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SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL EVALUATION OF NOVEL PYRAZOLYL AND BENZOFURANYL PYRIDYL SUBSTITUTED COUMARINS

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Abstract: A novel library of pyrazolyl and benzofuranyl pyridyl coumarins (3-(6-(benzofuran-2-yl)-4-(1,3-diphenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarins **(5a-r)** has been synthesized by the reaction of 3-(3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acryloyl)-2*H*-coumarins **(3a-f)** with benzofuranyl methyl pyridinium iodide salts **(4a-c)** in the presence of ammonium acetate in refluxing acetic acid which follows Krohnkes mechanism. Structure of all the newly synthesized compounds have been established by analytical and spectral analysis (IR, ^{1}H-NMR, ^{13}C-APT and Mass spectral data). All the synthesized compounds have been screened for their *in vitro* antimicrobial efficiency against representative panel of pathogenic strains specifically Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*), Gram-negative bacteria (*Escherichia coli*, *Salmonella typhi*) and Fungi (*Candida albicans*, *Aspergillus niger*). Upon evaluating the activity data it has been observed that almost all derivatives possess appreciable efficiency against Gram-positive bacteria and against Gram-negative bacteria. Some of the synthesized compounds exhibited moderate activity against tested fungi.

Keywords: Benzofuran, pyrazole, Krohnke reaction, antimicrobial activity, broth dilution method.

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1. INTRODUCTION

In current era, resistance of pathogenic bacteria to conventional drugs is major human health problem. The discovery and design of new efficient antimicrobial agents is crucial need to conquer the emerging multi-drug resistance pathogenic micro-organisms. At present, the role of heterocyclic compounds has become increasingly important in designing new class of structural entities of medicinal importance. Among the pharmacologically important heterocyclic compounds, coumarin and its derivatives have wide spectrum of biological activities.

Coumarin (*2H*-1-benzopyran-2-one) and its derivatives are widely distributed throught nature and many of them exhibit useful and diverse biological activities such as antitumor [1], anti-inflammatory [2] and antibacterial [3] activities. Coumarin derivatives especially pyridyl coumarins have been reported to have important biological activities like CNS depressant [4], antifungal [5], moth proofing activity [6], fish toxicity [7], MAO inhibitor [8], antibacterial agents [9] and antitubercular [10].

A large number of compounds having pyrazole nucleus in their structure are reported to have wide range of biological activities viz., antioxidant[11], antiinvasive[12], antiviral[13], anti-inflammatory[14] and are also used as agrochemicals[15] and dyestuff[16]. Phenylbutazone[17] has been used in the treatment of severe arthritis. Being so composed and having pharmaceutical effects on human, pyrazoles have significant importance in the field of medicinal chemistry.

Similarly, during our literature search we came across some benzofurans derivatives which are reported to have, anti-inflammatory, fungicidal and weed killing activity [18-20].

In view of the aforementioned properties of coumarins, pyrazoles and benzofuran pyrazoles moieties, it was thought worthwhile to synthesize a hybrid molecule incorporating all these moieties in a single scaffold so that one can expect novel biological properties. Keeping this objective in mind and in continuation of our work on synthesizing newer heterocyclic substituted coumarins[21], herein we report the synthesis of some various pyrazolyl and benzofuranyl pyridyl substituted coumarins using a *Krohnke's* reaction.

2. Materials and methods

2.1 EXPERIMENTAL:

All reactions were performed with commercially available reagents, and they were used without further purification. Organic solvents were purified by standard methods (Furniss et al., 2004) and stored over molecular sieves. All reactions were monitored by thin-layer

chromatography (TLC, on aluminum plates coated with silica gel 60 F254, 0.25 mm thickness, Merck), and UV radiation and/or iodine were used as the visualizing agents. Melting points were determined in open capillaries and are uncorrected. Infrared spectra were recorded on Shimadzu FTIR 8401 spectrophotometer using potassium bromide pellets in the range 4,000–400 cm^{-1}, and frequencies of only characteristic peaks are expressed in cm^{-1}. ^{1}H and ^{13}C Nuclear Magnetic Resonance spectra were recorded in $CDCl_3$ on a Bruker Avance 400 (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) using TMS signal as an internal standard at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm). The coupling constants (J) are given in Hertz (Hz). Mass spectrum of compound **5a** was scanned on a Shimadzu LCMS 2010 spectrometer (Shimadzu, Tokyo, Japan). The compounds were purified by column chromatography using silica gel (60–120 mesh).

Starting precursors 3-acetyl coumarins **1(a-b)** [22] and benzofurananyl methyl pyridinium iodide salts **4(a-c)** [23] were prepared using the reported procedures.

2.1.1. General procedure for the synthesis of 3-(3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acryloyl coumarin (3a-f)

In a 100 mL round bottom flask, an appropriate 3-acetyl coumarins (0.01 mol) and appropriate pyrazole aldehyde (0.01 mol) were taken in 50 mL of ethanol. Catalytic amount of piperidine (1.0 mL) was added and the reaction mixture was stirred for 10 minutes at room temperature. The reaction mixture was then refluxed on water bath for 4 hours. It was then allowed to cool to room temperature. A solid product separated out was filtered off, washed with cold ethanol and dried. It was recrystallized from ethanol.

Compound 1a: R=R_1=H, Yield: 86%, mp 232°C (lit.[24] mp 234°C)

Compound 1b: R=H, R_1=CH_3, Yield: 81%, mp 207°C (lit.[24] mp 208°C)

Compound 1c: R=H, R_1=OCH_3, Yield: 84%, mp 178°C (lit.[24] mp 180°C)

Compound 1d: R=OCH_3, R_1=H, Yield: 89%, mp 219°C (lit.[24] mp 220°C)

Compound 1e: R=OCH_3, R_1=CH_3, Yield: 91%, mp 158°C (lit.[24] mp 160°C)

Compound 1f: R=R_1=OCH_3, Yield: 90%, mp 187°C (lit.[24] mp 188°C)

2.1.2 General procedure for the synthesis of 3-{6-[benzofuran-2-yl-4-(1,3-diphenyl-*1H*-pyrazol-5-yl]pyridin-2-yl}coumarins(5a-r):

In a 100 mL round bottom flask equipped with a condenser, guard tube and magnetic needle, an appropriate benzofuranyl methyl pyridinium iodide salts **(4a-c)** (0.003 mole) in glacial acetic acid (15mL) was taken. To this, ammonium acetate (0.03 mole) was added with stirring at room temperature. Then a solution of an appropriate 3-(3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acryloyl coumarin (coumarin chalcone) **(3a-f)** (0.003 mole) in glacial acetic acid (15 mL) was added with stirring at room temperature and the reaction mixture was further stirred for 1 hour at room temperature. It was then refluxed for 12 hours at 140°C. It was then allowed to come to room temperature and was poured into ice-cold water (75 mL). A crude solid obtained was extracted with chloroform (3 x 30 mL). The organic layer was washed with 5% sodium bicarbonate solution (3 x 20 mL), water (2 x 20 mL) and dried over anhydrous sodium sulfate. The removal of chloroform under reduced pressure gave crude material which was subjected to column chromatography using silica gel and chloroform-ethyl acetate (7:3) as an eluent to give compounds **(5a-r)**. The compounds were recrystallized from chloroform-hexane.

The confirmation of all the eighteen synthesized **5a-r** compounds were carried out by their elemental analysis and IR , ^{1}H-NMR, ^{13}C- NMR, and representative mass spectral data given below.

3-(6-(Benzofuran-2-yl)-4-(1,3-diphenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin(5a): yellow solid; yield = 68% ; mp 230-232°C; Anal. Calcd. For $C_{37}H_{23}N_3O_3$: C, 78.75; H, 4.28; N, 10.80 %. Found: C, 78.62; H, 4.21; N, 10.73 %. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1726 (C=O stretching of δ-lactone of coumarin), 1576 and 1502 (aromatic C=C and C=N stretchings), 690 and 754(C-H bending vibration of monosubstituted benzene ring) 2923 (aliphatic C-H stretching), 3060 (aromatic C-H stretching), ^{1}H NMR (400MHz, $CDCl_3$, δ): 7.31-8.25 (20H, m, Ar-H), 8.66 (1H, s, C_3''-H of benzofuran ring), 9.04 (1H, s, C_5'''- H of pyrazole ring), 9.20 (1H, s, C_4-H of coumarin ring) , ^{13}C NMR (100MHz, $CDCl_3$, δ) : 105.68(CH), 111.64(CH), 114.04(CH), 116.47(CH), 119.62(C), 119.85(CH), 120.71(CH), 121.22(CH), 121.53(C), 122.92(CH), 123.79(CH), 123.96(CH), 124.57(CH), 124.62(CH), 125.61(C), 126.47(C), 127.31(CH), 128.12(CH), 128.57(C), 128.87(CH), 129.58(CH), 132.18(CH), 136.86(C), 139.49(C), 141.96(C), 142.65(CH), 149.31(CH), 151.03(C), 154.03(C), 154.87(C), 155.92(C), 156.02(C) and 159.47(CO of coumarin)δ. The mass spectrum of compound **3a** showed M^+ peak at 44(100%) (m/z %) ,77(85%) ,57(15%), 557(10%) along with some other fragments peaks etc. The appearance of molecular ion peak at 557 mass unit supports the structure of compound **5a**.

3-(6-(Benzofuran-2-yl)-4-(1-phenyl-3-p-tolyl-*1H*-pyrazol-4-yl)pyridin-2-ylcoumarin (5b): yellow solid; yield = 72% ; mp 218-220°C; Anal. Calcd. For $C_{38}H_{25}N_3O_3$: C, 76.63; H, 4.41; N, 10.21 %.

Found: C, 76.58; H, 4.37; N, 10.15 %. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1727 (C=O stretching of δ-lactone of coumarin), 1597 and 1457 (aromatic C=C and C=N stretchings), 832(C-H bending vibration of p-disubstituted benzene ring) 2923 (aliphatic C-H stretching), 3061 (aromatic C-H stretching), ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.33 (3H, s, CH_3), 6.68-8.26(19H, m, Ar-H), 8.36 (1H, s, C_3''-H of benzofuran ring), 8.46 (1H, s, C_5"'-H of pyrazole ring), 8.86 (1H, s, C_4-H of coumarin ring) , ^{13}C NMR (100MHz, $CDCl_3$, δ) : 21.47(CH_3), 105.17(C), 111.72 (CH), 114.89(CH), 116.37(CH), 118.56(CH), 119.22(CH), 119.51(C), 119.90(CH), 122.53(CH), 124.59(CH), 124.93(C), 126.37(CH), 126.85(CH), 127.47(CH), 128.59(CH), 129.09(C), 129.27(CH), 129.45(CH), 129.60(CH), 131.56(C), 132.26(CH),138.27(C), 139.68(C), 142.97(CH), 142.66(CH), 144.29(C), 144.95(C), 148.27(C), 151.31(C), 151.74(C), 154.01(C), 155.71(C),160.11(CO of coumarin).

3-(6-(Benzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl) coumarin (5c): White solid; yield = 69% ; mp 240°C; Anal. Calcd. For $C_{38}H_{25}N_3O_4$: C, 80.27; H, 4.25; N, 9.85%. Found: C, 80.19; H, 4.22; N, 9.77%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1729 (C=O stretching of δ-lactone of coumarin), 1597 and 1457 (aromatic C=C and C=N stretchings), 834 (C-H bending vibrations of p-disubstituted benzene ring), 3060 (aromatic C-H stretching), ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.93 (3H ,s, OCH_3) , 7.16 -8.26 (19H, m, Ar-H), 8.34 (1H, s, C_3''-H of furan ring), 8.425 (1H, s, C_5"' H pyrazole ring), 8.89 (1H, s, C_4-H of coumarin ring),.^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.35(OCH_3), 105.73(CH), 116.06(C), 117.26(C), 118.15(CH), 119.62(CH), 120.33(CH), 121.04(C), 121.11(C), 121.32(CH), 122.63(CH), 123.25(CH), 123.59(CH), 124.97(CH), 126.06(C), 127.53(CH), 127.97(CH), 128.38(C), 129.64(CH), 131.16(CH), 134.28(CH), 134.46(C), 135.03(CH), 139.35(C), 141.49(CH), 142.10(C), 148.43(CH), 149.14(C), 150.21(CH), 151.18(C), 152.80(C), 154.49(C), 154.84(C), 159.61 (CO of coumarin).

3-(4-(1,3-Diphenyl-*1H*-pyrazol-4-yl)-6-(4-methoxybenzofuran-2-yl)pyridin-2-yl)coumarin (5d):White solid; yield = 67% ; mp 194-196°C; Anal. Calcd. For $C_{38}H_{25}N_3O_4$: C,78.93; H, 4.54; N, 10.52%. Found: C, 78.87; H, 4.46; N, 40.45 %. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1725 (C=O stretching of δ-lactone of coumarin), 1598 and 1458 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of *para* disubstituted benzene ring), 2923 (aliphatic C-H stretching), 3061 (aromatic C-H stretching),^{1}H NMR (400MHz, $CDCl_3$, δ): 3.78 (3H, s, OCH_3), 6.66-8.20 (19H, m, Ar-H), 8.35 (1H, s, C_3''-H of furan ring), 8.43 (1H, s, C_5"' H pyrazole ring), 8.84 (1H, s, C_4-H of coumarin ring), ^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.88(OCH_3), 105.71(CH), 111.87(CH), 114.90(CH), 116.71(CH), 119.85(C), 120.92(CH), 121.43(CH), 121.48(CH), 121.58(CH), 123.14(CH), 124.01(CH), 124.19(CH), 124.78(CH), 124.81(CH), 125.90(C), 128.47(C), 128.87(CH), 129.11(C), 132.41(CH), 133.45(C), 137.11(CH), 141.80(C), 142.33(C), 142.88(CH), 149.50(C), 149.55(CH), 151.27(C), 154.28(C), 155.08(C), 156.20(C), 156.25(C), 159.16(C), 160.46 (CO of coumarin).

3-(6-(4-Methoxybenzofuran-2-yl)-4-(1-phenyl-3-p-tolyl-*1H*-pyrazol-4-yl)pyridin-2-yl)-coumarin (5e):Yellow solid; yield = 72% ; mp 223°C; Anal. Calcd. For $C_{39}H_{27}N_3O_4$: C, 76.85; H, 4.60; N,

9.96%. Found: C, 76.80 H, 4.57; N, 9.90%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1727 (C=O stretching of δ-lactone of coumarin), 1598 and 1458 (aromatic C=C and C=N stretchings), 823 (C-H bending vibrations of *p*-disubstituted benzene ring), 2921 (aliphatic C-H stretching), 3061 (aromatic C-H stretching), ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.41 (3H, s, CH_3),4.01 (3H, s, OCH_3), 6.74-7.92 (18H, m, Ar-H protons), 8.34 (1H, s, C_3''-H of furan ring), 8.44 (1H, s, C_5''' H pyrazole ring), 8.93 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 21.39(CH_3), 56.60 (OCH_3), 105.18(C), 105.33(CH), 109.21(CH), 116.39(CH), 118.60(CH), 119.23(CH), 119.53(C), 119.92(C), 122.56(CH), 124.61(CH), 124.98(C), 126.38(CH), 126.86(CH), 127.47(CH), 128.59(CH), 129.09(CH), 129.31(CH), 129.53(CH), 129.60(CH), 131.57(C), 132.28(CH), 138.28(C), 139.69(C), 142.68(C), 142.99(CH), 144.29(C), 144.96(C), 148.30(C), 151.33(C), 151.78(C),154.03(C), 155.73(C), 160.12(CO of coumarin).

3-(6-(4-Methoxybenzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5f):Yellow solid; yield = 74% ; mp 235-237°C; Anal. Calcd. For $C_{39}H_{27}N_3O_5$: C, 80.39; H, 4.50; N, 9.62%. Found: C, 80.31; H, 4.44; N, 9.57%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1725 (C=O stretching of δ-lactone of coumarin), 1598 and 1457 (aromatic C=C and C=N stretchings), 825 (C-H bending vibrations of *para* disubstituted benzene ring), 2930 aliphatic C-H stretching), 3060 (aromatic C-H stretching). ^{1}H NMR (400MHz, $CDCl_3$, δ): 3.95 (2×3H, s, OCH_3), 7.110-7.985 (18H, m, Ar-H protons), 8.39 (1H, s, C_3''-H of furan ring), 8.49 (1H, s, C_5''' H pyrazole ring), 8.71 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.86(OCH_3), 56.32(OCH_3), 106.02(CH), 112.35(CH), 114.93(CH), 117.41(C), 118.36(CH), 121.17(C), 121.25(CH), 121.35(CH), 121.43(CH), 123.19(CH), 123.99(C), 124.04(CH), 124.29(CH), 124.83(C), 126.82(C), 127.40(CH), 128.43(CH), 128.83(C), 131.25(CH), 133.38(C), 135.04(CH), 137.15(CH), 141.38(CH), 141.74(C), 142.43(C), 149.65(CH), 150.75(C), 153.02(C), 155.16(C), 156.02(C), 156.21(C), 159.31(C), 159.89 (CO of coumarin).

3-(6-(5-Bromobenzofuran-2-yl)-4-(1,3-diphenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5g): Yellow solid; yield = 75% ; mp 225-227°C; Anal. Calcd. For $C_{37}H_{22}BrN_3O_3$: C, 78.75; H, 4.28; N, 10.80%. Found: C, 78.67; H, 4.23; N, 10.71%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1726 (C=O stretching of δ-lactone of coumarin), 1599 and 1459 (aromatic C=C and C=N stretchings), 690 amd 748 (C-H bending vibrations of mono substituted benzene ring), 2926 (aliphatic C-H stretching), 3061 (aromatic C-H stretching). ^{1}H NMR (400MHz, $CDCl_3$, δ): 7.057-8.251 (19H, m, Ar-H protons), 8.30 (1H, s, C_3''-H of furan ring), 8.36 (1H, s, C_5''' H pyrazole ring), 8.77 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 108.54(CH), 110.07(C), 111.08(CH), 112.90(C), 115.73(C), 118.56(C), 118.71(CH), 119.28(C), 119.85(C), 121.04(CH), 122.32(CH), 122.76(CH), 124.07(CH), 124.30(CH), 124.94(CH), 126.49(CH), 127.93(C), 129.62(CH), 130.08(CH), 131.30(CH), 132.08(CH), 137.82(C), 138.29(CH), 142.36(C), 142.86(CH), 145.69(CH), 146.02(C), 147.26(C), 150.22(C), 152.63(C), 155.04(C), 160.66 (CO of coumarin).

3-(6-(5-Bromobenzofuran-2-yl)-4-(1-phenyl-3-*p*-tolyl-*1H*-pyrazol-4-yl)pyridin-2-yl)-coumarin (5h): Yellow solid; yield = 73% ; mp 195-197°C; Anal. Calcd. For $C_{38}H_{24}Br\ N_3O_4$: C,76.63; H, 4.36; N, 10.16%. Found: C, 76.63; H, 4.41; N, 10.21%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1726 (C=O stretching of δ-lactone of coumarin), 1598 and 1458 (aromatic C=C and C=N stretchings), 836 (C-H bending vibrations of *para* disubstituted benzene ring), 2925 (aliphatic C-H stretching), 3069 (aromatic C-H stretching).. ^{1}H NMR (400MHz, $CDCl_3$, δ) : 2.35 (3H, s, CH_3), 6.94-7.83 (18H, m, Ar-H), 8.54 (1H, s, C_5'''-H of furan ring), 8.56 (1H, s, C_5"'pyrazole ring), 8.91 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 21.87(CH_3), 105.54(CH), 112.31(CH), 114.89(CH), 117.35(C), 118.39(CH), 121.11(C), 121.25(CH), 121.35(CH), 121.43(CH), 123.17(CH), 123.93(C), 124.02(CH), 124.27(CH), 124.81(C), 126.82(C), 127.40(CH), 128.43(CH), 128.83(C), 131.25(CH), 133.38(C), 135.04(CH), 137.15(CH), 141.36(CH), 141.75(C), 142.41(C), 149.52(CH), 150.65(C), 153.02(C), 155.08(C), 155.99(C), 156.25(C), 159.16(C), 159.76 (CO of coumarin).

3-(6-(5-Bromobenzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5i): Yellow solid; yield = 65% ; mp 230°C; Anal. Calcd. For $C_{38}H_{24}BrN_3O_4$: C, 80.27; H, 4.25; N, 9.85%. Found: C, 80.21; H, 4.20; N, 9.77%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1726 (C=O stretching of δ-lactone of coumarin), 1599 and 1459 (aromatic C=C and C=N stretchings), 836 (C-H bending vibrations of *p*-disubstituted benzene ring), 2925 (aliphatic C-H stretching), 3069 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 3.92 (3H, s, OCH_3), 7.05-8.25 (18H, m, Ar-H), 8.30 (1H, s, C_3''-H of furan ring), 8.36 (1H, s, C_5"'pyrazole ring), 8.88 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 56.01(OCH_3), 105.99(CH), 111.82(CH), 115.24(CH), 116.43(CH), 118.67(CH), 118.77(CH), 119.67(C), 120.51(C), 120.92(CH), 121.53(CH), 121.89(CH), 123.26(CH), 123.75(CH), 124.97(CH), 125.28(C), 125.41(CH), 128.56(C), 130.13(CH), 133.05(C), 133.25(CH), 141.29(C), 142.17(C), 143.71(CH), 145.77(C), 148.10(C), 150.84(CH), 152.07(C), 153.96(C), 154.13(C), 154.73(C), 158.89(C), 159.83 (CO of coumarin).

8-Methoxy-3-(6-(benzofuran-2-yl)-4-(1,3-diphenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarins (5j):Yellow solid; yield = 66% ; mp 207-209°C; Anal. Calcd. For $C_{38}H_{25}N_3O_4$: C, 78.9.; H, 4.54; N, 10.52%. Found: C, 78.88; H, 4.48; N, 10.46 %. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1720 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 690 and 756 (C-H bending vibrations of *mono* substituted benzene ring), 2928 (aliphatic C-H stretching), 3058 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 3.85 (3H, s, OCH_3), 6.66-8.20 (19H, m, Ar-H), 8.35 (1H, s, C_3''-H of furan ring), 8.36(1H, s, C_5"'pyrazole ring), 8.84 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.63(OCH_3), 105.51(CH), 114.68(CH), 116.44(CH), 116.80(C), 119.54(C), 120.02(CH), 120.86(C), 121.26(CH), 121.32(CH), 122.49(CH), 123.19(CH), 123.55(CH), 124.70(CH), 124.85(CH), 125.05(C), 128.07(CH), 128.45(C), 129.03(CH), 132.36(CH), 133.06(C), 134.23(CH), 134.61(C), 141.43(C), 142.10(C), 142.98(CH), 148.53(CH), 150.10(CH), 151.70(C), 154.03(C), 154.35(C), 154.81(C), 159.02(C), 160.29 (CO of coumarin).

8-Methoxy-3-(6-(benzofuran-2-yl)-4-(1-phenyl-3-p-tolyl-*1H*-pyrazol-4-yl)pyridin-2-yl)-coumarins (5k):Yellow solid; yield = 72% ; mp 237°C; Anal. Calcd. For $C_{36}H_{26}N_3O_4$: C, 76.85; H, 4.66; N, 9.96%. Found: C, 76.82; H, 4.60; N, 9.91%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1719 (C=O stretching of δ-lactone of coumarin), 1599 and 1461 (aromatic C=C and C=N stretchings), 834 (C-H bending vibrations of p-disubstituted benzene ring), 2931 (aliphatic C-H stretching), 3061 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 2.34 (3H, s, CH_3) , 3.99 (3H, s, OCH_3), 7.22-7.99 (18H, m, Ar-H), 8.34 (1H, s, C_3''-H of furan ring), 8.44(1H, s, C_5'''pyrazole ring), 8.93 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 21.31(CH_3), 54.84(OCH_3), 105.70(CH), 116.45(C), 119.54(C), 119.64(CH), 120.09(CH), 121.24(C), 121.31(CH), 122.54(CH), 123.22(CH), 123.56(CH), 124.72(CH), 124.94(CH), 125.03(C), 127.50(CH), 128.00(CH), 128.41(C), 129.04(CH), 129.63(C), 132.39(CH), 134.23(CH), 134.58(C), 139.38(C), 141.89(C), 141.99(C), 143.02(CH), 148.57(CH), 149.18(C), 150.16(CH), 151.74(C), 154.05(C), 154.40(C), 154.84(C), 160.29 (CO of coumarin).

8-Methoxy-3-(6-(benzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)-coumarins (5l):Yellow solid; yield = 72% ; mp 236-238°C; Anal. Calcd. For $C_{38}H_{27}N_3O_5$: C, 75.84; H, 4.41; N, 6.80%. Found: C, 75.81; H, 4.39 N, 6.81%.IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1717 (C=O stretching of δ-lactone of coumarin), 1598 and 1478 (aromatic C=C and C=N stretchings), 836 (C-H bending vibrations of *p*-disubstituted benzene ring), 2930 (aliphatic C-H stretching) 3065 (aromatic C-H stretching).. ^{1}H NMR (400MHz, $CDCl_3$, δ) : 3.85 (3H, s, OCH_3), 4.02 (3H, s, OCH_3,) 6.95-7.87 (18H, m, Ar-H), 8.32 (1H, s, C_3''-H of furan ring), 8.44(1H, s, C_5'''pyrazole ring), 8.90 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.64(OCH_3), 56.32(OCH_3), 105.47(CH), 114.07(CH), 114.68(CH), 120.11(CH), 120.19(C), 120.42(CH), 120.87(C), 121.26(CH), 121.37(CH), 122.57(CH), 123.16(CH), 123.55(CH), 124.53(CH), 124.84(CH), 125.24(C), 128.14(CH), 128.45(C), 133.09(C), 134.22(CH), 134.62(C), 136.46(C), 142.14(C), 143.15(CH), 143.72(C), 146.98(C), 148.57(CH), 149.32(C), 150.13(CH), 151.70(C), 154.33(C), 154.81(C), 159.02(CO of coumarin).

8-Methoxy-3-(4-(1,3-diphenyl-*1H*-pyrazol-4-yl)-6-(4-methoxybenzofuran-2-yl)pyridin-2-yl)coumarin (5m): Yellow solid; yield = 69% ; mp 238°C; Anal. Calcd. For $C_{39}H_{27}N_3O_5$: C, 75.84; H, 4.41; N, 6.79%. Found: C, 75.80; H, 4.51; N, 6.80%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1721 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 690 and 755 (C-H bending vibrations of mono substituted benzene ring), 2926 (aliphatic C-H stretching), 3061 (aromatic C-H stretching) .^{1}H NMR (400MHz, $CDCl_3$, δ): 4.03 (2×3H, s, OCH_3,) 7.14-8.36 (18H, m, Ar-H), 8.43 (1H, s, C_3''-H of furan ring), 8.44(1H, s, C_5'''pyrazole ring), 8.89 (1H, s, C_4-H of coumarin ring)..^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.43(OCH_3), 56.82(OCH_3), 106.02(CH), 112.25(CH) 114.93(CH), 117.41(C), 118.36(CH), 121.17(C), 121.25(CH), 121.35(CH), 121.43(CH), 123.19(CH), 123.99(C), 124.04(CH), 124.29(CH), 124.83(C), 126.82(C), 127.40(CH), 128.43(CH),

128.83(C), 131.25(CH), 133.38(C), 135.04(CH), 137.15(CH), 141.38(CH), 141.74(C), 142.43(C), 149.65(CH), 150.75(C), 153.02(C), 155.16(C), 156.02(C), 156.21(C), 159.31(C), 159.89 (CO of coumarin).

8-Methoxy-3-(6-(4-methoxybenzofuran-2-yl)-4-(1-phenyl-3-p-tolyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5n): Yellow solid; yield = 65% ; mp 226-228°C; Anal. Calcd. For $C_{40}H_{29}N_3O_5$: C, 76.06; H, 4.63; N, 6.65%. Found: C, 76.01; H, 4.60; N, 6.67%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1721 (C=O stretching of δ-lactone of coumarin), 1598 and 1478 (aromatic C=C and C=N stretchings), 826 (C-H bending vibrations of *p*- disubstituted benzene ring), 2923 (aliphatic C-H stretching), 3061 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 2.34 (3H, s, OCH_3), 4.02 (2×3H, s, OCH_3,) 6.74-7.98 (21H, m, Ar-H), 8.32 (1H, s, C_3''-H of furan ring), 8.49(1H, s, C_5"'pyrazole ring), 8.93 (1H, s, C_4-H of coumarin ring). ^{13}C NMR (100MHz, $CDCl_3$, δ): 23.60(CH3), 60.74(OCH_3), 61.31(OCH_3), 105.26(CH), 110.73(CH), 116.55(CH), 119.94(CH), 120.01(CH), 124.93(C), 125.13(C), 125.21(CH), 125.62(CH), 125.92(CH), 126.23(CH), 126.61(CH), 127.93(CH), 128.46(CH), 129.72(C), 129.90(C), 130.12(CH), 133.30(C), 134.94(CH), 137.69(C), 145.49(C), 146.87(C), 148.00(C), 148.58(CH), 150.48(C), 151.45(C), 154.12(C), 155.53(CH), 156.66(C), 158.81(C), 159.41(C), 163.61(C), 164.27 (CO of coumarin).

8-Methoxy-3-(6-(4-methoxybenzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5o): Yellow solid; yield = 76% ; mp 236-238°C; Anal. Calcd. For $C_{40}H_{29}N_3O_6$: C, 74.18; H,4.51; N, 6.49%. Found: C, 74.16; H, 4.49; N, 6.51%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1722 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 824 (C-H bending vibrations of *p*-disubstituted benzene ring), 2927 (aliphatic C-H stretching), 3069 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 3.95 (3H, s, OCH_3), 3.92 (3H, s, OCH_3,) 3.84 (3H, s, OCH_3,) 6.77-8.24 (17H, m, Ar-H), 8.32 (1H, s, C_3''-H of furan ring), 8.33(1H, s, C_5"'pyrazole ring), 8.80 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.22 (OCH_3), 56.31(OCH_3), 56.35(OCH_3), 105.02(CH), 111.53(C), 113.87(CH), 114.08(CH), 118.41(CH), 119.13(CH), 119.35(CH), 119.84(CH), 120.11(C), 120.34(C), 121.16(CH), 121.60(CH), 122.06(CH), 123.18(CH), 124.38(C), 125.01(C), 125.12(CH), 125.18(CH), 127.48(C), 128.75(CH), 129.49(CH), 129.96(C), 139.64(C), 142.49(CH), 143.58(C), 146.84(C), 148.80(C), 150.92(C), 151.56(C), 155.11(C), 155.27(C) and 159.55(CO of coumarin).

8-Methoxy-(3-(6-(5-bromobenzofuran-2-yl)-4-(1,3-diphenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5p):Yellow solid; yield = 70% ; mp 252-254°C; Anal. Calcd. For $C_{38}H_{24}BrN_3O_4$: C, 68.48; H, 3.03; N, 6.30%. Found: C, 68.45; H, 3.01; N, 6.25%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1730 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 692 and 756 (C-H bending vibrations of mono substituted benzene ring), 2927 (aliphatic C-H stretching), 3064 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 4.01 (3H, s, OCH_3,) 7.28-8.37 (18H, m, Ar-H), 8.44 (1H, s, C_3''-H of furan ring), 8.58(1H, s, C_5"'pyrazole ring), 8.88

(1H, s, C_4-H of coumarin ring)..^{13}C NMR (100MHz, $CDCl_3$, δ) : 54.16(OCH_3), 106.24(CH), 111.85(CH), 116.44(CH), 119.30(CH), 119.67(C), 120.53(CH), 120.88(C), 121.53(CH), 121.96(CH), 123.32(CH), 123.78(CH), 124.85(C), 125.28(CH), 125.50(CH), 127.83(CH), 128.52(C), 130.14(CH), 130.23(CH), 133.26(CH), 139.37(C), 141.29(C), 142.05(C), 143.73(CH), 145.74(C), 148.05(C), 150.85(CH), 152.09(C), 153.96(C), 154.16(C), 154.70(C), 159.84(C),160.29(CO of coumarin).

8-Methoxy-3-(6-(5-bromobenzofuran-2-yl)-4-(1-phenyl-3-p-tolyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5q):Yellow solid; yield = 74% ; mp 248-250°C; Anal. Calcd. For $C_{39}H_{26}BrN_3O_4$: C, 68.83; H, 3.85; N, 6.17%. Found: C, 68.80 : H, 3.82; N, 6.14%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1716 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 837 (C-H bending vibrations of para disubstituted benzene ring), 2934 (aliphatic C-H stretching), 3069 (aromatic C-H stretching). ^{1}H NMR (400MHz, $CDCl_3$, δ): 2.42 (3H, s, OCH_3), 4.03 (3H, s, OCH_3,) 7.22-7.89 (17H, m, Ar-H), 8.34 (1H, s, C_3''-H of furan ring), 8.47(1H, s, C_5"'pyrazole ring), 8.89 (1H, s, C_4-H of coumarin ring).^{13}C NMR (100MHz, $CDCl_3$, δ) : 21.35(CH_3), 56.31(OCH_3), 105.30(CH), 111.65(C), 113.95(C), 116.29(CH), 119.64(CH), 120.24(C), 120.29(CH), 120.78(CH), 121.23(CH), 121.54(C), 122.89(CH), 123.87(CH), 123.95(CH), 124.40(CH), 124.61(CH), 127.30(CH), 128.17(CH), 128.57(C), 129.57(CH), 136.88(C), 139.51(C), 142.00(C), 142.82(CH), 147.01(C), 149.03(C), 149.29(CH), 151.02(C), 154.00(C), 154.86(C), 155.94(C), 156.03(C), 159.49(C), 160.23 (CO of coumarin).

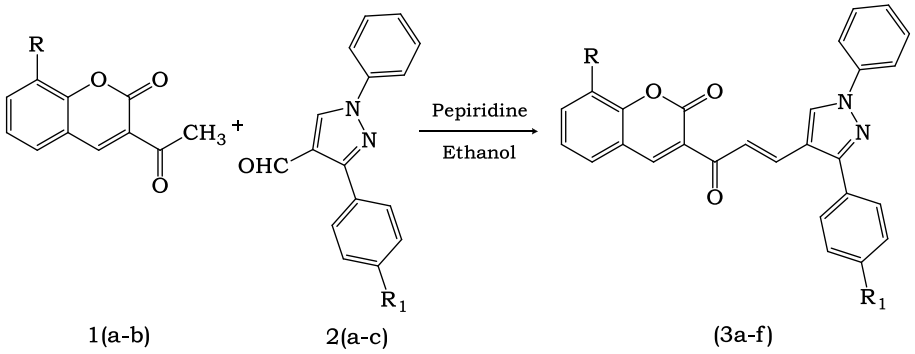
8-Methoxy-3-(6-(5-bromobenzofuran-2-yl)-4-(3-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazol-4-yl)pyridin-2-yl)coumarin (5r):Yellow solid; yield = 68% ; mp >280°C; Anal. Calcd. For $C_{39}H_{26}BrN_3O_5$: C, 67.25; H, 3.75; N,6.03%. Found: C, 67.21; H, 3.76; N, 6.05%. IR (KBr, ν_{max}, cm^{-1}); ν_{max} 1716 (C=O stretching of δ-lactone of coumarin), 1599 and 1478 (aromatic C=C and C=N stretchings), 832 (C-H bending vibrations of *p*-disubstituted benzene ring), 2934 (aliphatic C-H stretching), 3061 (aromatic C-H stretching).^{1}H NMR (400MHz, $CDCl_3$, δ): 3.93 (3H, s, OCH_3), 3.95 (3H, s, OCH_3,) 7.22-8.34 (17H, m, Ar-H), 8.42 (1H, s, C_3''-H of furan ring), 8.45(1H, s, C_5"'pyrazole ring), 8.87 (1H, s, C_4-H of coumarin ring)..^{13}C NMR (100MHz, $CDCl_3$, δ) : 55.28(OCH_3), 56.39(OCH_3), 105.68 (CH), 114.04(C), 116.47(C), 119.62(C), 119.85 (C), 120.71(CH), 121.22(CH), 121.53(C), 122.92(CH), 123.79(CH), 123.96(CH), 124.57(CH), 124.62(CH), 125.61(C), 126.47(C), 127.31(CH), 128.12(CH), 128.57(C), 128.87(CH), 129.58(CH), 132.18(CH), 136.86(CH), 139.49(C), 141.96(C), 142.65(CH), 149.31(CH), 151.03(C), 154.03(C), 154.87(C), 155.92(C), 156.02(C), 159.47(C) and 160.20(CO of coumarin).

In case of the compound **5g** the number of non-equivalent carbon signals observed is one less than expected. This may be due to identical chemical shifts of two carbons which may appear at same position.

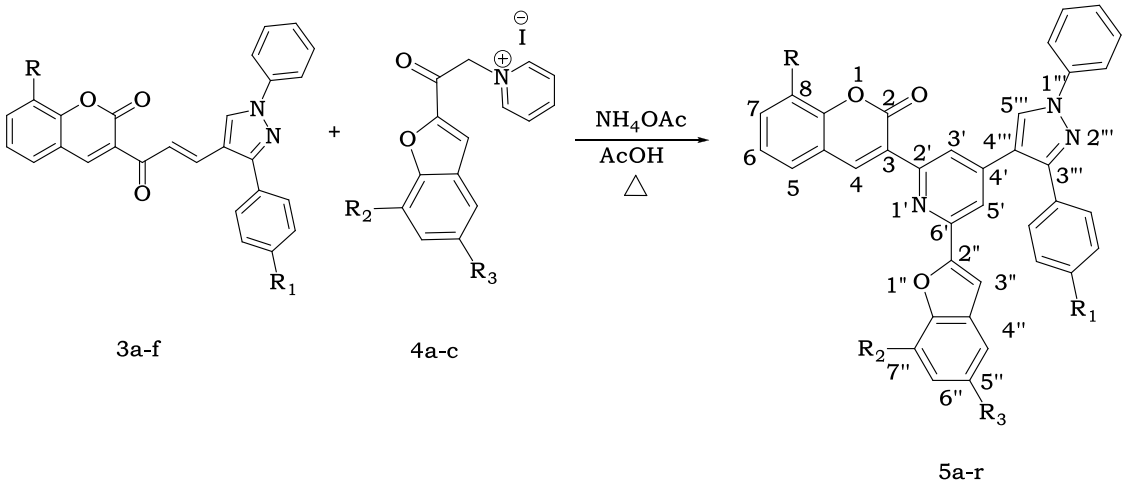
3. RESULTS AND DISCUSSION:

3.1. CHEMISTRY:

In the present work, synthesis of various 3-(6-(benzofuran-2-yl)-4-(1,3-diphenyl-1H-pyrazol-4-yl)pyridin-2-yl)coumarins **(5a-r) (Scheme.2)** have been carried out by the reaction of appropriate 3-(3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acryloyl)-2*H*-coumarins **(3a-f)** with benzofuranyl methyl pyridinium salts **(4a-c)** in the presence of ammonium acetate in refluxing acetic acid which under *Krohnke's* reaction condition. The starting material (3-(1,3-diphenyl-1*H*-pyrazol-4-yl)acryloyl)-2*H*-coumarins (coumarin chalcones) **(3a-f)** were prepared by the reaction of 3-acetyl coumarins **(1a-b)** with appropriate pyrazole aldehyde **(2a-c)** in the presence of piperidine in ethanol. **(Scheme-1).**



Scheme1.Synthesis of coumarin chalcones (3a-f)



Scheme-2: Synthetic scheme for the compounds (5a-r)

	R	R_1	R_2	R_3		R	R_1	R_2	R_3
5a	H	H	H	H	5j	OCH_3	H	H	H
5b	H	CH_3	H	H	5k	OCH_3	H	H	H
5c	H	OCH_3	H	H	5l	OCH_3	OCH_3	H	H
5d	H	H	OCH_3	H	5m	OCH_3	H	OCH_3	H
5e	H	CH_3	OCH_3	H	5n	OCH_3	CH_3	OCH_3	H
5f	H	OCH_3	OCH_3	H	5o	OCH_3	OCH_3	OCH_3	H
5g	H	H	H	Br	5p	OCH_3	H	H	Br
5h	H	CH_3	H	Br	5q	OCH_3	CH_3	H	Br
5i	H	OCH_3	H	Br	5r	OCH_3	OCH_3	H	Br

Table-1

3.2. BIOLOGICAL RESULTS:

3.2.1 ANTIMICROBIAL ACTIVITY

The *in vitro* antimicrobial activity of all newly synthesized compounds was carried out by broth dilution method as recommended by the National Committee for Clinical Laboratory Standards (NCCLS)[25]. All the synthesized compounds were screened for their antimicrobial activity against two Gram-positive bacteria *viz*. *Bacillus subtilis* (MTCC 441) and *Staphylococcus aureus* (MTCC 96), two Gram-negative bacteria *viz*. *Escherichia coli* (MTCC 443) and *Salmonella typhi* (MTCC 98) and two fungi *viz*. *Aspergillus niger* (MTCC 282) *and Candida albicans* (MTCC 227). In the present study, ampicillin and norfloxacin were used as standard antibacterial drugs, where as nystatin and griseofulvin were used as standard antifungal drugs. All MTCC cultures were collected from Institute of Microbial Technology, Chandigarh and tested against above mentioned known drugs. Mueller Hinton Broth was used as nutrient medium to grow and dilute the compound suspension for the test bacteria and Sabouraud Dextrose Broth was used for fungal nutrition. The size of the inoculum for the test strain was adjusted to 10^8 colony forming unit (CFU) per milliliter by comparing the turbidity. DMSO was used as a diluent to get the desired concentration of compounds to test upon standard bacterial strains. Each synthesized compound and standard drugs were diluted obtaining 2000 μgmL^{-1} concentration, as a stock solution. In primary screening 1000, 500 and 250 μgmL^{-1} concentrations of the synthesized drugs were taken. The active synthesized compounds found in this primary screening were further diluted to obtain 200, 125, 100, 62.5, 50, 25, 12.5 and 6.250 μgmL^{-1} concentrations for secondary screening to test in a second set of dilution against all microorganisms. 10 µL Suspensions from each well were further inoculated and growth was

noted after 24 and 48 h. The lowest concentration, which showed no visible growth (turbidity) after spot subculture was considered as MIC for each compound.

The investigation of the data summarized in **(Table-1)** reveals that many compounds were found to be active against Gram-positive bacteria while some of the compounds were found to be active against Gram-negative bacterial and fungal species as compared to that of the standard antimicrobial drugs.

3.2.2. ANTIMICROBIAL EVALUTION

The compounds were screened for their *in vitro* antibacterial and antifungal evaluation against various bacterial and fungal pathogens by broth dilution method. Ampicillin, Chloramphenicol, Norfloxacin, Griseofulvin and Nystatin were used as standard drugs. The values of MIC are summarized in **Table-1**.

All the newly synthesized compounds **5a-r** exerted significant activity against all the employed strains. Upon investigation of antimicrobial data, it was observed that compound **5d and 5n** (MIC= 62.5 µg/ml) showed excellent activity against gram positive strain *B. subtilis* as compared to Ampicillin (MIC= 250 µg/ml) and Norfloxacin (MIC= 100 µg/ml). The compounds **5b, 5k, 5r** (MIC= 100 µg/ml) showed excellent activity against *B. subtilis* upon comparison with first line drug Ampicillin (MIC= 250 µg/ml). In case of inhibiting *S. aureus*, compounds **5f and 5o** (MIC= 62.5 µg/ml) was found to be more potent upon comparison with reference drug Ampicillin (MIC= 250 µg/ml) and Norfloxacin (MIC= 100 µg/ml). The compounds **5c, 5l** (MIC= 100 µg/ml) exhibited excellent activity against *S. aureus* compared to Ampicillin (MIC= 250 µg/ml). The compound **5i** (MIC= 125 µg/ml) and compounds **5e, 5n and 5r** (MIC= 125 µg/ml) demonstrated improved activity compared to Ampicillin (MIC= 250 µg/ml) against *B. subtilis* and *S. aureus* respectively. The compounds 3a, 3c, 3e, 3h, 3j, 3m (MIC= 200 µg/ml) and **5a, 5k and 5m** (MIC= 200 µg/ml) depicted better activity against *B. subtilis* and *S. aureus* respectively compared to Ampicillin (MIC= 250 µg/ml).

Towards *E. coli*, compound **5c** (MIC= 62.5 µg/ml) demonstrated strong inhibition as compared to Ampicillin (MIC= 100 µg/ml) and compounds **5j** , **5e, 5g and 5q** were found to be equipotent against gram negative pathogens *E. coli* and *S. typhi* respectively compared to Ampicillin (MIC= 100 µg/ml).

Antifungal activity data of compounds revealed that, all the synthesized compounds have feasible antifungal profile compared to standard fungicidal drugs Nystatin and Griseofulvin. A few compounds **5o** (MIC= 250 µg/ml) and **5c, 5l and 5m** (MIC= 250 µg/ml) exhibited better activity against *A.niger* and *C. albicans* as compared to Griseofulvin (MIC= 500 µg/ml).

Compounds	Minimum Inhibitory Concentration (MIC, $\mu g mL^{-1}$)					
	Gram +ve bacteria		Gram –ve bacteria		Fungi	
	B.s.	*S.a.*	*E.c.*	*S.t.*	*A.n.*	*C.a.*
5a	**200**	**200**	250	200	>1000	**>1000**
5b	**100**	250	250	250	500	**>1000**
5c	**200**	**100**	**62.5**	125	>1000	**250**
5d	**62.5**	250	500	250	>1000	**>1000**
5e	**200**	**125**	125	**100**	1000	**1000**
5f	500	**62.5**	200	250	500	**500**
5g	250	250	125	**100**	>1000	**1000**
5h	**200**	250	500	250	500	**1000**
5i	**125**	250	250	250	1000	**>1000**
5j	**200**	250	**100**	125	1000	**500**
5k	**100**	**200**	125	200	1000	**1000**
5l	250	**100**	500	500	>1000	**250**
5m	**200**	**200**	250	200	>1000	**250**
5n	**62.5**	**125**	250	125	500	**500**
5o	250	**62.5**	250	250	**250**	**500**
5p	500	250	500	250	500	**1000**
5q	250	250	125	**100**	>1000	**1000**
5r	**100**	**125**	200	250	500	**1000**
Ampicillin	250	250	100	100	-	**-**
Chloramphenicol	50	50	50	50	-	**-**
Ciprofloxacin	50	50	25	25	-	**-**
Norfloxacin	100	10	10	10	-	**-**
Gentamycin	1	0.25	0.05	5	-	**-**
Griseofulvin	-	-	-	-	100	**500**
Nystatin	-	-	-	-	100	**100**

B.s.: Bacillus subtilis, S.a.: Staphylococcus aureus, E.c.: Escherichia coli, S.t.: Salmonella typhi, A.n.: Aspergillus niger, C.a.: Candida albicans

Table-1 : In *vitro* Antimicrobial activity of compounds (5a-r)

Majority of the synthesized compounds were active against Gram-positive bacteria *viz*. *Bacillus subtilis* (MTCC 441) and *Staphylococcus aureus* (MTCC 96), Gram-negative bacteria *viz*. *Escherichia coli* (MTCC 443) and *Salmonella typhi* (MTCC 98). Some of the synthesized compounds were found sufficiently potent to inhibit fungal pathogen *viz*. *Candida albicans* (MTCC 227). Thus compounds **5c**, **5e**, **5i**, **5l**, **5o** and **5q** were emerged as the proficient antimicrobial members of the series.

4. CONCLUSION:

Present study describes successful hybridization strategy of three bioactive moieties, pyridyl substituted coumarin, pyrazole and benzofuran in single scaffold. The target compounds were synthesized in good yield by adopting Krohnke's protocol. Majority of the compounds were found to be active against *Staphylococcus aureus* and *Bacillus subtilis*. Antimicrobial screening results revealed that compounds **5c**, **5e**, **5i**, **5l**, **5o** and **5q** were found to be the most proficient members of the series. Reviewing the antimicrobial data, it is worth mentioning here that coumarins bearing pyrazole and benzofuran entities as substitution serve as promising lead scaffolds for further generation of new antimicrobial agents.

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