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Design, synthesis, and antitubercular evaluation of novel series of 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanone and 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridin analogs

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ABSTRACT

Twenty-eight newer 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanone and 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridin analogs were synthesized by microwave irradiation method and evaluated for *in-vitro* and *in-vivo* antitubercular activity against multidrug-resistant *M. tuberculosis* stains. Structure–activity relationship study was carried out and found NO_2 (*o*) substituted 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridin was most potent antitubercular agent against *M. tuberculosis*, even better than standard drug isoniazid and comparable with rifampin. Other synthesized compounds **7j**, **7f**, **7a**, **7e** and **5d**, **5f** were found moderate to good activity in *in-vitro* model at lower IC_{50} values 85 μM, 154 μM, 157 μM, 164 μM, 170 μM and 190μML respectively. In *in-vivo* animal model compound **7j** was drastically reduced the bacterial load in lung and spleen tissues at the dose of 25 mg/kg body weight.

1. Introduction

Mycobacterium tuberculosis, the causative agent of tuberculosis (TB), is the greatest single infection cause of higher mortality worldwide; roughly two million peoples were killed by tuberculosis every year [1]. In addition; HIV-1 and 2 infections has been a major factor in the actual resurgence of tuberculosis [2]. Multidrug-resistant (MDR) strains of *M. tuberculosis* are another problem of antitubercular chemotherapy, two most effective chemotherapeutic agents, rifampin and isonicotinic acid hydrazide (INH) are to be resistant against *M. tuberculosis* [3]. Moreover, strains that are even more resistant than MDR, so-called extensively drug resistant (XDR) [4]. So there is a pressing need for new chemotherapeutic agents to combat the emergence of drugs resistance and shorten duration of treatment to improve the patient compliances. Nalidixic acid is the first lead quinolone antibiotic use in UTIs. Recently, quinolone analogs have been examined for different mycobacterial infections [5] as a result gatifloxacin and moxifloxacin are in last stage of antitubercular drug discovery pipeline, shortly FDA will approve gatifloxacin and moxifloxacin as antitubercular agents [6]. Pyridine ring is another heterocyclic interest has been present in isoniazid (INH), which was first reported as a potent antitubercular agent in 1952. Recent chemotherapy of tuberculosis, isoniazid and rifampin are the key components of first-line treatment of tuberculosis. The modification of pyridine and quinolone rings contributing broad-spectrum antimicrobial and potent antitubercular activity [7]. In recent years, 1,3,5 trisubstituted pyrazole bearing benzofuran derivatives were exhibited broad-spectrum antimicrobial activities [8,9,10,11]. Pyrazoline containing substituted benzofuran exhibited remarkable antitubercular activity [6,12,14]. All those finds, we inspired to design and synthesize different benzofuran pyrazoline containing pyridine and quinolone rings and examined for their *in-vitro* and *in-vivo* antitubercular activities. 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanones (**5a**–**5n**) and 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridins (**7a**–**7n**) are the great combination of pyrazoline, benzofuran with pyridine and quinolone rings. These types of novel ring systems have not been studied yet as antitubercular agents against multidrug-resistant *M. tuberculosis*.

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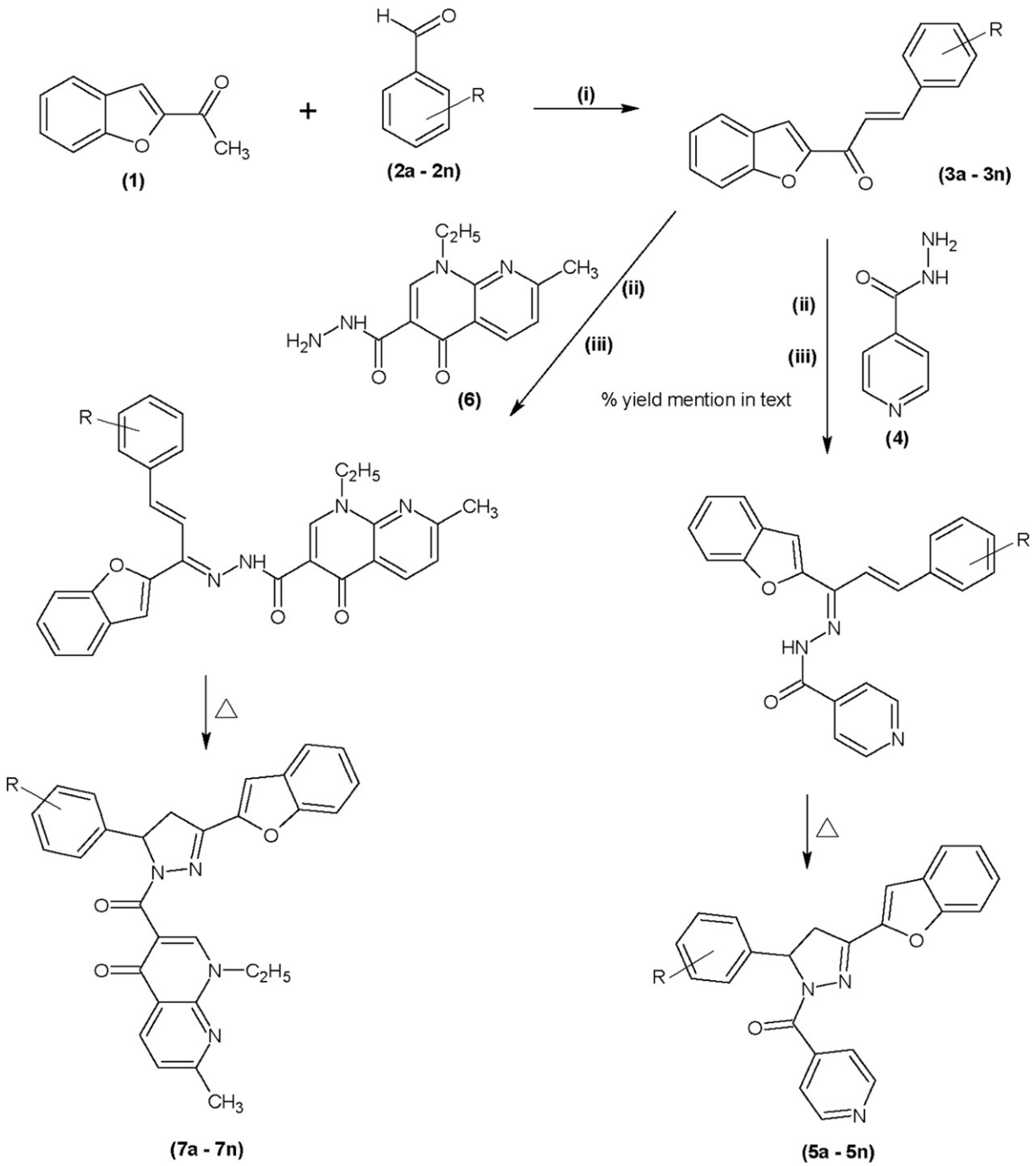
2. Chemistry

The moisture-sensitive reactions were carried out under nitrogen atmosphere. Most of the solvents and all reagents were obtained from commercial sources and used without further purification. All dry solvents were prepared according to standard procedures and stored over molecular sieves. First crucial intermediates 1-benzo[b]furan-2-yl-3-phenyl-2-propen-1-ones (chalcone) **3a**–**3n** were synthesized from 2-acetyl benzofuran **1** with various aromatic aldehydes **2a**–**2n**. The chalcones were further treated with two different hydrazides (isonicotinic acid hydrazide **4** and nalidixic acid hydrazide **6**) to give corresponding final compounds 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanones **5a**–**5n** and 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridins **7a**–**7n** (Scheme 1). Microwave irradiation method was adapted for the synthesis of all compounds to reduce the reaction time and better yield. Nalidixic acid hydrazide **6** was prepared from ester derivative of nalidixic acid as described [7].

3. Pharmacology

3.1. In-vitro antitubercular activity

The *in-vitro* antitubercular activity was performed by measuring the growth of *M. tuberculosis* ($H_{37}RV$) using *Lowensteine Jensen*



Scheme 1. Synthetic pathway of compounds **5a**–**5n** and **7a**–**7n**. Reagents and conditions: (i) EtOH, 10% KOH/20% NaOH sol., M.W.10–25 min. (ii) CH_3COOH. 6–10 h. (iii)CH_3COOH, M.W., 12–22 min.

medium (*L. J. medium*) [15,16]. Briefly, eggs were broken aseptically to obtain 200 mL of egg solution. The solution was filtered through a sterile muslin cloth into a sterile conical flask containing glass beads. Sterilized mineral salt solution (120 mL) (consisting of 4.0 g potassium phosphate, 0.4 g of magnesium sulfate, 1.6 g magnesium citrate, 6.0 g of asparagine, 20 mL of glycerol, distilled water makeup upto 1000 mL) and 4 mL of sterilized malachite green solution (2.0%) were added to the 200 mL of egg solution. The contents were mixed well to form a uniform medium. Compounds (10 mg) were dissolved in 10.0 mL of dimethyl sulfoxide (DMSO) and were diluted with DMSO to make 250 μg/mL and 10 μg/mL stock solutions. A 0.8 mL aliquot of each concentration was transferred into different McCartney bottles. To this, 7.2 mL of *L. J. medium* was added and mixed well. Isoniazid and rifampin (10 mg) were chosen as the standard drugs for the comparison of antitubercular activity. The drug was dissolved in DMSO and diluted as described above. The bottles were incubated at 75–80 °C for 3 days for solidification and sterilization.

Procedure for inoculation: A sweep from multidrug-resistant $H_{37}Rv$ strain of *M. tuberculosis* culture was transferred with the help of 22 S.W. nichrome wire loop of 3 mm external diameter into a sterile bijou bottle containing six 3 mm glass beads and 4 mL of sterile distilled water. Each loop of culture delivered approximately 4 mg of bacilli cells. The bottle was shaken with the help of vertex mixture for 2 min. The suspension was inoculated on the surface of each *L. J. medium* containing test compounds using 27 S.W.G nichrome wire loop of 3 mm external diameter and *L. J. medium* containing isoniazide and rifampin. The medium containing DMSO (control) was inoculated with the test organism for positive and negative controls. Medium without any test compound/DMSO was also inoculated with the test organism to check whether the media supports the growth of the tubercle bacilli or not. The inoculated bottles were incubated at 37 °C for 6 weeks, at the end of which readings were taken. Bacterial counts were measured and compared with the standard drugs and controls (vehicle-treated). *In-vitro* antitubercular activity was examined for all the synthesized compounds (**5a**–**5n** and **7a**–**7n**) and found satisfactory activity by measuring the growth of multidrug-resistant *M. tuberculosis* ($H_{37}RV$). The MICs of the compounds were obtained a satisfactory range at 85.45 μg/mL to 240.5 μg/mL. Compounds **5d**, **5f**, **5a**, **5g**, **7a**, **7e**, **7j** and **7g** were found moderate to good *in-vitro* antitubercular activity in Table 1. Among all the synthesized compounds, **7j** and **5d** exhibited maximum *in-vitro* antitubercular activity against both MTB and MDR-TB which could be compared with standard drugs. Rests of compounds were found moderate to low antitubercular activity.

3.2. In-vivo antitubercular activity

In-vivo antitubercular activity was examined in selective 6-week-old female CD-1 mice models against MTB at a dose of 25 mg/kg body weight, six animals per group. The stain was administered intravenously through the caudal vein with 10^6 to 10^7 viable *M. tuberculosis* ATCC 35801 [17]. Test drugs were administered by intra-peritoneal route initiated after 10 days of inoculation. After thirty-five days, the spleen and right lung were aseptically removed and grounded in a tissue homogenizer. The numbers of viable organisms were determined by serial 10-fold dilution and subsequent inoculation onto 7H10 agar plates. Cultures were incubated at 37 °C in ambient air for upto 6 weeks prior to the counts. Bacterial counts were measured and compared with the standard drugs and negative control (vehicle-treated). The bacterial load in lung and spleen tissues was reduced, when animals were treated with test drugs mention in Table 2. Compounds **7e**, **7a**, **7n** and **5d** were found to be most promising in reducing of bacterial count in lung and spleen tissues, which comparable with standard drug and control.

Table 1
In-vitro antitubercular activity and cytotoxic results of all the compounds against MTB and MDR-TB.

Name of comp.	–R	Results against MTB[a]	Results against MDR-TB[b]	IC_{50}[c] (μM)
		MIC (μg/mL)	MIC (μg/mL)	
5a	–OH (o)	3.7	6.2	>195.2
5b	$-OCH_3$ (o)	6.5	5.7	>202.4
5c	$-N(CH_3)_2$ (p)	9.2	11.5	>210.7
5d	–COOH (o)	2.2	3.2	>170.9
5e	$-NO_2$ (m)	7.5	6.9	>240.5
5f	–OH (o), OCH_3 (p)	3.3	4.5	>190.7
5g	–OH (p)	4.5	6.2	>200.3
5h	–Cl (p)	11.5	10.6	>220.7
5i	–Cl (o)	10.6	9.5	>210.6
5j	$-NO_2$ (o)	8.2	7.5	>245.4
5k	$-OCH_3$ (p)	6.8	5.5	>200.3
5l	–H	8.5	9.5	>209.6
5m	Furan Ring	9.6	10.4	>208.4
5n	–CH=CH–Ar	8.6	7.5	>212.2
7a	–OH (o)	1.2	6.4	>157.6
7b	$-OCH_3$ (o)	5.5	8.5	>187.5
7c	$-N(CH_3)_2$ (p)	9.2	10.6	>206.8
7d	–COOH (o)	4.5	7.8	>196.4
7e	$-NO_2$ (m)	2.3	3.7	>164.5
7f	–OH (o), OCH_3 (p)	4.2	5.4	>154.4
7g	–OH (p)	3.2	3.8	>148.5
7h	–Cl (p)	8.3	6.3	>160.5
7i	–Cl (o)	7.8	8.4	>178.4
7j	$-NO_2$ (o)	1.9	3.6	>85.4
7k	$-OCH_3$ (p)	6.3	8.5	>156.5
7l	–H	9.8	10.8	>210.4
7m	Furan Ring	7.5	8.5	>185.5
7n	–CH=CH–Ar	5.5	7.4	>168.6
Rifampin		0.60	4.2	>74.5
Isoniazid		0.32	8.5	>130.5

[a] *M. tuberculosis* stain $H_{37}RV$.
[b] Multidrug-resistant *M. tuberculosis.*
[c] Cytotoxicity in VERO cell line.

3.3. MICs determination

The minimum inhibitory concentrations (MICs) were determined for all the test drugs using fresh colonies of *M. tuberculosis* $H_{37}RV$. Fresh colonies were collected and suspended in distilled water; the turbidity of the suspension was adjusted with distilled water to match with standard 1 mg/mL suspension of *M. bovis* BCG (containing approximately 10^8 cfu per mL) [18]. The suspension was further diluted to 10^{-1} and 10^{-2} mg/mL. The MICs were measured using 10% oleic acid–albumin–dextrose–catalase-enriched 7H11 agar medium. All the test compounds, rifampin, and gatifloxacin (standard drugs) were dissolved and diluted with dimethyl formamide (DMF). One volume of drug solution was added to 99 volumes of culture medium, and made two fold dilutions, final concentration of test drugs and standards were in the range between 14 μg/mL to 0.12 μg/mL. The bacterial suspensions were plated in duplicate on both drug-free and drug-containing media. The result of MICs of all the test drugs and standard drugs were reported in Table 1.

3.4. Cytotoxicity study

Cytotoxic study was carried out for finding drug toxicity (IC_{50}) in a mammalian Vero cell line [19] at the concentration of 50 mg/mL. After 72 h of exposure, the viability was assessed on the basis of

Table 2
In-vivo antitubercular activities of all the synthesized compounds against *M. tuberculosis* ATCC 35801 in mice.

Name of comp.	−R	Lungs (log cfu ± SEM)	Spleen (log cfu ± SEM)
5a	−OH (o)	7.2 ± 0.12	9.45 ± 0.22
5b	$-OCH_3$ (o)	9.65 ± 0.24	10.6 ± 0.24
5c	$-N(CH_3)_2$ (p)	14.4 ± 0.56	15.8 ± 0.38
5d	−COOH (o)	6.24 ± 0.16	5.42 ± 0.22
5e	$-NO_2$ (m)	10.8 ± 0.42	11.6 ± 0.36
5f	−OH (o), OCH_3 (p)	6.98 ± 0.19	6.52 ± 0.15
5g	−OH (p)	7.46 ± 0.18	8.20 ± 0.20
5h	−Cl (p)	13.8 ± 0.21	12.4 ± 0.24
5i	−Cl (o)	12.5 ± 0.26	12.2 ± 0.22
5j	$-NO_2$ (o)	9.5 ± 0.18	10.5 ± 0.26
5k	$-OCH_3$ (p)	8.6 ± 0.16	9.24 ± 0.22
5l	−H	9.4 ± 0.21	10.6 ± 0.24
5m	Furan Ring	11.4 ± 0.22	12.6 ± 0.26
5n	−CH=CH−Ar	10.8 ± 0.21	11.6 ± 0.22
7a	−OH (o)	4.11 ± 0.62	5.36 ± 0.31
7b	$-OCH_3$ (o)	6.87 ± 0.27	6.13 ± 0.52
7c	$-N(CH_3)_2$ (p)	4.82 ± 0.42	6.53 ± 0.33
7d	−COOH (o)	5.12 ± 0.28	6.16 ± 0.36
7e	$-NO_2$ (m)	2.65 ± 0.43	3.25 ± 0.28
7f	−OH (o), OCH_3 (p)	8.42 ± 0.38	9.28 ± 0.24
7g	−OH (p)	5.49 ± 0.31	7.21 ± 0.22
7h	−Cl (p)	11.52 ± 0.23	12.12 ± 0.43
7i	−Cl (o)	10.85 ± 0.46	10.96 ± 0.21
7j	$-NO_2$ (o)	5.67 ± 0.22	6.12 ± 0.33
7k	$-OCH_3$ (p)	9.32 ± 0.42	10.77 ± 0.29
7l	−H	12.23 ± 0.37	12.98 ± 0.27
7m	Furan Ring	9.66 ± 0.38	10.52 ± 0.37
7n	−CH=CH−Ar	4.61 ± 0.12	6.32 ± 0.19
Control		8.24 ± 0.21	9.42 ± 0.19
Rifampin (25 mg/Kg)		3.21 ± 0.11	3.98 ± 0.09
Isoniazid (25 mg/Kg)		4.62 ± 0.10	5.45 ± 0.12

cellular conversion of [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] (MTT) into a formazan product using Promega Cell Titer 96 non-radioactive cell proliferation assay [20]. Cytotoxicity was reported in Table 1. Most of the tested compounds were found to be non-toxic in Vero cell line assay; compounds with nitrogen containing (**5e**, **5j** and **7e**, **7j**) showed 72–75% toxicity in Vero cell line.

3.5. Statistical analysis

The viable counts were converted to logarithms, which were then evaluated by a one-way ANOVA followed by a multiple comparison analysis of variance by a one-way Tukey test (SigmaStat software program). Differences were considered significant at the 95% level of confidence.

4. Results and discussion

The structures of the synthesize compounds were established on the basis of spectroscopic analysis. In ^{1}H NMR spectra, the signals of the individual protons of the drugs were verified by their chemical shifts, multiplicities and coupling constants. The structure of isonicotinic acid hydrazide **4** was established by IR peaks at 3366 cm^{-1} for NH, 1679 cm^{-1} for C=O, 1492 cm^{-1} for C=N. In ^{1}H NMR a sharp peak at 8.12 ppm was recorded for N**H**NH_2 (s, 1H) and 5.73 ppm (s, 2H) for NHN**H$_2$** were found and confirmed the hydrazide ring. The $NHNH_2$ characterized peaks were absent in final structure, in IR peaks at 3121–2963 cm^{-1} were recorded for aromatic CH starching, 1686 cm^{-1} for C=O and 1622, 1517 cm^{-1} for C=N and C=C in pyrazoline ring following peaks confirmed the structure of pyrazoline ring. In ^{1}H NMR, a sharp peaks at 7.23 ppm was recorded for one proton of furan (s, 1H), 6.30–5.8 ppm for CH of pyrazoline (m, 1H) and 3.6–4.00 ppm for CH_2 of pyrazoline (m, 2H) for the evidence of pyrazoline ring. The structure of compound **5a** was confirmed by ^{13}C NMR peaks at 34.7 (CH_2 in pyrazole ring), 167.4 (isonicotinic ring), 158.8, 152.6, 125.5 (C in benzofuran ring), 124.8, 122.6, 110.7, 15.5 (CH in benzofuran ring) and molecular ion peak of **5a** in mass spectra (FAB) was found identical with actual molecular weight of the compound at 383.98 (m + 1) and base peak was recorded at 145.20 (100%). Another thirteen derivatives of 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanone **5b**–**5n** were established similar way. Second series of 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridins were characterized by satisfactory spectral data. In second series compound **7a** was characterized by IR peak at 3368 cm^{-1} for OH(*o*) group in phenyl ring, other peaks like 3118–2952 cm^{-1} for aromatic CH, 1680 cm^{-1} for C=O, 1626 cm^{-1} for C=N, Pyrazoline, 1483–1448 cm^{-1} for aromatic C=C, 1352–1171 cm^{-1} for C–O, str. In ^{1}H NMR peaks were reconfirmed the structure at 10.12 ppm (s, OH) for hydroxyl one proton, 8.86 ppm peak was found for H-6 in naphthyridin ring (d, 1H, $J_{6\text{-}5} = 7.3$), 7.43 ppm for furan one proton (s, 1H), 6.32–5.84 ppm for CH of pyrazoline (m, 1H,) and 3.6–4.20 ppm for CH_2 of pyrazoline (m, 2H) established the structure of pyrazoline, 4.36 ppm (s, 2H), 2.32 ppm (s, 2H), 1.3 ppm (s, 3H) were also found for C_2H_5 group at C-1 position in naphthyridin ring. In ^{13}C NMR peaks were found like 180.27, 171.21, 164.63 (isonicotinic ring), 152.34, 143.77, 137.22, 133.81, 128.82, 123.26, 110.2, 106.8, 98.73, 45.7, 34.77 (CH_2 in pyrazole ring), 24.23, 14.27 (CH in benzofuran ring) were help to reconfirm the structure. In MS (FAB) *m*/*z* was found at 492.53 (m$^+$), which was same with actual molecular weight of the compound **5a** and 100% base peak of important fragment was recorded at 145.22 (100%). Another thirteen derivatives of 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridin **7b**–**7n** were interpreted and characterized similar way like **7a**. The elementals analysis confirmed the purity of the compounds, theoretical percentages were found similar ±0.4% with experimental elementals data.

5. Structure–activity relationships

The structure-activity relationship (structure-MTB/MDR activity) study demonstrated that, 2-[3-benzo[b]furan-2-yl-1-(2,3-dihydro-4-pyridinylcarbonyl)-4,5-dihydro-1H-5-pyrazolyl] phenyl derivatives (**5a-5n**) and 3-(3-benzo[b]furan-2-yl-5-phenyl-4,5-dihydro-1H-1-pyrazolylcarbonyl)-1-ethyl-7-methyl-1,4-dihydro [1,8]naphthyridin-4-one derivatives (**7a-7n**) exhibiting good to moderate antitubercular activity. The naphthyridin ring is more favorable group then pyridinylcarbonyl ring for the potent activity. The antitubercular activity was found by synthesized compounds, may be due to formation of free isonicotinoyl-NAD complex, which may be responsible for the inhibition of mycobacterium cell wall biosynthesis [13]. Carboxylic group containing compound **5d** was found more active against multidrug-resistant *M. Tuberculosis*. Hence, the acidic medium is favorable for the formation of isonicotinoyl-NAD complex, which produced by carboxylic group. The electron-withdrawing group (-NO_2 groups) containing naphthyridine ring (compound **7j**) produced better activity than presence of halogen, furan and other groups in same ring system. Nitro derivatives of pyrazoline containing benzofuran with naphthyridine or pyridines are highly favorable moieties for antitubercular activity.

6. Conclusion

In conclusion, the *in-vitro* and *in-vivo* antimycobacterial activity of the novel series of 3-benzofuran-5-aryl-1-pyrazolyl-pyridylmethanones and 3-benzofuran-5-aryl-1-pyrazolylcarbonyl-4-oxo-naphthyridin analogs were a new chemical classes endowed

with high antitubercular activity towards MDR-TB, exhibiting MICs values between 85 μg/mL to 240 μg/mL. The potency, selectivity and low cytotoxic compounds were valid leads for better antitubercular activity.

7. Experimental protocols

Microwave assisted synthetic routes were adopted for synthesizing all the compounds using microwave synthesizer, Synthon-3000, Anton Paar. Melting points were determined in one end open capillary tubes on a Buchi-530 melting point apparatus and were uncorrected. An infrared spectrum (FTIR) was recorded in Shimadzu-FTIR 8300 using KBr. Mass spectra, ^{1}H NMR and elemental analysis data were recorded using Joel-GSX 400 m, Advance Bruker (300 MHz) in DMSO-d_6 using TMS as an internal standard, Perkin–Elmer 2400 Series II analyzer respectively. ^{13}C NMR spectra were recorded in Bruker Aspect 300. The purity of compounds was confirmed by thin layer chromatography (TLC) using silica gel G glass plates and various solvent systems. The spots were visualized in iodine vapor. Elemental analysis results were reordered for C, H and N in the range of ±0.4% of the theoretical value. Chemicals and solvents were procured from E. Merck, SD-Fine, India, Sigma–Aldrich, USA, and Ranbaxy, India.

7.1. Synthesis of benzofuran chalcones **3a**–**3n**

Benzofuran chalcones were synthesized according to reported methods from 2-acetyl benzofuran and various aromatic aldehydes [21,22,23].

7.1.1. Microwave assisted synthesis of benzofuran chalcones **3a**–**3n**

2-acetyl benzofuran (0.05 mol) **1** and different aromatic aldehydes (0.05 mol) **2a**–**2n** were dissolved in 98% ethanol (2 mL) and added 10% KOH solution (1 mL) into the 5 mL polystyrene containers and then close the containers tightly with lids and live to exposed in microwave irradiation using 130 °C with 10 bar pressure for 10 min. at microwave synthesizer. Excess of solvent was removed under reduced pressure. The reaction solution was poured into 10 mL ice cold water and acidified with conc. HCl. and solid was separated by filtration.

7.2. Synthesis of 3-[(chlorooxy) carbonyl]-1-ethyl-7-methyl-1,8-naphthyridin-4(1H)-one [7,24]

Nalidixic acid (1 g) was taken into a dry 100 mL iodine flask, and then added 2 mL of thionyl chloride through dropping funnel. The thionyl chloride was added drop by drop inside the fuming hood with suitable air circulation. The reaction mixture was then kept in room temperature for 30 min for completing the reaction. Without separated and purified the acid chloride derivative of nalidixic acid was immediately used for the preparation of ester derivative using 2 mL of methanol. Methanol was added drop by drop with constant stirring in fuming hood with great care. Reaction mixture was then transferred into the 5 mL polystyrene containers and then exposed in microwave irradiation using 80 °C with 10 bar pressure for 6 min at microwave synthesizer. Ester derivatives was then poured into 10 mL ice cold water and extracted with diethyl ether.

7.3. Synthesis of 1-ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carbohydrazide [7,24]

0.005 mol amount of ester derivatives of nalidixic acid was equally distributed into the 5 mL polystyrene containers then added 0.02 mol of hydrazine hydrate through micropipette drop by drop, then close the container tightly with lids and live to exposed in microwave irradiation using 78 °C with 10 bar pressure for 4 min. at microwave synthesizer. After completing the reaction, the reaction mixture was poured into ice cold water. A yellowish-orange solid was separated immediately. Yield: 92%, m.p.: 217–219 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): I.R. (KBr): 3309 (Amide NH), 3205(NH_2), 1936, 1697, 1616 (C=O), 1496 (Ar. C=C), 1352 (C–N), 1255, 1220, 744; ^{1}H NMR (300 MHz, $CDCl_3$): 8.86 (d, 1H, $J_{6-5} = 7.30$, H-6), 8.65 (m, 1H, H-19), 7.73 (s, 1H, H-10), 6.80 (d, 1H, $J_{5-6} = 7.30$, H-5), 4.52 (q, 2H, $J_{11-12} = 6.80$, H-11), 2.70 (s, 3H, H-13), 1.40 (t, 3H, $J_{12-11} = 6.80$, H-12).

7.4. Synthesis of 2-[3-benzo[b]furan-2-yl-1-(2,3-dihydro-4-pyridinylcarbonyl)-4,5-dihydro-1H-5-pyrazolyl] phenyl derivatives (**5a**–**5n**) [23]

General procedure for the synthesis of 2-[3-benzo[b]furan-2-yl-1-(2,3-dihydro-4-pyridinylcarbonyl)-4,5-dihydro-1H-5-pyrazolyl] phenyl derivatives from different benzofuran chalcones (0.01 mol) and isoniazide (0.02 mol) were dissolved in 2 mL of glacial acetic acid into 5 mL polystyrene containers and then kept into the microwave synthesizer at 110 °C with 10 bar pressure for 12 min. Reactions were monitored by TLC using benzene and ethyl acetate (3:2 ratio) mobile phase system. The excess of solvent was evaporated under reduced pressure using rotary evaporator and resulting solution was poured in ice cold water with constant stirring. Solid was separated by vacuum filtration and recrystallized from suitable solvent.

7.5. Synthesis of 3-(3-benzo[b]furan-2-yl-5-phenyl-4,5-dihydro-1H-1-pyrazolylcarbonyl)-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one derivatives (**7a**–**7n**) [23]

General procedure for the synthesis 3-(3-benzo[b]furan-2-yl-5-phenyl-4,5-dihydro-1H-1-pyrazolylcarbonyl)-1-ethyl-7-methyl-1,4-dihydro[1,8]naphthyridin-4-one derivatives from benzofuran chalcones (0.01 mol) and nalidixic acid hydrazide (0.02 mol) were dissolved in 2 mL of glacial acetic acid into 5 mL polystyrene containers and then kept into the microwave synthesizer at 120 °C with 10 bar pressure for 14 min. Reactions were monitored by TLC using benzene and ethyl acetate (3:2 ratio) mobile phase system. The excess of solvent was evaporated under reduced pressure using rotary evaporator and resulting solution was poured in ice cold water with constant stirring. Solid was separated by vacuum filtration and recrystallized from suitable solvent.

Synthesized compounds and their spectral data are summarized below. FTIR, ^{1}H NMR, ^{13}C NMR, MS, and other data for characterization the structures.

7.6. 3-Benzo[b]furan-2-yl-5-(2-hydroxyphenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5a**)

Yield: 88%, m.p.: 145–146 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3373 (O–H str.), 3121–2963 (Ar-CH), 1686 (C=O), 1622 (C=N, Pyrazoline), 1517 (C=C), 1454 (Ar), 1345, 1169 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.92 (s, OH), 8.2 (m, 6H, $J = 3.43$, 6.3 Hz, Ar-H), 7.79 (dd, 2H, $J = 3.41$, 6.2 Hz), 7.75–7.39 (m, 12H, Ar-H), 7.23 (s, 1H, Furan-H), 6.30–5.8 (m, 1H, CH of pyrazoline), 3.6–4.00 (m, 2H, CH_2 of pyrazoline), 2.3 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.25, 158.21, 152.27, 150.56, 144.98, 131.45, 128.65, 122.5, 106.92, 45.52, 34.74; MS (FAB) m/z: 383.98 (m + 1), 145.20 (100%). Anal. calcd. for $C_{23}H_{17}N_3O_3$, C: 72.05, H: 4.47, N: 10.96%; found: C: 72.35, H: 4.42, N: 10.16%.

*7.7. 3-Benzo[b]furan-2-yl-5-(2-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5b**)*

Yield: 82%, m.p.: 120–121 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 1169–1026 (C–O–C str.), 2839 (CH_3 str.), 1456 (CH_3 def.); 3115–2981 (Ar-CH), 1682 (C=O), 1621 (C=N, Pyrazoline), 1516 (C=C), 1450 (Ar), 1341, 1167 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.33 (m, 6H, J = 4.43, 6.5 Hz, Ar-H), 7.87 (dd, 2H, J = 3.66, 6.42 Hz), 7.71–7.32 (m, 12H, Ar-H), 7.25 (s, 1H, Furan-H), 6.30–5.8 (m, 1H, CH of pyrazoline), 3.55–4.10 (m, 2H, CH_2 of pyrazoline), 2.32 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.46, 158.36, 152.26, 144.55, 132.32, 122.73, 56.53, 46.22, 34.62; MS (FAB) m/z: 397.12 (m+), 145.20 (100%). Anal. calcd. for $C_{24}H_{19}N_3O_3$, C: 72.53, H: 4.82, N: 10.57%; found: C: 72.12, H: 4.63, N: 10.22%.

*7.8. 3-Benzo[b]furan-2-yl-5-(4-dimethylaminophenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridyl methanone (**5c**)*

Yield: 72%; m.p.: 113–114 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 2925, 2804 (Ar–N–CH_3 str.), 1446 (CH_3 ban.), 1365, 1317 (C–N str.), 3131–2973 (Ar-CH), 1680 (C=O), 1624 (C=N, Pyrazoline), 1521 (C=C), 1451 (Ar), 1350, 1164 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.26 (m, 6H, J = 3.32, 6.42 Hz, Ar-H), 7.81 (dd, 2H, J = 3.53, 6.41 Hz), 7.72–7.42 (m, 12H, Ar-H), 7.28 (s, 1H, Furan-H), 6.28–5.86 (m, 1H, CH of pyrazoline), 3.42–4.11 (m, 2H, CH_2 of pyrazoline), 2.34 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.89, 157.93, 152.34, 150.55, 144.25, 137.21, 129.77, 122.16, 110.32, 53.52, 40.68, 34.45; MS (FAB) m/z: 410.88 (m + 1), 145.20 (100%). Anal. calcd. for $C_{25}H_{22}N_4O_2$, C: 73.15, H: 5.40, N: 13.65%; found: C: 73.42, H: 5.73, N: 13.22%.

*7.9. 2-[3-Benzo[b]furan-2-yl-1-(4-pyridylcarbonyl)-4,5-dihydro-1H-5-pyrazolyl]benzoic acid (**5d**)*

Yield: 86%; m.p.: 178–179 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3402 (carbonyl O–H str.), 3124–2961 (Ar-CH), 1715 (C=O str.), 1682 (C=O), 1171–1074 (C–O str.), 1624 (C=N, Pyrazoline), 1521 (C=C), 1455 (Ar), 1347, 1161 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.82 (s, OH), 8.24 (m, 6H, J = 3.45, 6.2 Hz, Ar-H), 7.82 (dd, 2H, J = 5.41, 6.44 Hz), 7.71–7.42 (m, 12H, Ar-H), 7.32 (s, 1H, Furan-H), 6.26–5.78 (m, 1H, CH of pyrazoline), 3.65–4.60 (m, 2H, CH_2 of pyrazoline), 2.33 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.55, 160.92, 157.57, 150.43, 141.34, 133.90, 124.82, 122.43, 110.23, 48.83, 35.15; MS (FAB) m/z: 411.89 (m + 1), 145.20 (100%). Anal. calcd. for $C_{24}H_{17}N_3O_4$, C: 70.07, H: 4.16, N: 10.21%; found: C: 70.26, H: 4.93, N: 10.22%.

*7.10. 3-Benzo[b]furan-2-yl-5-(2-nitrophenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5e**)*

Yield: 78%; m.p.: 110–111 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3118–2978 (Ar-CH), 1682 (C=O), 1620 (C=N, Pyrazoline), 1516 (C=C), 1527 (NO_2 str.), 1450 (Ar), 1346 (NO_2 str.), 1172 (C–O str.), 883 (C–N str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.26 (m, 6H, J = 3.46, 6.45 Hz, Ar-H), 7.77 (dd, 2H, J = 3.46, 6.24 Hz), 7.78–7.31 (m, 12H, Ar-H), 7.33 (s, 1H, Furan-H), 6.32–5.86 (m, 1H, CH of pyrazoline), 3.66–4.12 (m, 2H, CH_2 of pyrazoline), 2.35 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.77, 153.54, 150.32, 133.65, 123.54, 122.65, 106.82, 53.67, 34.42; MS (FAB) m/z: 416.11(m + 1), 145.84 (100%). Anal. calcd. for $C_{23}H_{16}N_4O_4$, C: 66.99, H: 3.91, N: 13.59%; found: C: 67.06, H: 3.93, N: 13.22%.

*7.11. 3-Benzo[b]furan-2-yl-5-(2-hydroxy-4-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5f**)*

Yield: 90%; m.p.: 123–124 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3372 (O–H str.), 3117–2955 (Ar-CH), 1676 (C=O), 1616 (C=N, Pyrazoline), 1521 (C=C), 1450 (Ar), 1383 (O–H ben.), 1346, 1170 (C–O str.), 1020 (C–O–C str.), 2927 (CH_3 str.), 1450 (CH_3 def.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.98 (s, OH), 8.30 (m, 6H, J = 3.66, 6.34 Hz, Ar-H), 7.68 (dd, 2H, J = 4.41, 6.28 Hz), 7.68–7.32 (m, 12H, Ar-H), 7.27 (s, 1H, Furan-H), 6.32–5.86 (m, 1H, CH of pyrazoline), 3.65–4.80 (m, 2H, CH_2 of pyrazoline), 2.34 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.34, 158.22, 152.25, 150.22, 148.55, 145.46, 125.53, 123.52, 122.74, 56.13, 46.67, 34.67; MS (FAB) m/z: 412.97 (m^+), 145.22 (100%). Anal. calcd. for $C_{24}H_{19}N_3O_4$, C: 69.72, H: 4.63, N: 10.16%; found: C: 69.26, H: 4.93, N: 10.22%.

*7.12. 3-Benzo[b]furan-2-yl-5-(4-hydroxyphenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5g**)*

Yield: 86%, m.p.: 154–156 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3367 (O–H str.), 3120–2960 (Ar-CH), 1680 (C=O), 1620 (C=N, Pyrazoline), 1516, 1450 (Ar, C=C), 1342, 1170 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.95 (s, OH), 8.28 (m, 6H, J = 3.66, 6.63 Hz, Ar-H), 7.86 (dd, 2H, J = 3.46, 6.28 Hz), 7.78–7.33 (m, 12H, Ar-H), 7.28 (s, 1H, Furan-H), 6.35–5.85 (m, 1H, CH of pyrazoline), 3.66–4.06 (m, 2H, CH_2 of pyrazoline), 2.35 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.85, 158.71, 151.27, 150.26, 145.18, 132.15, 126.85, 122.21, 107.12, 47.02, 35.24; MS (FAB) m/z: 383.88 (m + 1), 145.30 (100%). Anal. calcd. for $C_{23}H_{17}N_3O_3$, C: 72.05, H: 4.47, N: 10.96%; found: C: 72.26, H: 4.63, N: 11.02%.

*7.13. 3-Benzo[b]furan-2-yl-5-(4-chlorophenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5h**)*

Yield: 91%; m.p.: 113–114 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3128–2958 (Ar-CH), 1678 (C=O), 1622 (C=N, Pyrazoline), 1515, 1452 (Ar, C=C), 1350, 1168 (C–O str.), 786, 746 (C–Cl str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.27 (m, 6H, J = 3.49, 6.37 Hz, Ar-H), 7.82 (dd, 2H, J = 3.48, 6.23 Hz), 7.82–7.43 (m, 12H, Ar-H), 7.28 (s, 1H, Furan-H), 6.33–5.86 (m, 1H, CH of pyrazoline), 3.67–4.08 (m, 2H, CH_2 of pyrazoline), 2.35 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.55, 158.71, 152.47, 150.56, 144.22, 131.23, 128.45, 122.62, 107.12, 46.12, 34.34; MS (FAB) m/z: 401.55 (m^+), 144.95 (100%). Anal. calcd. for $C_{23}H_{16}N_3O_2Cl$, C: 68.74, H: 4.01, N: 10.46%; found: C: 68.26, H: 4.63, N: 10.02%.

*7.14. 3-Benzo[b]furan-2-yl-5-(2-chlorophenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5i**)*

Yield: 92%; m.p.: 135–136 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3118–2963 (Ar-CH), 1682 (C=O), 1622 (C=N, Pyrazoline), 1520, 1450 (Ar, C=C), 1344, 1174 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.28 (m, 6H, J = 4.43, 6.38 Hz, Ar-H), 7.82 (dd, 2H, J = 3.41, 6.2 Hz), 7.68–7.32 (m, 12H, Ar-H), 7.26 (s, 1H, Furan-H), 6.36–5.77 (m, 1H, CH of pyrazoline), 3.68–4.65 (m, 2H, CH_2 of pyrazoline), 2.38 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.95, 157.91, 152.57, 150.66, 144.12, 132.05, 125.85, 122.22, 107.12, 45.92, 35.74; MS (FAB) m/z: 402.12 (m + 1), 145.40 (100%). Anal. calcd. for $C_{23}H_{16}N_3O_2Cl$, C: 68.74, H: 4.01, N: 10.46%; found: C: 68.86, H: 4.23, N: 10.82%.

*7.15. 3-Benzo[b]furan-2-yl-5-(2-nitrophenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5j**)*

Yield: 94%; m.p.: 105–107 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3126–2963 (Ar-CH), 1683 (C=O), 1626 (C=N, Pyrazoline), 1552 (asy., NO_2 str.), 1516, 1450 (Ar, C=C), 1344 (sym., NO_2 str.), 1170 (C–O str.), 815 (C–N str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.2 (m, 6H, J = 3.43, 6.32 Hz, Ar-H), 7.79 (dd, 2H, J = 3.41, 6.2 Hz), 7.75–7.39 (m, 12H, Ar-H), 7.23 (s, 1H, Furan-H), 6.30–5.8 (m, 1H, CH of pyrazoline), 3.63–4.20 (m, 2H, CH_2 of pyrazoline), 2.33 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 167.75, 158.91, 152.17, 150.48, 144.17, 131.69, 128.55, 122.15, 106.22, 45.82, 34.94; MS (FAB) m/z: 411.88 (m^+), 145.14 (100%). Anal. calcd. for $C_{23}H_{16}N_4O_4$, C: 66.99, H: 3.91, N: 13.59%; found: C: 67.06, H: 3.63, N: 13.22%.

*7.16. 3-Benzo[b]furan-2-yl-5-(4-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5k**)*

Yield: 95%; m.p.: 164–165 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3126–2968 (Ar-CH), 2837 (CH_3 str.), 1678 (C=O), 1623 (C=N, Pyrazoline), 1520, 1454 (Ar, C=C), 1446 (CH_3 def.), 1170–1026 (C–O–C str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.42 (m, 6H, J = 3.63, 6.34 Hz, Ar-H), 7.82 (dd, 2H, J = 3.42, 6.24 Hz), 7.80–7.42 (m, 12H, Ar-H), 7.28 (s, 1H, Furan-H), 6.34–5.82 (m, 1H, CH of pyrazoline), 3.62–4.20 (m, 2H, CH_2 of pyrazoline), 2.36 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.96, 157.92, 152.27, 150.42, 144.75, 140.97, 130.68, 128.23, 127.85, 122.46, 110.22, 106.72, 53.22, 34.92; MS (FAB) m/z: 398.22 (m + 1), 145.20 (100%). Anal. calcd. for $C_{24}H_{19}N_3O_3$, C: 72.53, H: 4.82, N: 10.57%; found: C: 72.46, H: 4.93, N: 10.22%.

*7.17. 3-Benzo[b]furan-2-yl-5-phenyl-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5l**)*

Yield: 88%; m.p.: 115–116 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3118–2958 (Ar-CH), 1686 (C=O), 1626 (C=N, Pyrazoline), 1518, 1452 (Ar, C=C), 1348, 1170 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.62 (m, 6H, J = 4.43, 6.34 Hz, Ar-H), 7.82 (dd, 2H, J = 3.61, 6.22 Hz), 7.65–7.32 (m, 12H, Ar-H), 7.43 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.6–4.20 (m, 2H, CH_2 of pyrazoline), 2.32 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.45, 158.29, 152.77, 151.32, 143.81, 140.88, 125.66, 123.54, 122.18, 109.21, 103.83, 50.82, 34.76; MS (FAB) m/z: 368.12 (m + 1), 145.00 (100%). Anal. calcd. for $C_{23}H_{17}N_3O_2$, C: 75.19, H: 4.66, N: 11.44%; found: C: 75.46, H: 4.13, N: 11.22%.

*7.18. 3-Benzo[b]furan-2-yl-5-(2-furyl)-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5m**)*

Yield: 84%; m.p.: 185–187 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3122–2950 (Ar-CH), 1686 (C=O), 1622 (C=N, Pyrazoline), 1518 (furan), 1452 (Ar, C=C), 1346, 1170 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.66 (m, 6H, J = 4.33, 6.36 Hz, Ar-H), 7.86 (dd, 2H, J = 5.61, 6.82 Hz), 7.45–7.22 (m, 12H, Ar-H), 7.47 (s, 1H, Furan-H), 6.36–5.88 (m, 1H, CH of pyrazoline), 3.68–4.20 (m, 2H, CH_2 of pyrazoline), 2.37 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.62, 158.39, 152.82, 150.66, 144.15, 138.92, 132.03, 128.06, 122.27, 106.43, 56.45, 37.92; MS (FAB) m/z: 357.30 (m + 1), 145.10 (100%). Anal. calcd. for $C_{21}H_{15}N_3O_3$, C: 70.58, H: 4.23, N: 11.76%; found: C: 70.46, H: 4.13, N: 11.22%.

*7.19. 3-Benzo[b]furan-2-yl-5-[(E)-2-phenyl-1-ethenyl]-4,5-dihydro-1H-1-pyrazolyl-4-pyridylmethanone (**5n**)*

Yield: 72%; m.p.: 143–144 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3122–2942 (Ar-CH), 1680 (C=O), 1630 (C=N, Pyrazoline), 1520, 1450 (Ar, C=C), 1346, 1172 (C–O str.), 978 (–CH=CH–); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.86 (m, 6H, J = 6.42, 6.24 Hz, Ar-H), 7.77 (dd, 2H, J = 6.61, 6.82 Hz), 7.75–7.38 (m, 12H, Ar-H), 7.53 (s, 1H, Furan-H), 6.82–5.74 (m, 1H, CH of pyrazoline), 3.67–4.28 (m, 2H, CH_2 of pyrazoline), 2.35 (s, 2H); ^{13}C NMR (DMSO-d_6) δ ppm: 166.46, 157.19, 153.62, 151.06, 144.75, 138.12, 132.06, 128.09, 122.77, 106.43, 56.75, 37.32; MS (FAB) m/z: 394.13 (m + 1), 145.30 (100%). Anal. calcd. for $C_{25}H_{19}N_3O_2$, C: 76.32, H: 4.87, N: 10.68%; found: C: 76.46, H: 4.23, N: 10.22%.

*7.20. 3-[3-Benzo[b]furan-2-yl-5-(2-hydroxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7a**)*

Yield: 78%, m.p.: 172–173 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3368 (O–H str.), 3118–2952 (Ar-CH), 1680 (C=O), 1626 (C=N, Pyrazoline), 1483–1448 (Ar, C=C), 1352–1171 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 10.12 (s, OH), 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.3, H-6, naphthyridin), 8.62 (m, 6H, J = 4.43, 6.34 Hz, Ar-H), 7.82 (dd, 2H, J = 3.61, 6.22 Hz), 7.65–7.32 (m, 12H, Ar-H), 7.43 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.6–4.20 (m, 2H, CH_2 of pyrazoline), 4.36 (s, 2H, C_2H_5), 2.32 (s, 2H), 1.3 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.27, 171.21, 164.63, 152.34, 143.77, 137.22, 133.81, 128.82, 123.26, 110.2, 106.8, 98.73, 45.7, 34.77, 24.23, 14.27; MS (FAB) m/z: 492.53 (m^+), 145.22 (100%). Anal. calcd. for $C_{29}H_{24}N_4O_4$, C: 70.72, H: 4.91, N: 11.38%; found: C: 70.65, H: 4.92, N: 11.16%.

*7.21. 3-[3-Benzo[b]furan-2-yl-5-(2-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one(**7b**)*

Yield: 84%; m.p.: 218–219 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3123–2955 (Ar-CH), 1678 (C=O), 1620 (C=N, Pyrazoline), 1480–1452 (Ar, C=C), 1360 (C–N), 1350–1170 (C–O str.), 1169–1026 (C–O–C str.), 992 (Ar, CH); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.78 (d, 1H, $J_{6\text{-}5}$ = 7.42, H-6, naphthyridin), 8.82 (m, 6H, J = 6.42, 3.44 Hz, Ar-H), 7.62 (dd, 2H, J = 3.62, 6.24 Hz), 7.61–7.33 (m, 12H, Ar-H), 7.42 (s, 1H, Furan-H), 6.22–5.82 (m, 1H, CH of pyrazoline), 3.64–4.33 (m, 2H, CH_2 of pyrazoline), 4.34 (s, 2H, C_2H_5), 4.14 (s, 3H, OCH_3), 2.33 (s, 2H), 1.62 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 181.11, 171.73, 165.03, 152.34, 143.77, 138.22, 132.81, 126.82, 122.26, 107.2, 106.8, 98.53, 56.77, 45.27, 34.51, 24.77, 14.03; MS (FAB) m/z: 506.56 (m^+), 145.12 (100%). Anal. calcd. for $C_{30}H_{26}N_4O_4$, C: 71.13, H: 5.17, N: 11.06%; found: C: 71.53, H: 5.22, N: 11.57%

*7.22. 3-[3-Benzo[b]furan-2-yl-5-(4-dimethylaminophenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro [1,8]naphthyridin-4-one (**7c**)*

Yield: 82%; m.p.: 205–205 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3128–2942 (Ar-CH), 3005, 2820 (Ar–N–CH_3 str.), 1678 (C=O), 1631 (C=N, Pyrazoline), 1480–1450 (Ar, C=C), 1352 (C=N), 1347–1170 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.72 (d, 1H, $J_{6\text{-}5}$ = 6.56, H-6, naphthyridin), 8.77 (m, 6H, J = 4.54, 6.84 Hz, Ar-H), 7.42 (dd, 2H, J = 3.68, 6.82 Hz), 7.68–7.37 (m, 12H, Ar-H), 7.52 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.6–4.22 (m, 2H, CH_2 of pyrazoline), 4.36 (s, 2H, C_2H_5), 2.32 (s, 2H), 2.24 (s, 6H, N(CH_3)$_2$), 1.43 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.81,

170.53, 164.43, 156.14, 143.17, 136.02, 131.21, 124.82, 112.26, 106.28, 98.73, 49.77, 45.33, 40.21, 34.77, 15.13; MS (FAB) *m/z*: 520.60 (m + 1), 145.38 (100%). Anal. calcd. for $C_{31}H_{29}N_5O_3$, C: 71.66, H: 5.63, N: 13.48%; found: C: 71.42, H: 5.73, N: 13.22%.

*7.23. 3-[3-Benzo[b]furan-2-yl-5-(2-carboxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7d**)*

Yield: 87%; m.p.: 188–189 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3412 (O–H str.), 3116–2942 (Ar-CH), 1674 (C=O), 1616 (C=N, Pyrazoline), 1488–1452 (Ar, C=C), 1350–1174 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.97 (s, OH), 8.82 (d, 1H, $J_{6\text{-}5}$ = 7.66, H-6, naphthyridin), 8.64 (m, 6H, *J* = 5.43, 6.74 Hz, Ar-H), 7.68 (dd, 2H, *J* = 4.61, 6.42 Hz), 7.45–7.30 (m, 12H, Ar-H), 7.40 (s, 1H, Furan-H), 6.30–5.82 (m, 1H, CH of pyrazoline), 3.64–4.21 (m, 2H, CH_2 of pyrazoline), 4.42 (s, 2H, C_2H_5), 2.36 (s, 2H), 1.38 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.65, 171.21, 164.62, 157.34, 143.78, 137.32, 133.65, 124.66, 122.26, 106.98, 98.09, 45.67, 44.23, 35.67, 15.10; MS (FAB) *m/z*: 520.69 (m^+), 145.20 (100%). Anal. calcd. for $C_{30}H_{24}N_4O_5$, C: 69.22, H: 4.65, N: 10.76%; found: C: 69.26, H: 4.73, N: 10.52%.

*7.24. 3-[3-Benzo[b]furan-2-yl-5-(3-nirtophenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7e**)*

Yield: 78%; m.p.: 168–169 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3116–2950 (Ar-CH), 1682 (C=O), 1624 (C=N, Pyrazoline), 1532 (asy., NO_2 str.), 1350 (sym., NO_2 str.), 1483–1448 (Ar, C=C), 1352–1171 (C–O str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 10.12 (s, OH), 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.3, H-6, naphthyridin), 8.62 (m, 6H, *J* = 4.43, 6.34 Hz, Ar-H), 7.82 (dd, 2H, *J* = 3.61, 6.22 Hz), 7.65–7.32 (m, 12H, Ar-H), 7.43 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.6–4.20 (m, 2H, CH_2 of pyrazoline), 4.36 (s, 2H, C_2H_5), 2.32 (s, 2H), 1.3 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 181.22, 170.21, 164.23, 152.24, 144.13, 137.1, 132.81, 127.82, 122.26, 109.21, 105.8, 98.73, 46.7, 36.77, 25.23, 15.27; MS (FAB) *m/z*: 522.62 (m + 1), 145.19 (100%). Anal. calcd. for $C_{29}H_{23}N_5O_5$, C: 66.79, H: 4.44, N: 13.43%; found: C: 66.26, H: 4.53, N: 13.28%.

*7.25. 3-[3-Benzo[b]furan-2-yl-5-(2-hydroxy, 3-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro [1,8] naphthyridin-4-one (**7f**)*

Yield: 85%; m.p.: 142–143 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3216 (O–H str.), 3123–2952 (Ar-CH), 1676 (C=O), 1621 (C=N, Pyrazoline), 1360 (C–N), 1174 (C–O str.), 1622 (C=N), 1482–1452 (Ar, C=C), 1350–1176 (C–O str.), 1169–1026 (C–O–C str.), 992 (–CH); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 10.33 (s, OH), 8.76 (d, 1H, $J_{6\text{-}5}$ = 7.52, H-6, naphthyridin), 8.84 (m, 6H, *J* = 6.62, 3.47 Hz, Ar-H), 7.60 (dd, 2H, *J* = 4.62, 6.44 Hz), 7.60–7.34 (m, 12H, Ar-H), 7.42 (s, 1H, Furan-H), 6.22–5.82 (m, 1H, CH of pyrazoline), 3.64–4.33 (m, 2H, CH_2 of pyrazoline), 4.34 (s, 2H, C_2H_5), 4.14 (s, 3H, OCH_3), 2.33 (s, 2H), 1.62 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 181.27, 170.21, 165.63, 152.34, 143.75, 136.22, 134.81, 126.82, 122.26, 108.2, 103.8, 98.33, 45.7, 35.77, 24.23, 14.27; MS (FAB) *m/z*: 522.77 (m^+), 145.88 (100%). Anal. calcd. for $C_{30}H_{26}N_4O_5$, C: 68.96, H: 5.01, N: 10.72%; found: C: 68.76, H: 5.13, N: 10.52%.

*7.26. 3-[3-Benzo[b]furan-2-yl-5-(4-hydroxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7g**)*

Yield: 89%, m.p.: 186–187 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3343 (O–H str.), 3121–2952 (Ar-CH), 1672 (C=O), 1618 (C=N, Pyrazoline), 1358 (C–N), 1170 (C–O str.), 1624 (C=N), 1482–1454 (Ar, C=C), 1352–1172 (C–O str.), 1170–1024 (C–O–C str.), 992 (Ar, CH); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 10.88 (s, OH), 8.72 (d, 1H, $J_{6\text{-}5}$ = 6.62, H-6, naphthyridin), 8.86 (m, 6H, *J* = 6.46, 3.55 Hz, Ar-H), 7.32 (dd, 2H, *J* = 4.12, 6.33 Hz), 7.64–7.23 (m, 12H, Ar-H), 7.46 (s, 1H, Furan-H), 6.32–5.62 (m, 1H, CH of pyrazoline), 3.34–4.63 (m, 2H, CH_2 of pyrazoline), 4.24 (s, 2H, C_2H_5), 4.12 (s, 3H, OCH_3), 2.11 (s, 2H), 1.60 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 181.44, 170.21, 163.63, 150.34, 142.77, 135.22, 132.81, 128.82, 122.26, 110.2, 106.8, 98.73, 45.7, 34.77, 24.23, 14.27; MS (FAB) *m/z*: 493.74 (m + 1), 145.63 (100%). Anal. calcd. for $C_{29}H_{24}N_4O_4$, C: 70.72, H: 4.91, N: 11.38%; found: C: 70.66, H: 4.73, N: 11.22%.

*7.27. 3-[3-Benzo[b]furan-2-yl-5-(4-chlorophenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7h**)*

Yield: 78%; m.p.: 203–205 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3122–2950 (Ar-CH), 1682 (C=O), 1622 (C=N, Pyrazoline), 1480–1450 (Ar, C=C), 1350–1176 (C–O str.), 778, 753 (C–Cl str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.3, H-6, naphthyridin), 8.62 (m, 6H, *J* = 4.43, 6.34 Hz, Ar-H), 7.82 (dd, 2H, *J* = 3.61, 6.22 Hz), 7.25–7.33 (m, 12H, Ar-H), 7.23 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.62–4.23 (m, 2H, CH_2 of pyrazoline), 4.36 (s, 2H, C_2H_5), 2.33 (s, 2H), 1.34 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 181.11, 170.32, 163.22, 152.62, 143.63, 136.28, 132.81, 126.82, 122.26, 110.2, 109.8, 97.63, 45.64, 34.37, 23.23, 15.27; MS (FAB) *m/z*: 510.66 (m^+), 144.95 (100%). Anal. calcd. for $C_{29}H_{23}ClN_4O_3$, C: 68.17, H: 4.54, N: 10.96%; found: C: 68.28, H: 4.53, N: 10.82%.

*7.28. 3-[3-Benzo[b]furan-2-yl-5-(2-chlorophenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7i**)*

Yield: 82%; m.p.: 175–176 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3116–3002 (Ar-CH), 1680 (C=O), 1622 (C=N, Pyrazoline), 1481–1448 (Ar, C=C), 1352–1172 (C–O str.), 840, 748 (C–Cl str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 10.12 (s, OH), 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.3, H-6, naphthyridin), 8.64 (m, 6H, *J* = 5.43, 6.54 Hz, Ar-H), 7.62 (dd, 2H, *J* = 3.41, 7.22 Hz), 7.75–7.22 (m, 12H, Ar-H), 7.43 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.63–4.25 (m, 2H, CH_2 of pyrazoline), 4.36 (s, 2H, C_2H_5), 2.32 (s, 2H), 1.3 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.31, 170.82, 162.52, 153.33, 142.83, 135.12, 132.81, 124.82, 122.35, 110.27, 109.82, 96.63, 46.64, 34.37, 28.23, 14.27; MS (FAB) *m/z*: 510.26 (m^+), 144.75 (100%). Anal. calcd. for $C_{29}H_{23}ClN_4O_3$, C: 68.17, H: 4.54, N: 10.96%; found: C: 68.58, H: 4.21, N: 10.76%.

*7.29. 3-[3-Benzo[b]furan-2-yl-5-(2-nitrophenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7j**)*

Yield: 84%; m.p.: 165–167 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3119–2942 (Ar-CH), 1674 (C=O), 1616 (C=N, Pyrazoline), 1565 (asy., NO_2 str.), 1488–1452 (Ar, C=C), 1350–1174 (C–O str.), 1338 (sym., NO_2 str.), 822 (C–N str.); ^{1}H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.82 (d, 1H, $J_{6\text{-}5}$ = 7.66, H-6, naphthyridin), 8.64 (m, 6H, *J* = 5.43, 6.74 Hz, Ar-H), 7.68 (dd, 2H, *J* = 4.61, 6.42 Hz),

7.46–7.30 (m, 12H, Ar-H), 7.64 (s, 1H, Furan-H), 6.40–5.62 (m, 1H, CH of pyrazoline), 3.64–4.31 (m, 2H, CH_2 of pyrazoline), 4.32 (s, 2H, C_2H_5), 2.16 (s, 2H), 1.38 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.42, 170.81, 163.26, 153.28, 143.13, 136.1, 130.81, 126.82, 122.24, 108.21, 104.8, 97.73, 45.7, 36.12, 25.03, 14.87; MS (FAB) *m/z*: 521.58 (m^+), 145.34 (100%). Anal. calcd. for $C_{29}H_{23}N_5O_5$, C: 66.79, H: 4.44, N: 13.43%; found: C: 66.06, H: 4.23, N: 13.29%.

*7.30. 3-[3-Benzo[b]furan-2-yl-5-(4-methoxyphenyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8] naphthyridin-4-one (**7k**)*

Yield: 78%; m.p.: 264–265 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3124–2955 (Ar-CH), 1668 (C=O), 1622 (C=N, Pyrazoline), 1478–1456 (Ar, C=C), 1354–1172 (C–O str.), 1162–1033 (C–O–C str.); ^1H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.36, H-6, naphthyridin), 8.62 (m, 6H, J = 5.23, 6.72 Hz, Ar-H), 7.82 (dd, 2H, J = 5.31, 6.45 Hz), 7.55–7.20 (m, 12H, Ar-H), 7.46 (s, 1H, Furan-H), 6.32–5.83 (m, 1H, CH of pyrazoline), 3.65–4.25 (m, 2H, CH_2 of pyrazoline), 4.46 (s, 2H, C_2H_5), 2.30 (s, 2H), 1.44 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.11, 172.73, 165.63, 153.34, 142.77, 137.22, 133.81, 124.82, 122.11, 107.28, 106.82, 97.54, 55.57, 45.22, 34.32, 23.77, 15.03; MS (FAB) *m/z*: 507.15 (m + 1), 145.55 (100%). Anal. calcd. for $C_{30}H_{26}N_4O_4$, C: 71.13, H: 5.17, N: 11.06%; found: C: 71.26, H: 5.13, N: 11.22%.

*7.31. 3-[3-Benzo[b]furan-2-yl-5-phenyl-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8]naphthyridin-4-one (**7l**)*

Yield: 76%; m.p.: 195–196 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3120–2946 (Ar-CH), 1674 (C=O), 1616 (C=N, Pyrazoline), 1482–1452 (Ar, C=C), 1350–1172 (C–O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ, ppm): 9.97 (s, OH), 8.82 (d, 1H, $J_{6\text{-}5}$ = 7.66, H-6, naphthyridin), 8.64 (m, 6H, J = 5.43, 6.74 Hz, Ar-H), 7.68 (dd, 2H, J = 4.61, 6.42 Hz), 7.45–7.30 (m, 12H, Ar-H), 7.40 (s, 1H, Furan-H), 6.30–5.82 (m, 1H, CH of pyrazoline), 3.64–4.21 (m, 2H, CH_2 of pyrazoline), 4.42 (s, 2H, C_2H_5), 2.36 (s, 2H), 1.38 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.51, 170.23, 165.63, 152.34, 144.17, 129.82, 124.26, 106.2, 98.73, 45.25, 33.51, 24.77, 14.93; MS (FAB) *m/z*: 477.68 (m + 1), 145.71 (100%). Anal. calcd. for $C_{29}H_{24}N_4O_3$, C: 73.09, H: 5.08, N: 11.76%; found: C: 73.26, H: 5.13, N: 11.62%.

*7.32. 3-[3-Benzo[b]furan-2-yl-5-(2-furyl)-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro[1,8]naphthyridin-4-one (**7m**)*

Yield: 87%; m.p.: 287–288 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3121–2952 (Ar-CH), 1684 (C=O), 1624 (C=N, Pyrazoline), 1548 (furan), 1483–1452 (Ar, C=C), 1355–1174 (C–O str.); ^1H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.86 (d, 1H, $J_{6\text{-}5}$ = 7.3, H-6, naphthyridin), 8.64 (m, 6H, J = 4.43, 6.34 Hz, Ar-H), 7.82 (dd, 2H, J = 3.61, 6.22 Hz), 7.25–7.33 (m, 12H, Ar-H), 7.23 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.62–4.24 (m, 2H, CH_2 of pyrazoline), 4.34 (s, 2H, C_2H_5), 2.33 (s, 2H), 1.35 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.11, 170.23, 164.03, 150.34, 142.27, 136.22, 132.41, 126.12, 122.26, 106.42, 97.25, 53.72, 45.17, 34.71, 24.27, 14.13; MS (FAB) *m/z*: 467.52 (m + 1), 145.72 (100%). Anal. calcd. for $C_{27}H_{22}N_4O_4$, C: 69.52, H: 4.75, N: 12.01%; found: C: 70.46, H: 4.13, N: 11.22%.

*7.33. 3-[3-Benzo[b]furan-2-yl-5-[(E)-2-phenyl-1-ethenyl]-4,5-dihydro-1H-1-pyrazolylcarbonyl]-1-ethyl-7-methyl-1,4-dihydro [1,8]naphthyridin-4-one (**7n**)*

Yield: 88%; m.p.: 212–213 °C. Spectroscopic analysis: IR (KBr) υ_{max} (cm^{-1}): 3118–2946 (Ar-CH), 1678 (C=O), 1620 (C=N, Pyrazoline), 1483–1454 (Ar, C=C), 1354–1173 (C–O str.), 972 (–CH=CH–); ^1H NMR ($CDCl_3$, 300 MHz, δ, ppm): 8.82 (d, 1H, $J_{6\text{-}5}$ = 7.32, H-6, naphthyridin), 8.63 (m, 6H, J = 5.43, 6.54 Hz, Ar-H), 7.85 (dd, 2H, J = 3.71, 6.27 Hz), 7.95–7.73 (m, 12H, Ar-H), 7.23 (s, 1H, Furan-H), 6.32–5.84 (m, 1H, CH of pyrazoline), 3.62–4.23 (m, 2H, CH_2 of pyrazoline), 4.34 (s, 2H, C_2H_5), 2.37 (s, 2H), 1.37 (s, 3H, C_2H_5); ^{13}C NMR (DMSO-d_6) δ ppm: 180.11, 170.73, 164.03, 152.34, 143.67, 137.22, 132.21, 128.82, 125.26, 122.2, 106.8, 99.53, 51.77, 45.27, 36.51, 23.77, 14.93; MS (FAB) *m/z*: 502.77 (m^+), 145.30 (100%). Anal. calcd. for $C_{31}H_{26}N_4O_3$, C: 74.09, H: 5.21, N: 11.15%; found: C: 74.26, H: 5.23, N: 11.22%.

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