ANTIBACTERIAL, ANTIFUNGAL ACTIVITY OF NEWLY SYNTHESIZED 1, 8-NAPHTHYRIDINYL HETEROCYCLES

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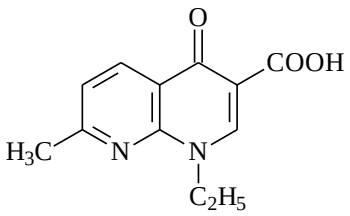
I. INTRODUCTION

Due to the utility of these composites as medicines, heterocyclic chemistry is veritably important to medicinal druggists. Multitudinous heterocyclic substances are being used as medicinal agents and are also necessary for mortal life. 1,8-Naphthyridine Derivations Are a Significant Class of Heterocyclic Chemicals Due to Their Wide Range of Natural Conduct. Numerous 1,8- naphthyridine derivations were created as a result of nalidixic acid's remarkable clinical effectiveness as an antibacterial medicine. Gram-negative bacteria that beget patient urinary tract infections have been demonstrated to respond well to the treatment with nalidixic acid **1**.



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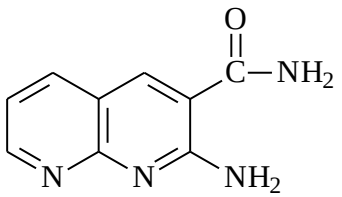
Numerous 1,8-naphthyridine derivatives have undergone in-depth research as physiologically active substances with a range of properties, including antibacterial2, antimalarial3, anti-hypertensive4, anti-tumor5, and anti-inflammatory6 properties. The diuretic properties of 2-amino-1,8-naphthyridine-3-carboxamide 2 and its hydrochloride monohydrate have been described by Gorecki and Hawes7.



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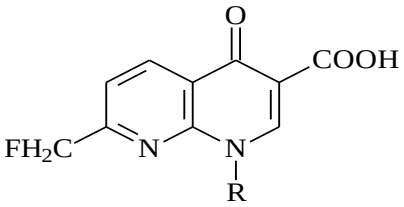
The creation of 7-fluoromethyl-1, 8-naphthyridine derivatives **3** and their antibacterial activity have been described by Tani et al.8



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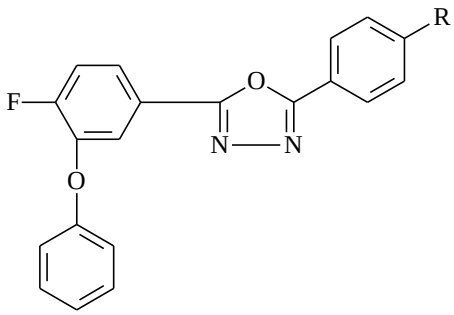
Some 1,3,4-oxadiazoles **4** with phenoxy fluorophenyl groups were synthesized, according to Mohan et al. (9), who also documented their insecticidal properties.



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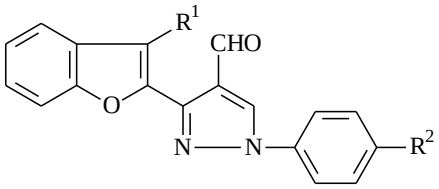
According to Kumar et al., 1-aryl-3-(1-benzofuran-2-yl)-1H-pyrazole-4-carbaldehydes 5 has antibacterial and antifungal activities.10



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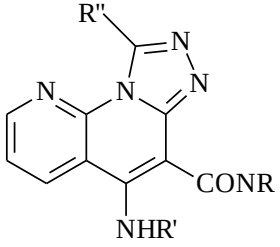
N,N-dialkyl-4-(alkylaminocycloalkylamino)[1, 2, 4] has been synthesized and its anti-inflammatory and anti-aggressive properties have been described by Roma et al **11**.-triazolo[4,3-a][1,8]six-carboxamides of naphthalidine **6**.



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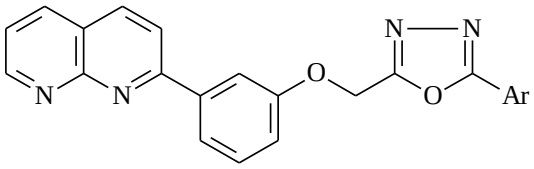
II. PRESENT WORK

Due to their numerous biological actions, 1,8-naphthyridine derivatives have garnered a lot of attention. Because of the wide range of pharmacological and microbiological actions they display, different Phthalazine-1,4-diones, pyrazoles, and 1,3,4-oxadiazoles play an important role in medicinal chemistry.There have been reports of fascinating and varied biological and pharmacological activities in fused 1,2,4-triazoles. Encouraged by these findings, several novel 1,8-naphthyridines have been synthesized (both substituted and fused)(7–10) to test their antibacterial properties.

1. 3 - (1, 8-naphthyridin-2-yl) phenoxymethyl]-5-aryl-2the 1, 3, 4-Oxadiazoles 7



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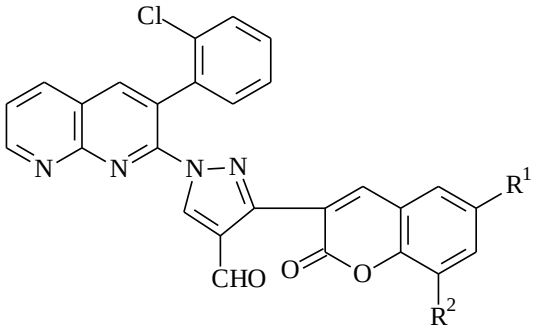
2. 1-[3-(2-Chlorophenyl)[1,8]naphthyridin-2-yl]-3-(2-oxo-2*H*-3-chromenyl)-1*H*-4-pyrazolecarbaldehydes 8



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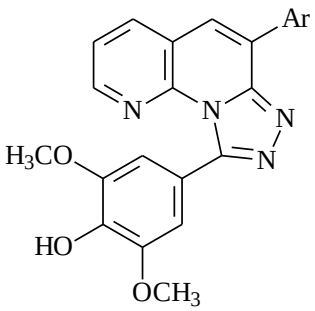
3. 9-(3, 5-dimethoxy-4-hydroxyphenyl)6-Aryl--1,2,4-triazolo[4,3-*a*][1,8] naphthyridines 9



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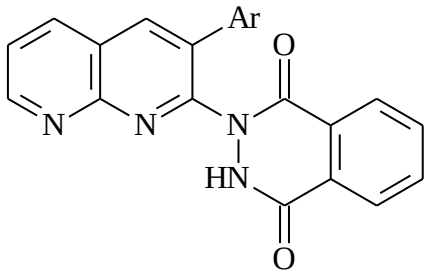
4. Tetrahydrophthalazine-1, 4-diones of 2-(3-Aryl-1, 8-naphthyrdin-2-yl)



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III. ANTIBACTERIAL ACTIVITY

The antibacterial activity of all the generated compounds (7–10) was evaluated against the bacterium Escherichia coli and Bacillus subtilis using the filter paper disc technique of Vincent and Vincent12. These drugs' efficacy was assessed at 250 and 500 μg /disc concentrations. Gentamycin was used as the standard for comparison. The results are shown in Tables I through IV.

1. **2-[*3*-(1, 8-naphthyridin-2-yl) 5-Aryl phenoxymethyl] the 1, 3, 4-oxadiazoles 7:** The chemicals were tested for antibacterial properties 7 (Table I) revealed that, at a concentration of 250 μg / disc, every compound was effective against both bacteria. The kind and position of the substituent affect the compound's action. The action is significantly increased by the addition of substituents, particularly methyl, methoxy, and chloro groups. The most active substance in the group was 7e, which shown activity on par with Gentamycin. All other substances have good or average efficacy against the two bacteria.

2. **1-[3-(2-Chlorophenyl) [1, 8] naphthyridin-2-yl] – 3 - (2-oxo-2H-3-chromenyl) One Hydroxy - 4- pyrazolecarbaldehydes 8:** At a concentration of 250 μg / disc, all of the compounds **8** were effective against both Gram-negative and Gram-positive bacteria (**Table II**). The bulk of the compounds had positive antibacterial activity, according to the results. The amounts of inhibition in the test chemical and the bacterium were different, though. The activity is increased when specific substituents, such as chloro and methoxy groups, are present in the phenyl ring. The 8c compound was the series' most energetic substance. The remaining compounds displayed average to good activity.

3. **6 – Aryl - 9 - (3, 5-dimethoxy-4-hydroxyphenyl)-1, 2, 4-triazolo [4, 3-a] [1, 8] 9 naphthalyridines:** Table III displays the results of experiments testing the compounds 9 for their antibacterial activity against E. Coli and b. subtilis. The results demonstrate that the majority of the compounds exhibit detectable action against both test bacteria at a concentration of 250 μg /disc. Compound 9h displayed antibacterial activity against both bacteria that was comparable to Gentamycin's. In comparison to these species, the remaining chemicals displayed either good or moderate activity.

4. **2-(3-Aryl-1, 8-naphthyrdin-2yl)-1, 2, 3, 4-tetrahydrophthalazine-1, 4-diones 10:** According to the screening results in **Table IV**, the synthesized compounds 10 demonstrated moderate to good action to the test bacteria at the concentration of 250 μg /disc.The most effective substance in the group was 10f, which shown activity similar to that of Gentamycin.

IV. ANTIFUNGAL ACTIVITY

The antifungal activity of all the compounds (7–10) against Curvularia lunata and Fusarium oxysporum was tested in vitro at concentrations of 250 and 500 μg /disc using the filter paper disc technique of Vincent and Vincent12. Commercial fungicide carbendazim was frequently employed.Even at a concentration of 250 μg /disc, the chemicals exhibited little antifungal action.

V. EXPERIMENTAL SECTION

1. **Antibacterial Activity:** The filter paper disc approach of Vincent and Vincent12 was used to assess the antibacterial activity of the resulting compounds. In the current experiment, Gram-positive Bacillus subtilis and Gram-negative Escherichia coli were the microorganisms utilised. The chemicals were evaluated at two different concentrations (250 and 500 μg /disc) after being dissolved in acetone. After being seeded with diverse bacteria on nutrient agar plates, the Whatman filter paper discs (6 mm in diameter), which contained various chemicals, were grown for 72 hours at 37 + 1°C in an aseptic environment.At the end of the incubation period, the diameter of the growth inhibition zones was measured. The observation was carried out twice and at least ten paper discs were utilized.

2. **Antifungal Activity:** The filter paper disc method was used to assess the antifungal activity of the developed compounds12. The current work used the test organisms Curvularia lunata and Fusarium oxysporum. Acetone was used to dissolve the medication, which was tested at two distinct concentrations (250 and 500 μg /disc). The diverse fungi were planted on nutrient agar plates, and the Whatman filter paper discs (6 mm in diameter) were aseptically inserted on those plates. The plates were then grown for 7 days at 28 + 2°C. The diameter of the growth inhibition zones was determined at the conclusion of the incubation period. Each test chemical concentration was double-checked on at least ten paper discs.

Table 1: Information about 1, 3, 4-oxadiazolesand 5-Aryl-2-[3-(1,8-naphthyridin-2-yl)-phenoxymethyl]'s antibacterial activity 7

Compd	Ar	Inhibition zone (in mm)			
		E. coli at		*B. subtilis* at	
		250 μg /disc	500 μg /disc	250 μg /disc	500 μg /disc
7a	C_6H_5	7.6	9.4	6.1	8.2
7b	4-$CH_3C_6H_4$	10.0	19.5	6.5	12.0
7c	4-$CH_3OC_6H_4$	9.5	15.0	6.0	9.5
7d	2-ClC_6H_4	10.5	16.5	6.5	10.5

7e	4-ClC_6H_4	11.5	21.0	7.0	13.5
7f	3-$NO_2C_6H_4$	6.5	8.5	6.0	7.5
7g	4-$NO_2C_6H_4$	8.0	11.5	7.0	9.5
7h	3,4-$(CH_3O)_2C_6$	7.5	9.5	5.5	7.5
	Gentamycin	12.0	22.0	8.0	15.0

Table 2: Results of antibacterial screening 1-[3-(2-Chlorophenyl)-[1,8]- naphthalyridin-2-yl]-3-(2-oxo-2H-3-chromenyl)-1H-4-pyrazolecarbaldehydes 8

Compd	**R^1**	**R^2**	**Inhibition zone (in mm)**			
			***E. coli* at**		***B. subtilis* at**	
			250 µg /disc	**500 µg /disc**	**250 µg /disc**	**500 µg /disc**
8a	H	H	8.6	10.6	6.1	8.6
8b	H	OCH_3	10.6	13.6	6.5	9.6
8c	Cl	H	11.4	18.1	7.6	13.4
8d	Cl	Cl	10.1	14.1	5.5	10.6
8e	Br	H	9.1	10.5	5.6	6.6
8f	Br	Br	10.0	13.0	6.0	8.0
8g	NO_2	H	6.5	8.0	5.5	7.0
8h	5,6-Benzo		8.0	11.0	6.5	8.0
	Gentamycin		12.0	22.0	8.0	15.0

Table 3: Results of 6-Aryl-9-(3, 5-dimethoxy-4-hydroxyphenyl)-1, 2, 4-triazolo [4, 3-a]'s antibacterial activity Naphthyridines, [1, 8] 9

Compd	**Ar**	**Inhibition zone (in mm)**			
		***E. coli* at**		***B. subtilis* at**	
		250 µg /disc	**500 µg /disc**	**250 µg /disc**	**500 µg /disc**
9a	C_6H_5	6.6	9.5	6.1	8.0
9b	4-$CH_3OC_6H_4$	7.0	10.5	5.5	7.0
9c	2-ClC_6H_4	8.0	12.0	5.5	7.5
9d	3-ClC_6H_4	7.5	11.0	5.0	6.5
9e	4-ClC_6H_4	11.0	18.5	6.5	10.0
9f	2-F C_6H_4	9.5	12.5	6.0	8.5
9g	3-F C_6H_4	8.5	11.5	5.5	7.5
9h	4-F C_6H_4	11.5	20.0	7.0	11.5
	Gentamycin	12.0	22.0	8.0	15.0

Table 4: 2-(3-Aryl-1,8-naphthyrdin-2yl)-1,2,3,4-tetrahydrophthalazine- 1,4-dione antibacterial screening data 10

Compd	**Ar**	**Inhibition zone (in mm)**			
		***E. coli* at**		***B. subtilis* at**	
		250 µg/disc	**500 µg/disc**	**250 µg/disc**	**500 µg/disc**
10a	2-FC_6H_4	9.0	11.5	6.5	9.5
10b	3-FC_6H_4	8.5	10.0	6.0	7.5

10c	4-FC_6H_4	11.0	17.5	7.0	11.5
10d	2-$CF_3C_6H_4$	10.5	13.5	7.0	10.5
10e	3-$CF_3C_6H_4$	9.5	12.0	6.5	9.5
10f	4-$CF_3C_6H_4$	11.5	21.0	7.5	14.0
	Gentamycin	12.0	22.0	8.0	15.0

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