SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL 2-ARYL-PYRAN-4-ONES OF 1,8-NAPHTHYRIDIN AND ITS DERIVATIVES

Narendar Atmakuri, Laxminarayana Eppakayala† & Thirumala Chary Maringanti*

JNTUH College of Engineering, Nachupally, Karimnagar -505 327 (A.P.) INDIA
†Mahatma Gandhi Institute of Technology, Gandipet, Hyderabad-500075 (A.P.) INDIA

ABSTRACT
In the present study, a series of pyranone derivatives of 1,8-naphthyridines (6a-j) were synthesized by condensation of 1-(2-hydroxy-1,8-naphthyridin-3-yl)ethanone (3) and different aromatic aldehydes in ethanolic solution of potassium hydroxide followed by cyclization. Several pyranones have been synthesized and their biological activity (Antimicrobial) investigated using the Ampicillin and Nalidixic acid as standards. The results showed that compound (6d and 6e) shows the higher anti-bacterial activity against gram positive bacteria. The synthesized compounds have been characterized by using Mass, IR and 1H NMR Spectral data together with elemental analysis.

Key words: 2-Amino-pyridine-3-carbaldehyde, Pyranones ring cyclisation, Antimicrobial activity.

INTRODUCTION
1,8-Naphthyridine derivatives have attracted considerable attention because the 1,8-naphthyridine skeleton is present in many compounds that have been isolated from natural substances, with various biological activities, antibacterial,1,2 antymycobacterial,3 antitumor,4 antiinflam matory,5 antiplt elet,6 gastric antisecretary,7 antiallergic,8 local anaesthetic9 and benzodia zepine receptor activity.10 Nalidixic acid, for example, possesses strong antibacterial activity and used mainly for the treatment of urinary tract infections with gram negative pathogens11. In addition, Gemifloxacin is antimicrobial and antibacterial12. A survey of the literature shows that the major synthetic approache that are used to prepare various types of
1,8-naphthyridine system involves Friedländer condensation of 2-aminonicotinaldehyde with carbonyl compounds containing active methylene compounds, aldehydes, acyclic and cyclic ketones or diketones group in the presence of an acid or base catalyst. Flavones occupy a special place in the realm of natural and synthetic Organic chemistry owing to their useful biological activities such as anti-oxidant, Anxiolytic, anti cancer, and anti microbial. During the past few years various methods have been reported for the synthesis of pyrone ring system. In view of above facts, it was contemplated to design and synthesis of some flavone (contains pyrone ring) derivatives from the corresponding chalcone by using DMSO/I2 as an oxidizing agent. The structure of flavone derivatives were confirmed by melting point, TLC and spectral data.

**MATERIALS AND METHODS**

**General Procedure for the synthesis of 2-hydroxy-[1,8] naphthyridine-3-carbonitrile (1)**

To a stirred solution of 2-amino-pyridine-3-carboxaldehyde (1.0g, 8.19 mmol) in ethanol (10 mL), was added ethylcyano acetate (1.11g, 9.83 mmol), piperidine (0.83g, 9.83 mmol). The resulting solution was heated at 90°C for about 6h. The resulting light yellow solids were filtered and washed with ethanol, dried to afford the desired product as light yellow solid (1.35g, 7.80 mmol, yield: 96%); mp >300°C; ¹H NMR (200 MHz, DMSO-d6): 8.89 (s, 1H), 8.64 (d, 1H, J=7.5 Hz), 8.21 (d, 1H, J=7.2 Hz), 7.37 (m, 1H), 5.86 (brs, 1H, OH); ¹³C NMR (200 MHz, DMSO-d6): 164.3 (C-OH), 150.8, 146.6, 138.6, 136.7, 122.4, 118.0, 108.8, 106.0; MS (EI): m/z (M+1) 172 ; IR (ν/cm⁻¹): 3076 and 2215 due to (OH) and (CN).

**2-methoxy-1,8-naphthyridine-3-carbonitrile (2)**

To a solution of 2-hydroxy-1,8-naphthyridine-3-carbo nitrile (1), (1.0g, 5.84 mmol) in DMF (10 mL), was added K₂CO₃ (1.61g, 11.69 mmol) at -5-0°C, the resulting solution was stirred for 10 min, then methyliodide (2.47g 17.52 mmol) was added slowly, the resulting solution was slowly allowed to room temperature, stirred for about 16h, poured in ice-cold water and filtered the solid compound, washed with ethanol, dried to offorded yellow solid ( 0.98g, 5.29
mmol, yield: 91%). mp 266-268 °C; 1H NMR (200 MHz, DMSO-d6): 8.87 (m, 2H), 8.34 (d, 1H, J=6.2 Hz), 7.47 (m, 1H), 3.72 (s, 3H, OCH3); 13C NMR (200 MHz, DMSO-d6): 172.3 (C-OCH3), 153.1 (N-C-N), 151.2 (C-N), 142.6, 137.7, 125.8, 122.0, 109.3 (CN), 103.0, 56.7 (OCH3); MS (EI): m/z (M+1) 186.1; IR (ν/cm⁻¹): 2220 (CN) 2220 and 3115 (OCH3).

1-(2-methoxy-1,8-naphthyridin-3-yl)ethanone (3)

To a solution of 2-methoxy-1,8-naphthyridine-3-carbonitrile (2) (1.0 g, 5.40 mmole) in dry tetrahydrofuran (20 mL), was added methylmagnesiumiodide (1.79 g, 10.81 mmol, 3.0 M solution in diethylether) by dropwise over a period of 20 min, at -78°C, the resulting solution was slowly allowed to room temperature and stirred for about 1h, the solution was quenched with 2N HCl solution (10mL), extracted with ethyl acetate, dried over anhydrous Na2SO4, evaporated the solvent under reduced pressure. The resulting crude compound was purified by column chromatography by using 100-200 mesh silicagel, eluted with dichloromethane in methanol (9:1), to afford 1-(2-methoxy-1,8-naphthyridin-3-yl)ethanone (3) as light yellow solid (0.45 g, 2.22 mmol, yield: 42%); mp 204-206 °C; 1H NMR (500 MHz, CDCl3): 8.82 (d, 1H, J= 6.8Hz), 8.74 (s, 1H ), 8.19 (d, 1H, J= 7.2Hz), 7.32 (m, 1H), 4.25 (s, 3H, OCH3), 2.04 (s, 3H, COCH3); 13C NMR (200 MHz, CDCl3): 198.2 (C=O), 175.3, 153.3, 149.6, 141.6, 139.7, 125.4, 125.0, 111.8, 58.0 (O-CH3), 28.2 (CO-CH3); IR (ν/cm⁻¹): 1676 (C=O); MS (EI): m/z (M+1) 203.1;Analysis (% Cal/fou) for C11H10N2O2: C: 65.34/65.04, H: 4.98/ 4.52, N: 13.85/13.25.

General procedure for the synthesis of chalcone derivatives (4a-j)

To a solution of acetophenone (3), (1.0 mmol) in dry dimethyl formamide (10 mL) was added aq KOH (5%, 10mL) and aldehydes (1.0 mmol) at -5-0°C. The resulting solutions stirred for about 4-6 h at room temperature. The reaction mixture was diluted with ice cold water, acidified with cold dilute HCl and extracted with ether. The ether layer was washed with water, dried over anhydrous Na2SO4 and the solvent was evaporated. The reaction mixture was purified by recrystallization from aq. ethanol afforded corresponding Chalcone derivatives (4a-j) in pure form.

The following compounds were synthesized using this method:

1-(2-methoxy-1,8-naphthyridin-3-yl)-3-phenylprop -2-en -1-one (4a)

Orange solid, Yield: 87%; m.p. 216-218 °C; 1H NMR (200 MHz, CDCl3): 9.23-9.28 (d, 1H, J= 6.3 Hz), 8.46 (m, 1H), 8.12-8.18(m, 1H, 1CH), 7.51-7.29 (m, 3H), 7.26-7.02 (m, 4H), 3.54 (s, 3H, OCH3); 13C NMR (200 MHz, CDCl3): 193.5(CO), 165.2, 163.8, 158.3, 154.6, 144.4,
142.2, 132.2, 128.3, 129.3, 131.2, 133.7, 131.9, 114.5 51.21 (OCH$_3$); IR (v/cm$^{-1}$); 3275 (CO); MS (EI): m/z (M+1), 291 Analysis (% Cal/fou) for C$_{18}$H$_{14}$N$_2$O$_2$, C: 74.47/ 74.21, H: 4.86/ 4.21, N: 9.65/ 9.15.

1-(2-Methoxy-[1,8]naphthyridin-3-yl)-3-p-tolyl-propenone (4b)
Orange solid (4b); Yield: 82%; m.p. 222-224°C; $^1$H NMR (200 MHz, CDCl$_3$): 9.13 (d, 1H, J= 8.0 Hz), 8.56 (bs, 1H), 8.30 (d, 1H, J= 8.0 Hz), 7.59-7.19 (m, 2H), 7.31-7.02 (m, 4H, 4CH), 6.14 (s, 1H), 3.34 (s, 3H, OCH$_3$), 2.14 (s, 3H, CH$_3$); $^{13}$C NMR (200 MHz, CDCl$_3$): 191.5 (CO), 162.2 (CH), 161.2 (CH), 148.3, 144.6, 133.4, 132.2, 131.2, 129.3, 122.3, 121.2, 119.7, 114.9, 113.5 55.21 (OCH$_3$), 22.6 (CH$_3$); IR (v/cm$^{-1}$); 1725 (CO); MS (EI): m/z (M+1) 305.3, Analysis (% Calculated/found) for C$_{19}$H$_{16}$N$_2$O$_2$ (Mwt 304.24) C: 74.98/ 74.18, H: 5.30/ 4.63, N: 9.20/ 8.65.

1-(2-Methoxy-[1,8]naphthyridin-3-yl)-3-(4-nitro-phenyl)-propenone (4c)
Light yellow solid, Yield: 78%; m.p: 228-230°C; $^1$H NMR (200 MHz, CDCl$_3$) : 9.22 (d, 1H, J=8.3 Hz), 8.71 (bs, 1H), 8.42 (d, 1H, J=8.5 Hz), 8.38 (dd, 2H, J=6.8 Hz), 7.78 (s, 1H), 7.51 (t, 1H, J=7.5 Hz) , 7.46 (d, 2H, J=8.5 Hz), 7.12 (s, 1H), 3.64 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, CDCl$_3$): 193.2 (CO), 164.2 (CH), 154.2 (CH), 146.3, 142.6, 140.4, 131.2, 130.2, 128.3, 122.3, 121.9, 118.7, 112.9, 112.5 53.21 (OCH$_3$); IR (v/cm$^{-1}$); 1725 (CO); Analysis (% Calculated/found) for C$_{18}$H$_{13}$N$_3$O$_4$ C: 64.47/ 64.38, H: 3.91/ 3.63, N: 12.53/ 12.25. MS (EI): m/z (M+1) 336.

3-(4-Chloro-phenyl)-1-(2-hydroxy-[1,8]naphthyridin-3-yl)-propenone (4d)
Light orange solid, Yield: 90%; m.p: 228-230°C; $^1$H NMR (200 MHz, CDCl$_3$) : 9.14 (d, 1H, J=8.3 Hz), 8.78 (s, 1H), 8.43(d, 1H, J=8.6 Hz), 8.38 (dd, 2H, J=6.5 Hz), 7.66 (s, 1H), 7.52 (t, 1H, J=7.5 Hz) , 7.49 (d, 2H, J=8.7 Hz), 7.14 (s, 1H), 3.68 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, CDCl$_3$): 191.2 (CO), 164.2, 153.2, 146.3, 142.6, 141.4, 131.2, 132.2, 128.3, 125.3, 121.9, 119.7, 112.9, 110.8 52.26 (OCH$_3$); IR (v/cm$^{-1}$); 1729 (CO); Analysis (% Calculated/found) for C$_{17}$H$_{11}$ClN$_2$O$_2$ C: 65.71/64.38, H: 3.57/3.27, N: 9.02/8.62. MS (EI): m/z (M+1) 311.

3-(4-Bromo-phenyl)-1-(2-methoxy-[1,8]naphthyridin-3-yl)-propenone (4e)
Light orange solid, Yield: 88%; m.p: 225-227°C; $^1$H NMR (200 MHz, CDCl$_3$) : 9.18 (d, 1H, J=8.2 Hz), 8.75 (s, 1H), 8.43 (d, 1H, J=8.4 Hz), 8.36 (dd, 2H, J=6.6 Hz), 7.76 (s, 1H), 7.52 (t, 1H, J=7.5 Hz) , 7.48 (d, 2H, J=8.5 Hz), 7.13 (s, 1H), 3.66 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, CDCl$_3$): 192.2 (CO), 163.2, 154.2, 147.3, 143.6, 141.4, 132.2, 131.2, 127.3,124.3,
123.9, 118.7, 111.9, 110.5 53.21 (OCH$_3$); IR (v/cm$^{-1}$); 1724 (CO); Analysis (% Cal/fou) for C$_{13}$H$_{15}$BrN$_2$O$_2$: 58.56/57.38, H: 3.55/3.25, N: 7.59/7.02. MS (EI): m/z (M+1) 369.

3-(4-Fluoro-phenyl)-1-(2-methoxy-[1,8]naphthyridin-3-yl)-propenone (4f)
Orange solid, Yield: 72%; m.p: 206-208 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): 9.16 (d, 1H, J=8.0 Hz), 8.72 (s, 1H), 8.23 (d, 1H, J=8.2 Hz), 7.76 (s, 1H), 7.54 (t, 1H, J=7.5 Hz) 7.36 (dd, 2H, J=6.4 Hz , 7.18 (d, 2H, J=8.5 Hz), 7.03 (s, 1H), 3.68 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, DMSO-d$_6$):195.2 (CO), 163.2 (CH), 155.2 (CH), 149.3, 147.6, 141.4, 133.2, 132.2, 129.3,124.3, 122.9, 119.7, 112.9, 111.5 48.21 (OCH$_3$); IR (v/cm$^{-1}$); 1728 (CO); Analysis (% Calculated/found) for C$_{18}$H$_{14}$FN$_2$O$_2$: 70.12/70.02, H: 4.25/3.85, N: 9.09/8.72. MS (EI): m/z (M+1) 309.

3-(4-Hydroxy-phenyl)-1-(2-methoxy-[1,8] naphthyridin-3-yl)-propenone (4g)
Off-White solid, Yield: 96%; m.p: 240-242 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): 9.20 (d, 1H, J=7.8 Hz), 8.78 (s, 1H), 8.26(d, 1H, J=8.2 Hz), 7.66 (s, 1H), 7.58 (t, 1H, J=7.5 Hz) 7.39 (dd, 2H, J=6.4 Hz , 7.28 (d, 2H, J=8.5 Hz), 7.08 (s, 1H), 4.58 (s, 1H, OH), 3.59 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, DMSO-d$_6$): 191.2 (CO), 164.2 (CH), 154.2 (CH), 146.3, 142.6, 140.4, 131.2, 130.2, 128.3,122.3, 121.9, 118.7, 112.9, 112.5 43.21 (OCH$_3$); IR (v/cm$^{-1}$); 1725 (CO); Analysis (% Calculated/found) for C$_{18}$H$_{14}$FN$_2$O$_2$: 70.58/70.22, H: 4.61/4.15, N: 9.15/8.72. MS (EI): m/z (M+1) 307.

1-(2-methoxy-1,8-naphthyridin-3-yl)-3-(pyridin-2-yl)prop-2-en-1-one (4h)
Light yellow crystals, 93.0 %; m.p: 248-250 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): 9.23 (d, 1H, J=7.8 Hz), 8.73 (d, 1H, J=7.5 Hz), 8.46 (s, 1H), 8.13 (d, 1H, J=7.3 Hz), 7.86 (s, 1H), 7.53 (t, 1H, J=6.8 Hz), 7.42-7.32 (m, 2H), 7.26-7.08(m, 2H), 3.41 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, DMSO-d$_6$): 186.5(CO), 169.2, 168.2, 159.3, 154.6, 153.4, 142.2, 141.2, 139.3,132.3, 131.2, 119.7, 116.9, 113.5 42.51 (OCH$_3$); IR (v/cm$^{-1}$); 1715 (CO); Analysis (% Cal/fou) for C$_{17}$H$_{13}$N$_3$O$_2$ (Mwt 291.2) C: 70.09/69.32, H: 4.50/ 4.23, N: 14.42/ 14.02.

1-(2-methoxy-1,8-naphthyridin-3-yl)-3-(pyridin-3-yl)prop-2-en-1-one (4i)
Light yellow crystals: Yield: 90 %; m.p: 246-248 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): 9.24 (d, 1H, J=7.8 Hz), 8.63 (d, 1H, J=7.5 Hz), 8.48 (s, 1H), 8.23 (d, 1H, J=7.3 Hz), 7.76 (s, 1H), 7.53 (t, 1H, J=6.7 Hz), 7.46-7.38 (m, 2H), 7.28-7.06(m, 2H), 3.46 (s, 3H, OCH$_3$); $^{13}$C NMR (200 MHz, DMSO-d$_6$):187.9(CO), 166.2(C-OCH3), 164.2,156.3, 154.6, 153.4, 142.2, 138.2,
136.3, 133.3, 132.2, 118.7, 116.3, 114.3 53.51 (OCH$_3$); IR (v/cm$^{-1}$); 1718 (CO); MS (EI): m/z (M+1) 292, Analysis (% Cal/fou) for C$_{17}$H$_{13}$N$_3$O$_2$ (Mwt 291.2) C: 70.09/ 69.38, H: 4.50/ 4.33, N: 14.42/ 14.12.

1-(2-methoxy-1,8-naphthyridin-3-yl)-3-(thiophen-2-yl)prop-2-en-1-one (4j)

Off-White solid, Yield: 89 %; m.p. 224-226 °C; $^1$H NMR (200 MHz, DMSO-d$_6$) : 9.18 (d, 1H, J=7.7 Hz), 8.28 (s, 1H), 8.13 (d, 1H, J=7.3 Hz), 7.73 (d, 2H, J=7.5 Hz), 7.56 (t, 1H, J=6.7 Hz), 7.46 (s, 1H), 7.26 (t, 1H, J=6.7 Hz), 6.38 (s, 1H), 3.49 (s, 3H, OCH$_3$); IR (v/cm$^{-1}$); 1715 (CO); MS (EI): m/z (M+1) 297.3, Analysis (% Cal/fou) for C$_{16}$H$_{12}$N$_2$O$_2$S (Mwt 296.54) C: 64.85/ 64.25, H: 4.08/ 4.03, N: 9.45/ 9.25.

General Procedure for the Synthesis of 1-(2-hydroxy-1,8-naphthyridin-3-yl)-3-phenyl prop-2-en-1-one (5a)

To a solution of 1-(2-methoxy-1,8-naphthyridin-3-yl)-3-phenyl prop-2-en-1-one (4a), (0.2g, 0.68 mmol) in unhydrous dichloromethane (10 mL) was added BBr$_3$ (0.25g, 1.03 mmol) by drop wise at 0°C, the resulting solution was heated to reflux for about 16h, evaporated the dichloro methane completely and purified by column chromatography, eluted with dichloromethane in methanol (9:2) to provide the title compound as offwhite solid (0.15g, 2.96 mmol, 80 %), mp. 247-249 °C; $^1$H NMR (200 MHz, DMSO-d$_6$) : 9.28 (d, 1H, J= 7.5Hz, CH), 8.66 (s, 1H), 8.25 (d, 1H, J= 6.8 Hz), 7.86 (s, 1H), 7.79 (t, 1H, J=8.0 Hz), 7.65 (d, 2H, J=12Hz), 741 (t, 2H, J=12Hz), 723 (t, 1H, J=8.0Hz), 6.64 (s, 1H, CH), 5.36 (bs, 1H, OH); $^{13}$C NMR (200 MHz, DMSO-d$_6$): 189.5(C=O), 164.2 (C-OH), 151.3, 144.6, 143.4, 142.2, 129.2, 128.3, 127.3, 125.4, 125.8, 124.8, 123.4, 122.2, 103.7; IR (v/cm$^{-1}$); 3365 (OH), 1710 (CO); MS (EI): m/z (M+1) 277, Analysis (% Cal/fou) for C$_{16}$H$_{12}$N$_2$O$_2$ (Mwt 276.29) C: 73.90 / 73.52, H: 4.38 / 4.21, N: 10.14 / 9.85.

The following compounds were synthesized using this method:

1-(2-Hydroxy-[1,8]naphthyridin-3-yl)-3-p-tolyI-propeno ne (5b)

Off-white solid, Yield: 87 %; m.p. 262-264 °C; $^1$H NMR (200 MHz, DMSO-d$_6$): 9.26 (d, 1H, J=8.2 Hz), 8.46 (s, 1H), 8.35 (d, 1H, J=6.4 Hz), 7.74 (s, 1H), 7.69 (t, 1H, J=8.2 Hz), 7.64 (d, 2H, J=12Hz), 741 (t, 2H, J=12Hz), 6.64 (s, 1H, CH), 5.36 (bs, 1H, OH), 2.54 (s, 3H, CH$_3$); $^{13}$C NMR (200 MHz, DMSO-d$_6$):189.5(C=O),167.2(C-OH),151.3,144.6,143.4, 142.2, 136.2, 133.3,129.6, 113.2, 114.5 23.21 (CH$_3$); IR (v/cm$^{-1}$); 3325 (OH), 1710 (CO); MS (EI): m/z
(M+1) 291.3, Analysis (% Ca/fou) for C$_{18}$H$_{14}$N$_2$O$_2$ (Mwt 290.1) C: 74.47 / 73.52, H: 4.86 / 4.32, N: 9.65 / 9.12.

1-(2-Hydroxy-[1,8]naphthyridin-3-yl)-3-(4-nitro-phenyl)-propenone (5c)

Off-white solid, Yield: 77 %; m.p. 232-234 °C; $^1$H NMR (200 MHz, DMSO-d6) : 9.26 (d, 1H, J=8.5 Hz), 8.36 (s, 1H), 8.25 (d, 1H, J=6.7 Hz), 7.64 (s, 1H), 7.64 (t, 1H, J=8.4 Hz), 7.48 (d, 2H, J=10Hz), 7.41 (t, 2H, J=8.7Hz), 6.68 (s, 1H), 5.38 (bs, OH); $^{13}$C NMR (200 MHz, DMSO-d6): 188.6 (C=O), 168.1 (C-OH), 161.4 (C-OCH3), 152.3, 143.6(N=C=N), 142.4, 142.5, 135.2, 132.3,125.2, 124.6, 123.2, 113.2, 114.5; IR (v/cm$^{-1}$); 3325 (OH), 1710 (CO); MS (EI): m/z (M+1) 291.3, Analysis (% Ca/fou) for C$_{18}$H$_{14}$N$_2$O$_2$ (Mwt 290.1) C: 74.47 / 73.52, H: 4.86 / 4.32, N: 9.65 / 9.12.

3-(4-Chloro-phenyl)-1-(2-hydroxy-[1,8]naphthyridin-3-yl)-propenone (5d)

Off-white solid, Yield: 77 %; m.p. 234-236 °C; $^1$H NMR (200 MHz, DMSO-d6) : 9.28 (d, 1H, J=8.5 Hz), 8.39 (s, 1H), 8.35 (d, 1H, J=6.8 Hz), 7.54 (s, 1H), 7.48 (t, 1H, J=8.4 Hz), 7.32 (d, 2H, J=12Hz), 7.47 (t, 2H, J=8.8Hz), 6.69 (s, 1H), 5.28 (bs, OH); $^{13}$C NMR (200 MHz, DMSO-d6) : 190.6 (C=O), 164.1 (C-OH), 162.4, 152.4, 146.4, 143.4, 141.5, 136.2, 130.3,125.3, 124.2, 124.8, 123.3, 122.6, 113.2; IR (v/cm$^{-1}$); 3335 (OH), 1722 (CO); MS (EI): m/z (M+1) 311; Analysis (% Cal/fou) for C$_{17}$H$_{11}$ClN$_2$O$_2$ C: 65.71 / 64.52, H: 3.57 / 3.32, N: 9.02 / 8.92.

3-(4-Bromo-phenyl)-1-(2-hydroxy-[1,8]naphthyridin-3-yl)-propenone (5e)

Off-white solid, Yield: 80 %; m.p. 236-238 °C; $^1$H NMR (200 MHz, DMSO-d6) : 9.22 (d, 1H, J=8.4 Hz), 8.36 (s, 1H), 8.31 (d, 1H, J=6.4 Hz), 7.51 (s, 1H), 7.42 (t, 1H, J=8.2 Hz), 7.31 (d, 2H, J=9.2Hz), 7.43 (t, 2H, J=8.4 Hz), 6.62 (s, 1H), 5.21 (bs, OH); $^{13}$C NMR (200 MHz, DMSO-d6) : 189.2 (C=O), 163.1 (C-OH), 161.4, 154.2, 151.6, 146.4, 144.5, 138.2, 133.3,128.3, 127.2, 126.8, 125.3, 124.6, 114.2; IR (v/cm$^{-1}$); 3325 (OH), 1710 (CO); MS (EI): m/z (M+1) 311; Analysis (% Cal/fou) for C$_{17}$H$_{11}$BrN$_2$O$_2$ C: 57.49/ 56.52, H: 3.12/ 3.02, N: 7.89 / 7.12.

3-(4-Fluoro-phenyl)-1-(2-hydroxy-[1,8]naphthyridin-3-yl)-propenone (5f)

Light yellow solid, Yield: 76 %; m.p. 218-220 °C; $^1$H NMR (200 MHz, DMSO-d6) : 9.18 (d, 1H, J=8.4 Hz), 8.32 (s, 1H), 8.26 (d, 1H, J=6.2 Hz), 7.48 (s, 1H), 7.42 (t, 1H, J=8.0 Hz), 7.28 (d, 2H, J=9.1Hz), 7.41 (t, 2H, J=8.1 Hz), 6.57 (s, 1H), 5.26 (bs, OH); $^{13}$C NMR (200 MHz, DMSO-d6) : 186.2 (C=O), 162.1 (C-OH), 160.4, 154.2, 150.6, 144.4, 143.5, 136.2,
132.3, 129.3, 128.2, 127.8, 126.3, 125.6, 112.2; IR (ν/cm⁻¹): 3322 (OH), 1716 (CO); MS (EI): m/z (M+1) 295; Analysis (% Cal/fou) for C₁₇H₁₁FN₂O₂: C: 69.38/ 68.52, H: 3.77/ 3.22, N: 9.52/ 9.12.

1-(2-Hydroxy-[1,8]naphthyridin-3-yl)-3-(4-hydroxy-phenyl)-propenone (5g)

Off-white solid, Yield: 72 %; m.p. 262-254 °C; ¹H NMR (200 MHz, DMSO-d₆): 9.13 (d, 1H, J=7.5 Hz), 8.26 (s, 1H), 8.15 (d, 1H, J=6.8 Hz), 7.54 (s, 1H), 7.34 (t, 1H, J=8.1 Hz), 7.28 (d, 2H, J=8.0 Hz), 7.11 (t, 2H, J=8.7Hz), 6.66 (s, 1H), 5.18 (bs, 2H, OH); ¹³C NMR (200 MHz, DMSO-d₆): 183.9 (C=O), 166.1 (C-OH), 159.4 (C-OH), 151.3, 148.6, 147.4, 145.5, 133.2, 131.3, 128.2, 126.6, 124.2, 113.2; IR (ν/cm⁻¹); 3328 (OH), 1720 (CO); MS (EI): m/z (M+1) 293.2; Analysis (% Calculated/found) for C₁₇H₁₁N₂O₃: C: 69.86/ 68.92, H: 4.14/ 4.01, N: 9.58/ 9.10.

1-(2-hydroxy-1,8-naphthyridin-3-yl)-3-(pyridin-2-yl)prop-2-en-1-one (5h)

Off-white solid, 94.0%; m.p. 258-260 °C; ¹H NMR (200 MHz, DMSO-d₆): 9.26 (d, 1H, J=7.2 Hz), 8.66 (s, 1H), 8.53 (d, 1H, J=6.8 Hz), 8.13 (d, 1H, J=7.3 Hz), 7.84(s, 1H), 7.56 (t, 1H, J=6.3 Hz), 7.42-7.33 (m, 2H), 7.28-7.04(m, 2H), 5.43 (s, 1H, OH); ¹³C NMR (200 MHz, DMSO-d₆): 186.5(CO), 168.2, 153.3, 148.4, 147.2, 146.7, 136.3,135.3, 134.2, 130.7, 129.9, 123.5,122.3,121.4, 112.51; IR (ν/cm⁻¹); 3345 (OH), 1735 (CO); MS (EI): m/z 278.3 (M+1), Analysis (% Calculated/found) for C₁₆H₁₁N₃O₂ (Mwt 277.28): C: 69.31/ 69.21, H: 4.00/ 3.87, N: 15.15/ 14.12.

1-(2-hydroxy-1,8-naphthyridin-3-yl)-3-(pyridin-3-yl)prop-2-en-1-one (5i)

Off-white solid, 84.0%; m.p. 262-264 °C; ¹H NMR (200 MHz, DMSO-d₆): 9.28 (d, 1H, J=7.1 Hz), 8.56 (s, 1H), 8.51 (d, 1H, J=6.7 Hz), 8.11(d, 1H, J=7.1 Hz), 7.82(s, 1H), 7.52 (t, 1H, J=6.4 Hz), 7.41-7.32 (m, 2H), 7.26-7.02(m, 2H), 5.42 (s, 1H, OH); ¹³C NMR (200 MHz, DMSO-d₆): 184.5(CO), 167.2, 152.3, 149.4, 149.9, 147.7, 135.3,134.3, 133.2, 131.7, 129.9, 122.1,122.9,121.8, 112.3; IR (ν/cm⁻¹); 3329 (OH), 1735 (CO); MS (EI): m/z 278.2 (M+1), Analysis (% Calculated/found) for C₁₆H₁₁N₃O₂ (Mwt 277.28): C: 69.31/ 69.21, H: 4.00/ 3.87, N: 15.15/ 14.12.

1-(2-hydroxy-1,8-naphthyridin-3-yl)-3-(thiophen-2-yl)prop-2-en-1-one (5j)

Off-white solid, Yield: 72 %; m.p. 234-236 °C; ¹H NMR (200 MHz, DMSO-d₆): 9.08 (d, 1H, J=7.3 Hz), 8.29 (s, 1H), 8.14 (d, 1H, J=7.3 Hz), 7.83 (d, 2H, J=7.5 Hz), 7.66 (t, 1H, J=6.3 Hz), 7.56 (s, 1H), 7.46 (t, 1H, J=6.6 Hz), 6.32 (s, 1H), 4.52 (s, 1H, OH); ¹³C NMR
(200 MHz, DMSO-d6): 193.5 (C=O), 165.2 (C-OH), 163.8, 158.3, 151.6, 144.4, 142.2, 136.2, 134.3, 129.3, 126.1, 126.9, 125.3, 124.6, 123.7, 117.9, 106.5; IR (ν/cm⁻¹): 3325 (OH), 1700 (CO); MS (EI): m/z 283 (M+1), Analysis (% Cal/fou) for C₁₅H₁₀N₂O₂S (Mwt 282.32) C: 63.81/63.67, H: 3.57/3.51, N: 9.92/9.42.

General Procedure for the Synthesis of Flavones (6a-j)

Iodine (0.1 mmol) was added to the solution of chalcone derivatives (5a-j) (1.0 mmol) in DMSO (10 mL). The mixture was refluxed for 30-60 min. The completion of reaction was monitored by TLC; the mixture was cooled, diluted with ethyl acetate and filtered. The filtrate was washed with dilute sodium thiosulphate to remove I₂ and subsequently washed with water. After evaporation of ethyl acetate, the crude mixture was purified by column chromatography using dichloromethane in methanol (9:1) eluent to afforded corresponding (6a-j) flavones.

2-Phenyl-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6a)

Off-white solid, Yield: 92%; m.p. 228-230 °C; ¹H NMR (500 MHz, DMSO-d6) : 9.17 (d, 1H, J=7.5 Hz), 8.45 (s, 1H), 7.61 (d, 1H, J=8.4 Hz), 7.46 (t, 1H, J=6.5 Hz), 7.38 (d, 2H, J= 6.1 Hz), 7.21 (t, 2H, J=6.4 Hz), 7.05 (t, 1H, J=7.1 Hz), 5.45 (s, 1H); ¹³C NMR (500 MHz, DMSO-d6) : 189.2 (C=O), 165.6, 165.2, 148.3, 146.6, 133.4, 132.2, 131.2, 129.3, 122.3, 121.2, 114.9, 98.4; IR (ν/cm⁻¹): 1755 (CO); MS (EI): m/z 275 (M+1), Analysis (% Calculated/found) for C₁₇H₁₀N₂O₂ (Mwt 274.27) C: 74.44/74.18, H: 3.67/4.23, N: 10.21/9.85.

The following compounds were synthesized using this method:

2-(4-Tolyl)-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6b)

Off-white solid, Yield: 84%; m.p. 234-236 °C; ¹H NMR (500 MHz, DMSO-d6) : 9.20 (d, 1H, J=7.4 Hz), 8.38 (s, 1H), 7.51 (d, 1H, J=8.2 Hz), 7.42 (t, 1H, J=6.5 Hz), 7.32 (d, 2H, J= 6.3 Hz), 7.23 (t, 2H, J=6.2 Hz), 7.08 (t, 1H, J=7.0 Hz), 5.48 (s, 1H), 2.32 (s, 3H, CH₃), ¹³C NMR (500 MHz, DMSO-d6) : 188.3 (C=O), 164.4, 165.6 (C-O), 148.6, 146.2, 135.4, 134.2, 130.2, 129.3, 122.5, 121.2, 118.7, 112.9, 111.5, 96.4, 24.5 (CH₃); IR (ν/cm⁻¹): 1740 (C=O); MS (EI): m/z 289.1 (M+1), Analysis (% Calculated/found) for C₁₈H₁₂N₂O₃ (Mwt 288.09) C: 74.99/73.48, H: 3.67/4.23, N: 10.21/9.85.

2-(4-Nitro-phenyl)-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6c)

Light yellow solid, Yield: 79%; m.p. 226-228 °C; ¹H NMR (500 MHz, DMSO-d6) 9.14 (d,
$^{1}$H, $J$=6.5 Hz), 8.34 (s, 1H), 7.63 (d, 1H, $J$=7.2 Hz), 7.48 (t, 1H, $J$=6.4 Hz), 7.32 (d, 2H, $J$=6.1 Hz), 7.28 (t, 2H, $J$=6.2 Hz), 5.38 (s, 1H); $^{13}$C NMR (500 MHz, DMSO-d6) : 186.4 (C=O), 166.4, 165.4 (C-O), 149.6(C-NO$_2$), 144.2, 135.2, 133.2, 131.8, 128.3,126.9, 123.2, 122.7, 112.9, 96.4; IR ($\nu$/cm$^{-1}$): 1745 (C=O); MS (EI): m/z (M+1) 320; Analysis (% Cal/fou) for C$_{17}$H$_9$N$_3$O$_4$ C: 63.95/ 63.48, H 2.84/ 2.23, N: 13.16/ 12.15.

2-(4-Chloro-phenyl)-4H-pyrano[2,3-b][1,8]naphthyridin- 4-one (6d)
Pale yellow solid, Yield: 86 %; m.p. 232-234 °C; $^1$H NMR (500 MHz, DMSO-d6) : 9.22 (d, 1H, $J$=6.4 Hz), 8.48 (s, 1H), 8.14 (d, 1H, $J$=7.2 Hz), 7.62 (t, 1H, $J$=6.1 Hz), 7.13 (t, 2H, $J$=6.2 Hz), 5.28 (s, 1H); $^{13}$C NMR (500 MHz, DMSO-d6) : 184.7 (C=O), 164.2, 164.8, 147.3, 145.6, 135.4, 134.3, 133.2, 129.3,127.5, 126.2, 123.7, 109.9, 97.4; IR ($\nu$/cm$^{-1}$): 1755 (C=O); MS (EI): m/z (M+1) 309.3; Analysis (% Cal/fou) for C$_{17}$H$_9$ClN$_2$O$_2$ C: 66.14/ 65.48, H 2.94/ 2.43, N: 9.07/8.77.

2-(4-Bromo-phenyl)-4H-pyrano[2,3-b][1,8] naphthyridin-4-one (6e)
Light yellow solid, Yield: 82 %; m.p. 223-225 °C; $^1$H NMR (500 MHz, DMSO-d6) : 9.26 (d, 1H, $J$=6.2 Hz), 8.32 (s, 1H), 8.12 (d, 1H, $J$=7.0 Hz), 7.60 (t, 1H, $J$=6.0 Hz), 7.38 (d, 2H, $J$=6.0 Hz), 7.12 (t, 2H, $J$=6.0 Hz), 5.24 (s, 1H); $^{13}$C NMR (500 MHz, DMSO-d6) : 183.3 (C=O), 165.4, 164.7, 149.2, 149.8, 135.6, 134.4, 132.2, 131.4, 128.3,127.5, 126.2, 123.7, 110.2, 99.4; IR ($\nu$/cm$^{-1}$): 1746 (C=O); MS (EI): m/z (M+2) 353; Analysis (% Cal/fou) for C$_{17}$H$_9$BrN$_2$O$_2$ C: 57.81/ 56.48, H 2.57/ 2.23, N: 7.93/ 7.15.

2-(4-Fluoro-phenyl)-4H-pyrano[2,3-b][1,8] naphthyridin-4-one (6f)
Light yellow solid, Yield: 78 %; m.p. 213-215 °C; $^1$H NMR (500 MHz, DMSO-d6) : 9.13 (d, 1H, $J$=5.6 Hz), 8.42 (s, 1H), 8.22 (d, 1H, $J$=6.3 Hz), 7.63 (t, 1H, $J$=5.1 Hz), 7.36 (d, 2H, $J$=6.0 Hz), 7.10 (t, 2H, $J$=6.0 Hz), 5.34 (s, 1H); $^{13}$C NMR (500 MHz, DMSO-d6) : 182.4 (C=O), 166.4, 165.7, 148.2, 148.8, 136.6, 135.4, 133.2, 131.4, 130.3,127.5, 123.7, 106.2, 96.4; IR ($\nu$/cm$^{-1}$): 1742 (C=O); MS (EI): m/z (M+2) 293; Analysis (% Cal/fou) for C$_{17}$H$_9$FN$_2$O$_2$ C: 69.86/ 69.18, H 3.10/ 3.05, N: 9.58/ 9.12.

2-(4-Hydroxy-phenyl)-4H-pyrano[2,3-b][1,8] naphthyridin-4-one (6g)
Off-white solid, Yield: 76 %; m.p. 252-254 °C; $^1$H NMR (500 MHz, DMSO-d6) : 9.13 (d, 1H, $J$=8.5 Hz), 8.74 (s, 1H), 7.73 (d, 1H, $J$=7.5 Hz), 7.43 (t, 1H, $J$=6.2 Hz), 7.28 (d, 2H, $J$= 6.1 Hz), 7.18 (d, 2H, $J$=6.2 Hz), 5.23 (s, 1H), 4.83 (bs, 1H, OH); $^{13}$C NMR (500 MHz, DMSO-d6) : 187.3 (C=O), 166.4, 165.2, 149.6, 147.2, 136.2, 135.2, 133.6, 134.3,128.5, 127.2, 126.7,
122.9, 109.5, 93.4; IR (v/cm\(^{-1}\)): 1746 (C=O); MS (EI): m/z (M+2) 291; Analysis (% Cal/fou) for C\(_{17}\)H\(_{10}\)N\(_2\)O\(_3\): C: 70.34/ 69.38, H: 3.47/ 3.15, N: 9.65/ 9.02.

2-(pyridin-2-yl)-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6h)

Off-white solid, Yield: 76%; m.p. 264-266 °C; \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) : 9.15 (d, 1H, J=6.2 Hz), 8.86 (d, 1H, J=6.0 Hz), 8.67 (s, 1H), 8.16 (d, 1H, J=6.0 Hz), 7.82 (t, 1H, J=6.8 Hz), 7.52-7.34 (m, 2H), 7.22 (t, 1H, J=6.5 Hz), 6.32 (s, 1H, CH); \(^{13}\)C NMR (500 MHz, DMSO-\(d_6\)) : 192.3 (C=O), 165.4 (N=C), 162.6 (C-O), 147.6, 145.2, 136.4, 134.2, 131.2, 128.3, 126.5, 124.2, 118.9, 114.9, 112.5, 96.8; IR (v/cm\(^{-1}\)) ; 1746 (C=O); MS (EI): m/z 275 (M+1), Analysis (% Calculated/found) for C\(_{16}\)H\(_9\)N\(_3\)O\(_2\): C: 69.81/ 69.48, H: 3.30/ 3.23, N: 15.27/ 15.17.

2-(pyridin-3-yl)-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6i)

Off-white solid, Yield: 78%; m.p. 261-263 °C; \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) : 9.19 (d, 1H, J=6.0 Hz), 8.72 (d, 1H, J=6.2 Hz), 8.63 (s, 1H), 8.18 (d, 1H, J=6.3 Hz), 7.85 (t, 1H, J=6.5 Hz), 7.62-7.44 (m, 2H), 7.32 (t, 1H, J=6.5 Hz), 6.23 (s, 1H, CH); \(^{13}\)C NMR (500 MHz, DMSO-\(d_6\)) : 193.3 (C=O), 166.4 (N=C-O), 164.6 (C-O), 148.6, 146.2, 139.4, 136.2, 134.2, 131.3, 128.5, 127.2, 116.9, 114.9, 113.5, 107.6, 98.8; IR (v/cm\(^{-1}\)); 1753 (CO); MS (EI): m/z 275 (M+1), Analysis (% Cal/fou) for C\(_{16}\)H\(_9\)N\(_3\)O\(_2\): C: 69.81/ 69.48, H: 3.30/ 3.23, N: 15.27/ 15.12.

2-(Thiophen-2-yl)-4H-pyrano[2,3-b][1,8]naphthyridin-4-one (6j)

Off-white solid, Yield: 73%; m.p. 252-254 °C; \(^1\)H NMR (500 MHz, DMSO-\(d_6\)) : 9.23 (d, 1H, J=6.0 Hz), 8.68 (s, 1H), 8.54 (d, 1H, J=5.8 Hz), 7.69 (d, 2H, J=5.4 Hz), 7.41-7.29 (m, 2H), 5.34 (s, 1H, CH); \(^{13}\)C NMR (500 MHz, DMSO-\(d_6\)) : 184.5 (C=O), 169.4 (N=C-O), 164.6 (C-O), 148.3, 147.6, 136.4, 135.2, 133.2, 130.8, 127.3, 126.2, 125.6, 124.7, 122.9, 112.5, 94.6; IR (v/cm\(^{-1}\)); 1756 (CO); MS (EI): m/z 281 (M+1), Analysis (% Cal/fou) for C\(_{15}\)H\(_8\)N\(_2\)O\(_3\)S (Mwt 280.3) C: 64.27/ 64.07, H: 2.88/ 2.21, N: 9.99/ 9.35.

RESULTS AND DISCUSSION

All reagents used were Aldrich or Fluka Company; and used without further purification, or were prepared according to the procedure described in the literature. Reactions were monitored by Thin layer chromatography (TLC) performed with E.-Merck precoated silica gel plates (60 F-254) visualizing with ultraviolet light or iodine vapors. Melting points were determined in Fisher-Johns apparatus and are uncorrected. IR spectra were recorded on
2-Amino pyridine-3-carboxaldehyde reacts with ethy cyanoc acetate to offord 2-hydroxy-1,8-napthyridine-3-carbonitrile\(^1\) (1), which on further reacts with methyl iodide to provide 2-methoxy-1,8-napthyridine-3-carbonitrile (2), further which on reacts with methyl magnesium iodide, yields 1-(2-hydroxy-1,8-napthyridin-3-yl)ethanone (3). Further compound (3) on reacts with different aromatic aldehydes to yields chalcones (4a-j) which on demethylated by using borantribromide (BBr\(_3\)) to yields compounds (5a-j) which on cyclisation by using I\(_2\) as catalyst furnished cyclised pyranone compounds\(^2\) (6a-j).

**Scheme 1**

Scheme 1. Synthesis of 2-Aryl-4H-pyran[2,3-b][1,8]naphthyridin-4-ones (6a-j). Reagents and conditions: (i) Ethy cyanoc acetate/ Piperidine/ Ethanol (ii) CH\(_3\)I/ K\(_2\)CO\(_3\)/DMF, (iii) CH\(_3\)Mgl (2.0 eq),THF/-78°C - Rt/ 2h (iv) Ar-CHO / DMF,Rt 2h, (v) BBr\(_3\)/ DCM, (vi) I\(_2\)/ DMSO

**Antimicrobial Evaluation**

The Pyranone derivatives (6a-j) were evaluated for their *in vitro* growth inhibitory activity against different microbes. The bacterial strains used were *Staphylococcus aureus*, *Streptococcus mutans* and *Bacillus subtilis* (all Gram positive) and *Ecscherichia coli,*
Salmonella typhi and Pseudomonas aeruginosa (all Gram negative). For testing the antifungal activity of the synthesized compounds the fungal strains Candida albicans, Aspergillus flavus and Aspergillus niger were used. The inhibition zones of synthesized compounds were determined using disc diffusion method. In this method, paper disks (6 mm) containing specific amounts of an antimicrobial agent (300 µg for the synthesized compounds) were placed on the surface of an agar plate inoculated with a standardized suspension of the microorganisms tested. The plates were incubated at 35°C for 24 and 48 h, respectively for bacteria and fungi. Ampicillin (10 µg) for Gram positive bacteria, Nalidixic acid (30 µg) for Gram negative bacteria, Amphotericin B (30 µg) for fungi, were used as standard drugs. Paper disks with only DMSO were utilized as negative control. All experiments were carried out three times and the average reading was taken. The inhibition zones produced by the various synthesized compounds on the microbial growth were measured (diameter in mm). The data on antimicrobial activity of compounds (6a-j) are shown in Table-1&2.

The results of antimicrobial studies of newly synthesized compounds reveal that the compounds possess significant antibacterial activities. In general, the inhibitory activity against the Gram-positive bacteria was higher than that of the Gram-negative bacteria. Compounds 6d, 6e, 6f and 6g with chloro, bromo fluoro, and hydroxyl substitutions at the 4-position of 2-Phenyl-4H-pyrano subunit were found to be most potent compounds of the series with antibacterial activity higher than that of standard drug i.e., Nalidixic acid against S. aureus and B. subtilis. The Compounds 6a, 6b, 6c and 6j phenyl, methyl and nitro substituents on phenyl ring at 2-Phenyl-4H-pyrano subunit moiety of final compounds displayed moderate activities against S. aureus and B. subtilis. The outstanding properties of this new class of antibacterial substances deserve further investigation in order to clarify the mode of action at molecular level, responsible for the activity observed. More extensive study is also warranted to determine additional physicochemical and biological parameters to have a deeper insight into structure-activity relationship and to optimize the effectiveness of this series of molecules. As can be seen in Table-2, although all the compounds are not as active as standard Amphotericin B, compounds 6a and 6g were found to be more active against Candida albicans and Aspergillus flavus. Again in antifungal activity compounds 6c 6h, 6i and 6j showed less or negligible activity than the other derivatives of the same series. Although the rest of the compounds showed varying degree of inhibition, none were as effective as Amphotericin B.
Table-1 Antimicrobial activity of 2-Aryl-4H-pyrano [2,3-b][1,8] naphthry di-4-ones (6a-j) (Inhibition Zone in mm)

<table>
<thead>
<tr>
<th>Antibacterial activity</th>
<th>Gram-positive bacteria</th>
<th>Gram-negative bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Compound</strong></td>
<td><em>S.aureus</em></td>
<td><em>S. mutans</em></td>
</tr>
<tr>
<td>6a</td>
<td>32</td>
<td>20</td>
</tr>
<tr>
<td>6b</td>
<td>35</td>
<td>18</td>
</tr>
<tr>
<td>6c</td>
<td>33</td>
<td>16</td>
</tr>
<tr>
<td>6d</td>
<td>36</td>
<td>18</td>
</tr>
<tr>
<td>6e</td>
<td>38</td>
<td>16</td>
</tr>
<tr>
<td>6f</td>
<td>38</td>
<td>13</td>
</tr>
<tr>
<td>6g</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
<td>6h</td>
<td>32</td>
<td>13</td>
</tr>
<tr>
<td>6i</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>Ampicillin&lt;sup&gt;b&lt;/sup&gt;</td>
<td>38</td>
<td>22</td>
</tr>
<tr>
<td>Nalidixic acid&lt;sup&gt;b&lt;/sup&gt;</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

<sup>−</sup>Indicates bacteria are resistant to the compound.

<sup>a</sup>Values are mean (n = 3)

<sup>b</sup>Ampicillin (10 µg/disc) and Nalidixic acid (30 µg/disc) used as positive reference; synthesized

Compounds (300 µg/disc)

‘−’ indicates no sensitivity or mean inhibition zone diameter lower than 7 mm

Table 2. Antifungal activity of compounds (6a–6j).

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Candida albicans</th>
<th>Aspergillus niger</th>
<th>Aspergillus flavus</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>26</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>6b</td>
<td>22</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>6c</td>
<td>19</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>6d</td>
<td>20</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>6e</td>
<td>21</td>
<td>20</td>
<td>22</td>
</tr>
</tbody>
</table>

<sup>a</sup>Mean zone inhibition (in mm)

<sup>b</sup>Values are mean (n = 3)
CONCLUSION
In conclusion, a series of novel 2-Aryl-4H-pyran-2,3-b[1,8] naphthyridin-4-ones (Flavone derivatives) (6a-6j) were systematically designed and synthesized using Friedlander condensation. The antimicrobial activity of these compounds was evaluated against various Gram-positive, Gram-negative bacteria and fungi. Among the synthesized compounds, almost all compounds showed good activity against bacteria and moderate activity against fungi and emerged as potential molecules for further development.

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