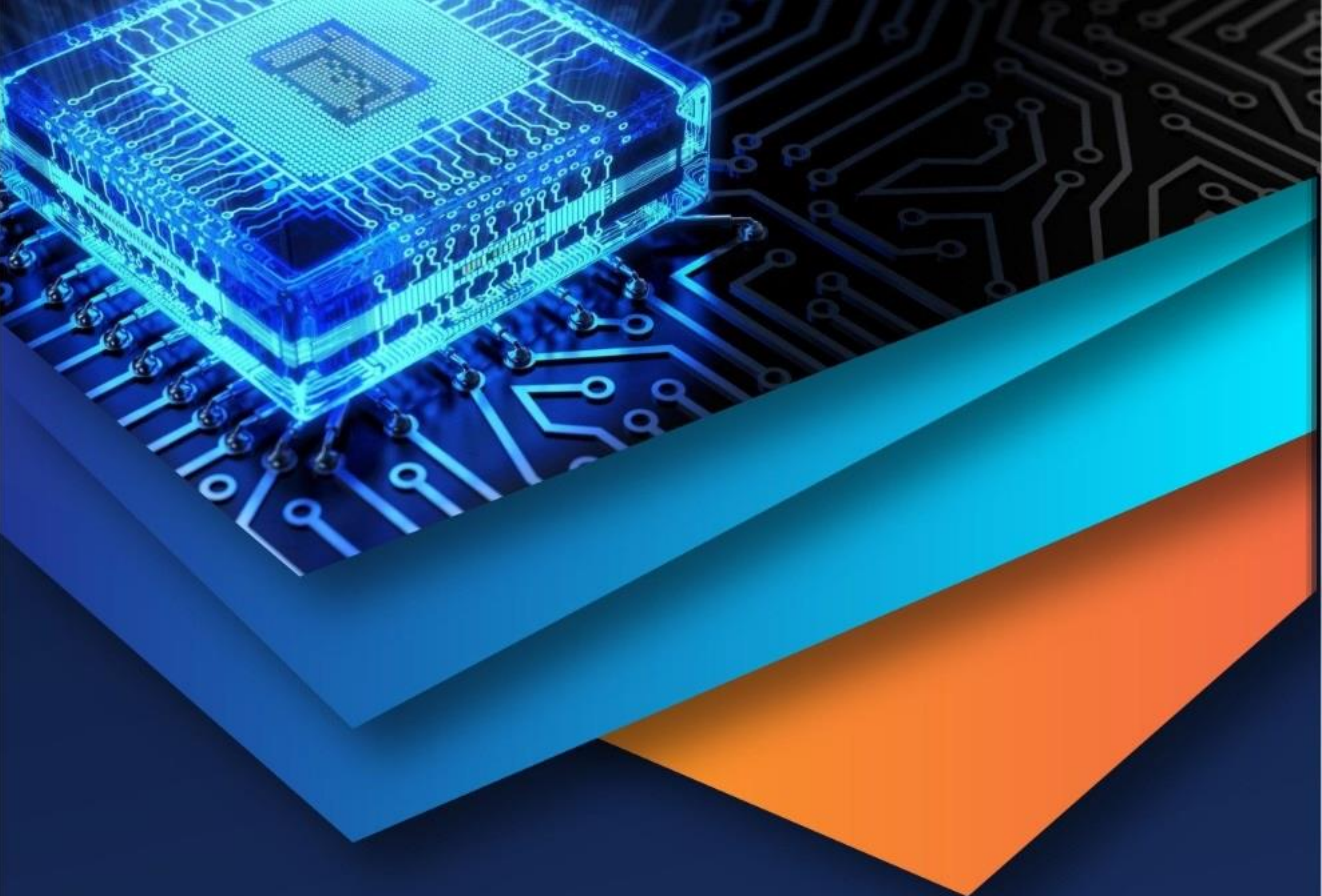

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