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Synthesis and Anti-Microbial Activity of 2-(Coumarinyl-4-Oxy)-4, 6-Dichloro-1,3,5-Triazine Pyrazole-1-Carboxamide Derivatives.

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KEYWORDS

S-Triazine, Chalcones, 4-Hydroxy Coumarin, Substituted Pyrazoline, Disubstituted Triazine Derivatives, Anti-bacterial and Anti-fungal Activities.

ABSTRACT:

The Pyrazoline scaffold containing heterocyclic compounds are vital biological active class of organic chemistry. The literature has proven that compounds with an s-triazine core exhibiting other heterocyclic compounds frequently exhibit significant biological activities. s-triazine and pyrazoline, substituted pyrazoline are the major structural core systems found in many pharmacologically active Compounds. In the present study, Substituted Pyrazoline derivatives are coupled with 4-hydroxy Coumarin comprising s-triazine molecule which contributes to enhance pharmacological activities of Pyrazolines. In this paper we designed and successfully synthesized new series of substituted pyrazoline and structures were confirmed by 1HNMR, IR and Mass Spectroscopy. All Synthesised compounds (9a-j) were screened for Anti-Bacterial and Anti-fungal activities.

INTRODUCTION

Because of potent biological activity, heterocycles that include nitrogen have drawn a lot of attention in recent decades. One such heterocycle is 1, 3, 5-triazine. It is a six-membered heterocyclic molecule with the general formula $C_3H_3N_3$, three nitrogen atoms, and three chlorine atoms that are readily substituted by a variety of nucleophiles. s-triazines and substituted s-triazines are among the many nitrogen-containing heterocycles that are particularly useful in drug discovery due to their wide range of possible biological actions[1]**.** beside from its usage as pharmacophores in medicinal chemistry, s-triazine is widely researched due to its numerous applications in biological systems as an anticancer, antibacterial, antiviral, and antifungal agent[2]. The 1,3,5-triazine ring provides an excellent framework for the synthesis of physiologically active substances with a variety of medicinal uses and anti-protozoa qualities[3]. s-triazine hold a special place in the field of medicinal chemistry. It functions as a protective group in organic chemistry. It's a group of molecule that are reactive and malleable to many synthetic transformations[4]. One of the earliest chemical compounds ever discovered is s-triazine; some of its derivatives have been understood for at least 150 years[5]**.** Decades of research have revealed a broad synthetic range of properties of s-triazine derivatives[6]**.** Because the fact that s-triazine is present in various pharmaceutical drug its chemistry has been thoroughly investigated[7]**.** Because of the wide variety of biological activity revealed by the s-triazine based Chalcones and their derivatives, they have generally been the subject of substantial research[8]**.** A remarkable structural core system shared by a fascinating class of heterocyclic compounds known as triazines and chalcones is present in many pharmacologically active substances[9]**.**

Coumarin is an oxygen-heterocyclic molecule that is a member of the lactone family. Another name for it is benzo-fused lactone. It shares a skeletal structure with benzopyrones[10]. Among all the coumarin derivatives, 4-hydroxy coumarins have demonstrated promise for use in anticancer, antimalarial, antifungal, antiviral, and anticoagulant medicinal applications. Coumarin derivatives have been crucial to medicinal chemistry due

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to their diverse biological applications. They have produced notable results as antibiotics (Novobiocin), anti-AIDS drugs, and anticancer drugs (Gelparvarin). Several of these drugs have been developed using 4-hydroxycoumarin, which has a promising biological activity, following substantial research[11].

Pyrazolines are heterocyclic compounds that have a five-membered unsaturated ring structure and two nitrogen atoms near to three carbon atoms. Many pyrazoline compounds exhibit noteworthy pharmacological characteristics, making them important tools for drug discovery[12]. Due to their numerous biological effects, pyrazoline have drawn the interest of researcher[13]. The broad spectrum of pharmacological actions of pyrazoline-linked heterocyclic compounds was well established. A redesigned pyrazoline ring linked to additional heterocyclic moieties has shown strong biological activity with decreased toxicity[14]. Chalcones and their pyrazoline derivatives are very important compounds in pharmaceutical chemistry because of their biological characteristics, which include antibacterial, antiviral, antifungal, anti-inflammatory, antihypertensive, and anticancer properties[15–17]. Many chemical and biological substances contain pyrazolines, which are highly useful heterocyclic molecules that contain nitrogen and improve their biological importance[18]. In chemical biology and medicinal chemistry, pyrazolines are one of the most active groups of molecules with a vast array of pharmacological characteristics. [19]. Following up on our earlier research on the pure synthesis and antimicrobial assessment of s-triazine containing derivatives of Chalcones, our goal in this work is to synthesize a new series of s-triazine derivatives with stronger antibacterial and antifungal properties.

EXPERIMENTAL

Experimental section:

All the Melting points were determined in open capillaries. ^{1}HNMR spectral dada was recorded at 500 MHz (Bruker Avance) Cryo-magnet Spectrometer in $CDCl_3$ or DMSO Solvent using TMS as an internal standard. IR spectral data were recorded on a FT Infra-Red Spectrophotometer Model RZX Perkin Elmer. The synthesised products were confirmed by the comparison of their Mass, IR, ^{1}HNMR spectral data. TLC was carried out on Silica gel G (Merk) plates with n-Hexane/Ethyl Acetate (8:2) system.

Chemicals and Materials

Synthesis of 2-(Coumarinyl-4-oxy)-4,6-dichloro-s-triazine (3)

To a stirred solution of s-triazine (0.05 mol) in acetone (60 ml) at 0-5°C, the solution of 4-hydroxy Coumarin (0.05 mol) in 10% $NaHCO_3$ (50 ml) was added drop wise with stirring for 2 hours. The progress of the reaction was being monitored by TLC using n-Hexane/Ethyl Acetate (8:2) as Eluent. After reaction completion, the stirring of reaction mixture was stopped and the reaction mixture was poured in to crushed ice. The obtained product was filtered and dried. The crude product was purified and recrystalized from acetone to give the compound (3); yield 90%, M.P. 207-209°C. The physical data is recorded and correlated with reference[11, 20].

General Procedure for the Preparation of 1-(4-aminophenyl)-3-phenylprop-2-en-1-ones (6a-j): - Equimolar quantity (0.01mol) of 4-Amino Acetophenone and respective aryl aldehyde were mix and dissolved in 30 ml of alcohol. To this add aqueous potassium hydroxide (KOH 20%) solution then it was continuously stirred for 24 hours at room temperature and the reactions progress was monitored on Thin Layer Chromatography (n-Hexane/Ethyl Acetate, 8:2), after completion of reaction, it was poured on crushed Ice and neutralized with dil. HCL and the obtained product was filtered, dried and recrystallized from alcohol. The physical data is recorded and correlated with reference[21-23].

General Procedure for the Preparation of 3-(4-aminophenyl)-5-substitutedphenyl-4,5-dihydro-1H-pyrazole-1-carboxamide (8a-j). A Mixture of Chalcones (0.01mol) and Semi carbazide hydrochloride (0.01mol) was taken in Ethanol (30ml) and reflex the reaction mixture for 15 hrs. the reactions progress was monitored on Thin Layer Chromatography (n-Hexane/Ethyl Acetate, 8:2), after completion of reaction, it was poured on crushed Ice filtered, dried and recrystallized from alcohol. The physical data is recorded and correlated with reference[8].

General Procedure for the Preparation 4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-

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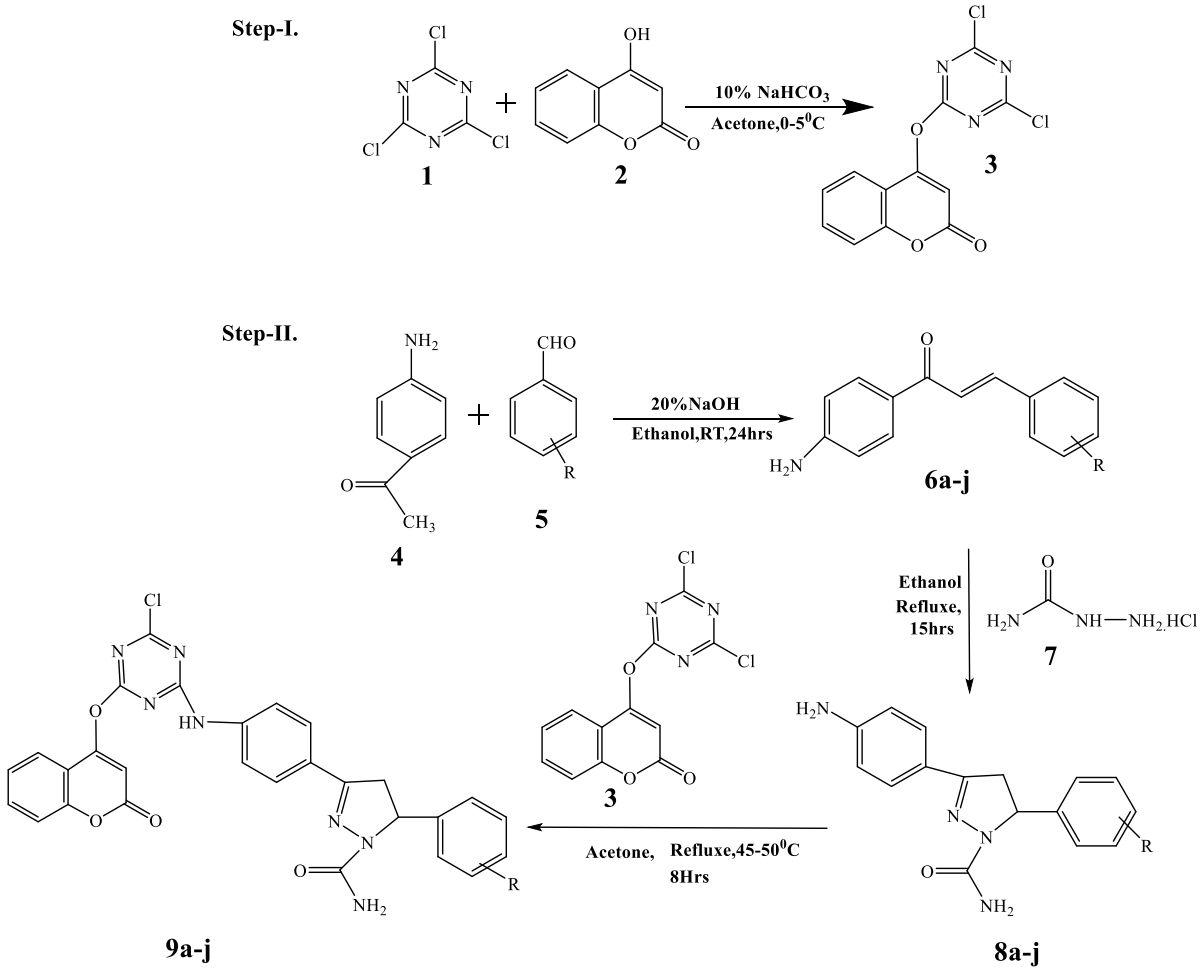
yl)amino)substitutedphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide Derivatives (9a-j): To the stirred solution (0.001mol) of compound 3 in 20 ml acetone add Compound **8a-j**, (0.001mol) ,and stirred the reaction mixture for 8 hrs, maintaining the temp 40°C the pH was kept neutral by the appropriate addition of 10% $NaHCO_3$ Solution. The temperature was steadily raised to 45°C during 3 hours and further maintained for 6 hrs. the reactions progress was monitored on Thin Layer Chromatography (n-Hexane/Ethyl Acetate, 8:2), after completion of reaction, it was poured on crushed Ice. The solid obtained product was filtered and dried. The crude was purified and recrystallized from Acetone.



Scheme III: - 4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)substitutedphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide Derivatives.

Spectral Analysis and Physical Data of Synthesized Compound (9a-j):

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-phenyl-2,3-dihydro-1H-pyrrole-1-carboxamide (9a): Yield 65%, m.p.145-147°C. IR (KBr, ν_{max}, cm^{-1}): 3460, 3130 (-NH-stretching), 2950(-C-H-stretch in Ar-H), 1715, 1606(-C=O stretch in Coumarin, amide), 1563(C=N stretch), 1215(-C-O-C- stretch in Coumarin).

^{1}H NMR (DMSO,500 MHz, δ ppm): 9.80 (s,1H,-NH-,exchangeable with D_2O), 6.22 (s,2H,-NH-),7.72(d,2H),7.35(d,2H),7.30(d,2H),7.26(m,1H,),7.25(d, 2H),7.35-7.70(m,4H), 5.70(s,1H), 3.80(dd,1H,H_a), 3.60(dd,1H,H_b), 4.02(m,1Hx). Mass (m/z):553.13[m+1],

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Anal. Calcd. For $C_{27}H_{20}ClN_7O_4$, C: 60.17, H: 3.64, N: 17.70, Found C: 60.12, H: 3.62, N: 17.68.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(2-chlorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9b): Yield 85%, m.p.182-184^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3449,3294 (-NH- stretch), 2881(-C-H- stretch in Ar), 1733,1686 (-C=O stretch in Coumarin, amide), 1562 (C=N), 1218 (-C-O-C- stretch in Coumarin), 752 (C-Cl stretch).^{1}HNMR (DMSO,500 MHz, δ ppm): 9.43 (s, 1H, -NH-, exchangeable with D_2O), 6.85 (s,2H,-NH-), 7.74 (d, 2H), 7.66 (d,1H), 7.20-7.28 (m,3H), 7.25 (d,2H,), 7.35-7.70(m,4H), 5.70(s,1H), 3.90(dd,1H,H_a), 3.62(dd,1H,H_b), 4.06(m,1Hx). Mass (m/z): 588.41 [m+1], Anal. Calcd. For $C_{28}H_{19}Cl_2N_7O_4$, C:57.16, H: 3.25, N:16.16, Found C:57.12, H: 3.22, N:16.14.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(4-chlorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9c): Yield 86%, m.p.166-168^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): IR (KBr, ν_{max}, cm^{-1}): 3490,3126 (-NH- stretch), 2885(-C-H- stretch in Ar), 1721,1620 (-C=O stretch in Coumarin, Amide), 1564 (C=N), 1220 (-C-O-C- stretch in Coumarin), 765 (C-Cl stretch).^{1}H NMR (DMSO,500 MHz, δ ppm): 9.46 (s, 1H, -NH-, exchangeable with D_2O), 6.90 (s,2H,-NH-), 7.76 (d, 2H), 7.47 (d,2H), 7.46 (d,2H), 7.27 (d,2H,), 7.35-7.70(m,4H), 5.72(s,1H), 3.92(dd,1H,H_a), 3.63(dd,1H,H_b), 4.09(m,1Hx). Mass (m/z): 588.41 [m+1], Anal. Calcd. For $C_{28}H_{19}Cl_2N_7O_4$, C:57.16, H: 3.25, N:16.16, Found C:57.12, H: 3.22, N:16.14

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(2,4-dichlorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9d): Yield 72%, m.p.235-237^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3486,3210 (-NH- stretch), 2985(-C-H-stretch in Ar), 1722,1680 (-C=O stretch in Coumarin ,Amide), 1555 (C=N), 1220 (-C-O-C- stretch in Coumarin), 765 (C-Cl stretch).^{1}HNMR (DMSO,500 MHz, δ ppm): 9.44 (s, 2H, -NH-, exchangeable with D_2O), 6.80 (s,1H,-NH-), 7.75 (d, 2H), 7.71 (s,1H), 7.40 (d,1H), 7.26 (d,2H,),7.01(d,1H), 7.35-7.70(m,4H), 5.69(s,1H), 3.93(dd,1H,H_a), 3.62(dd,1H,H_b), 4.07(m,1Hx). Mass (m/z): 579.82 [m+1], Anal. Calcd. For $C_{28}H_{18}Cl_3N_7O$, C:54.09, H: 2.91, N:15.74, Found C:54.06, H: 2.85, N:15.70

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(2-fluorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9e): Yield 62%, m.p.196-198^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3410,3110 (-NH- stretch), 2985(-C-H- stretch in Ar), 1720,1680 (-C=O stretch in Coumarin, Amide), 1520 (C=N), 1215 (-C-O-C- stretch in Coumarin), 978 (C-F stretch).^{1}H NMR (DMSO,500 MHz, δ ppm): 9.38 (s, 1H, -NH-, exchangeable with D_2O), 6.75 (s,2H,-NH-), 7.73 (d, 2H), 7.70 (m,1H), 7.20-7.60 (m,3H), 7.24 (d,2H,), 7.35-7.70(m,4H), 5.65(s,1H), 3.89(dd,1H,H_a), 3.60(dd,1H,H_b), 4.03(m,1Hx). Mass (m/z): 571.95 [m+1], Anal. Calcd. For $C_{28}H_1ClFN_7O_4$, C:58.80, H: 3.35, N:17.40,Found C:58.75, H: 3.33, N:17.38.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(4-fluorophenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9f): Yield 72%, m.p.142-44^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3486,3129 (-NH- stretch), 2828(-C-H- stretch in Ar), 1722,1616 (-C=O stretch in Coumarin, Amide), 1569 (C=N), 1210 (-C-O-C- stretch in Coumarin), 979 (C-F stretch).^{1}H NMR (DMSO,500 MHz, δ ppm): 9.47 (s, 1H, -NH-, exchangeable with D_2O), 6.80 (s,2H,-NH-), 7.72 (d, 2H), 7.24 (d,2H), 7.20 (d,2H), 7.21 (d,2H,), 7.35-7.70(m,4H), 5.69(s,1H), 3.89(dd,1H,H_a), 3.59(dd,1H,H_b), 4.04(m,1Hx). Mass (m/z): 571.95 [m+1], Anal. Calcd. For $C_{28}H_1ClFN_7O_4$, C:58.80, H: 3.35, N:17.40,Found C:58.75, H: 3.33, N:17.38.

2-(4-bromophenyl)-4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9g): Yield 80%, m.p.161-63^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3400,3210 (-NH- stretch), 2880(-C-H- stretch in Ar), 1715,1630 (-C=O stretch in Coumarin, Amide), 1600 (C=N), 1205 (-C-O-C- stretch in Coumarin), 810 (C-Br stretch).^{1}HNMR (DMSO,500 MHz, δ ppm): 9.38 (s, 1H, -NH-, exchangeable with D_2O), 6.90 (s,2H,-NH-), 7.71 (d, 2H), 7.69 (d,2H), 7.16 (d,2H), 7.23 (d,2H,), 7.35-7.70(m,4H), 5.68(s,1H), 3.90(dd,1H,H_a), 3.60(dd,1H,H_b), 4.03(m,1Hx).Mass (m/z): 632.86 [m+1], Anal. Calcd. For $C_{28}H_{19}ClBrN_7O_4$, C:53.14, H: 3.03, N:15.49, Found C:53.10, H: 3.00, N:15.46.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(o-tolyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9h): Yield 76%, m.p.180-182^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3405,3190 (-NH-stretch), 2882(-C-H- stretch in Ar), 1720,1690 (-C=O stretch in Coumarin, Amide), 1570 (C=N), 1210 (-C-O-C- stretch in Coumarin).^{1}H NMR (DMSO,500 MHz, δ

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ppm): 9.25 (s, 1H, -NH-, exchangeable with D_2O), 6.76 (s,2H,-NH-), 7.69 (d, 2H), 7.30 (m,1H), 6.90-7.20 (m,3H), 7.20 (d,2H), 7.35-7.70(m,4H), 5.50(s,1H), 3.75(dd,1H,H_a), 3.89(dd,1H,H_b), 4.01(m,1Hx),2.26(s,3H).Mass (m/z): 567.99 [m+1], Anal. Calcd. For $C_{29}H_{22}ClN_7O_4$, C:61.32, H: 3.90, N:17.26, Found C:61.26, H: 3.86, N:17.21.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(p-tolyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9i) : Yield 75%, m.p.165-167^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3495,3190 (-NH- stretch), 2870(-C-H- stretch in Ar), 1715,1682 (-C=O stretch in Coumarin, Amide), 1586 (C=N), 1200 (-C-O-C- stretch in Coumarin).^{1}HNMR (DMSO,500 MHz, δ ppm): 9.22 (s, 1H, -NH-, exchangeable with D_2O), 6.65 (s,2H,-NH-), 7.68 (d, 2H), 7.20 (d,2H), 7.05 (d,2H), 7.19 (d,2H), 7.35-7.70(m,4H), 5.62(s,1H), 3.68(dd,1H,H_a), 3.79(dd,1H,H_b), 3.00(m,1Hx),2.27(s,3H). Mass (m/z): 567.99 [m+1], Anal. Calcd. For $C_{29}H_{22}ClN_7O_4$, C:61.32, H: 3.90, N:17.26, Found C:61.26, H: 3.86, N:17.21.

4-(4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)phenyl)-2-(4-methoxyphenyl)-2,3-dihydro-1H-pyrrole-1-carboxamide (9j): Yield 76%, m.p.176-178^{0}C**.** IR (KBr, ν_{max}, cm^{-1}): 3395,3285 (-NH- stretch), 2800(-C-H- stretch in Ar), 1705,1695 (-C=O stretch in Coumarin, Amide), 1580 (C=N), 1200 (-C-O-C- stretch in coumarin), 1121(-C-O-C-). ^{1}HNMR (DMSO,500 MHz, δ ppm): 9.20 (s, 1H, -NH-, exchangeable with D_2O), 6.50 (s,2H,-NH-), 7.63 (d, 2H), 7.19 (d,2H), 6.86 (d,2H), 7.16 (d,2H,),7.35-7.70(m,4H), 5.69(s,1H), 3.65(dd,1H,H_a), 3.77(dd,1H,H_b), 4.00(m,1Hx),3.78(s,3H). Mass (m/z): 583.99 [m+1], Anal. Calcd. For $C_{29}H_{22}ClN_7O_5$, C:59.64, H: 3.80, N:16.79, Found C:59.61, H: 3.78, N:16.73.

Biological Activity:

Anti-bacteria and Anti-fungal Activities.

All the novel synthesized compounds from the series (**9a-j**) were screened for antibacterial activity against two Gram-Positive Bacteria viz. B. subtilis, and Gram-Negative Bacteria viz. E.coli by disk diffusion assay [24]. Using Chloramphenicol (100 µs/disk) the reference standard for comparing the results. The Anti-bacterial activity was screened by using nutrient agar obtained from Hi-media. Composition (gL^{-1}). Sodium chloride-5 : Beef extract-3: Penton 5.0 (P^H 7.2).The novel synthesized series of compounds (**9a-j**) were also screened for Anti-fungal activity against A.niger and C. albicans by agar diffusion assay [25] , Using Amphotericin B (100 units /disk) as the reference standard. The Antifungal activity is screened by using Sabouraud Agar Media and DMSO as control Solvent. The diameter of the Zone is measured by Vernier Calliper. The Anti-Bacterial and Anti-Fungal Activity of the 4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)substitutedphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide compound derivatives (**9a-j**) is shown in

Table No.1.

TABLE NO 1.

Anti-bacterial and Anti-fungal Screening of Compounds (9a-j)

Compound		Anti-bacterial Activity		Anti-Fungal Activity
		B.subtilis	E.Coli	C. albicans
9a	H	8	7.9	10.0
9b	2-Cl	-	8.7	13.8
9c	4-Cl	7.2	8.4	9.9
9d	2,4-Cl	-	7.4	10.0
9e	2-F	7.5	9.0	11.0
9f	4-F	9.8	7.1	10.7
9g	4-Br	10.4	8.2	9.5

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9h	2-Me	12.7	7.0	10.2
9i	4-Me	8.9	8.7	11.4
9j	4-OCH_3	-	9.0	12.3
Chloramphenicol		19	27.1	-
Amphotericin B		NA	NA	18.03

RESULT AND DISCUSSION

Literature survey reveals that there are no reports of 4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)substitutedphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide, hence it was planned to synthesize these compounds. In the present study step-I, 1,3,5-triazine **(1)** is reacted with 4-Hydroxy Coumarin **(2)** in the presence of aq. $NaHCO_3$ in acetone to the yield 2-(Coumarinyl-4- oxy)-4,6-dichloro-s-triazine **(3)** in good yield**.** In the step-II, 4-Amino acetophenone **(4)** is reacted with the substituted aryl aldehydes **(5)** in the presence of NaOH followed by condensation reaction to yield 1-(4-aminophenyl)-3-phenylprop-2-en-1-one compound derivatives **(6a-6j)** with good yield. Further synthesis, Compounds **(6a-6j)** reacted with the compound **(7)** which yield compound **(8a-j),** in the final step compound **(8a-j)** reacted with compound **(3)** in the presence of aq. $NaHCO_3$ and Acetone as solvent to Yield **(9a-9j)** with excellent yield. The IR spectra of **(9c)** show strong absorption band at 3449 cm^{-1} and 3294 cm^{-1} indicated the Stretching frequency of -NH- functional group. 1733 cm^{-1} is stretching of (-C=O) in Coumarin ring, 1616cm^{-1} is the value for (-C=N) stretching in pyrazoline confirm the synthesis of coupling of pyrazoline derivatives with s-triazine. ^{1}H NMR Spectrum of **(9c)** show that, Singlet at δ 9.90 ppm for (–NH-) gives confirmation of secondary amine, again singlet at δ 6.40 ppm confirm the (-NH-) of amide whereas δ 5.85 ppm for (-C-O-C-) confirm that the coupling of s-triazine and 4-hydroxy Coumarin. The Mass Spectra shows the molecular Ion peak at 588.90 [m+1]. All these Spectral analyses show that the Confirmation of synthesis of **(9a-9j)** compounds.

Screening of the biological activities of synthesized compounds revealed that, compound **9a-9j** show good Anti-bacterial activity against Gram negative bacteria i.e. E.Coli. and Gram-positive B.subtilis. Compounds **9i, 9j** having electron donating show good Anti-bacterial activity against Gram-negative bacteria i.e. E.coli. Compounds No any compound show antibacterial activity against Gram-Negative bacteria i.e. E.coli and B.subtilis. The Investigation of Anti-fungal activity data revealed that, the compound which has chlorine,methoxy substituent shows less zone of inhibition as compare to another substituent against C. albicans. Fungal strain compared with the standard Amphotericin B drug.

CONCLUSION

In the present research, we have reported the synthesis of new series 4-((4-chloro-6-((2-oxo-2H-chromen-4-yl)oxy)-1,3,5-triazin-2-yl)amino)substitutedphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carboxamide derivatives (**9a-j**). All the Compound shows promising Anti-bacterial activities as compared to the standard Chloramphenicol drug. All synthesized compound shows potent Antifungal activities against standard Amphotericin B. drug. But chlorine, methyl, methoxy substituent has more antifungal activity as compare to another substituent. All the synthesized series of compound shows excellent to moderate activity against the Pathogens and are very promising core molecule as potent Antifungal agents, further investigation is needed

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