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Synthesis, Characterization and Antihelminthic Activity of Some Pyrazole Derivative

Ekta Yadav[1, 3], Sarita[2], Anjali Srivastava[3]

1, Research scholar department of pharmaceutical chemistry sagar institute of technology and management department of pharmacy,faizabad road, barabanki, 225001.

2, Associate professor Department of pharmaceutical chemistry sagar institute of technology and management department of pharmacy,faizabad road, barabanki, 225001

3. Assitant Professor, Nova College of pharmacy, kh. No. 74 stp road behind ganpativihar colony, khargapur, gomtinagar, extention, uttarpradesh 226010

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ABSTRACT:A novel series of 1H-pyrazole derivatives was synthesized. This was followed by reaction of glacial acetic acid as catalysis, an equimolar solution of phenyl hydrazine and substituted phenyl acetophenone in absolute ethanol will be refluxed over a water bath for two hours. From pure alcohol, the crude product will be separated and crystallized. In the next step The Vilsmayer-Haack reagent (1E)-1-(substituted phenyl) ethanone phenyl hydrazine (0.01M) was added and refluxed for five hours after being made by dropping three millilitres of POCl3 into twenty-five millilitres of ice-cooled DMF. After adding the reaction mixture was kept to the ice bath, sodium bicarbonate was used to neutralize it. From the ethanol, the crude product will be crystallized and separated. The anthelmintic action of all the recently compounds (4a-f) was evaluated using earth warms in comparison to Albendazole. All the synthesized compounds has reported good anthelmintic activity out of witch 4d and 4f were found to be potent when compared to the ordinary drug albendazole. But compound 4d has expressed maximum active to standard drug. The earth warms were divided into three groups, each of which had two earth warms that are almost identical in size. The tests were conducted at ambient temperature throughout. A very little amount of DMSO was used to dissolve the test and standard compounds, and the volume was subsequently adjusted to 10 millilitres using regular saline. The concentrations of the test and standard solutions were 0.25%, and 0.50% w/v. Normal saline was used for the control group. The time was recorded for both the phases of study i.e. paralysis and Death of earth warms.

KEYWORDS: Carbazole anthelmintic action, earth warms and paralysis

I. INTRODUCTION

Anthelmintic Agents a medication used to cure infections in animals caused by parasitic worms is called an anthelmintic. Anthelmintic are sometimes referred to as anthelminthic or vermis fudges, are a class of antiphrastic medications used to extravagance parasitic young insect diseases in both individuals and beasts. They function by either killing or stunning the worms without seriously harming the host. Many parasite infections, including those brought on by roundworms like nematodes and flatworms like flukes and tapeworms, can be treated with anthelmintic.

Helminthic Infection With a projected 1.5 billion sick individuals, or 24 percent of the global inhabitants, Soil Transmitted Helminthiasis (STH) contaminations are between the most predominant illnesses globally. With the maximum occurrence recorded from Asia, America, China, and Africa, these illnesses primarily afflict the most impoverished and deprived groups with little admittance to hygienic water, cleanliness, and sanitization in subtropical settings. They spread through the eggs found in anthropological faces, which pollute the loam in unsanitary locations. These parasites are highly transmissible in places where they affect about 260 million kindergarten-stage offspring, 654 million school-age teen-agers, 108 million young females, and 138.8 million in the family way and lactating moms. These populations require treatment and preventive measures. Symptoms of Helminthic Infection Most of the time, people with light-intensity infections (few worms) are not ill. Intestinal signs (diarrhoea and stomach discomfort), malnourishment, general dissatisfaction and faintness, and poor development and corporeal development are only a few of the

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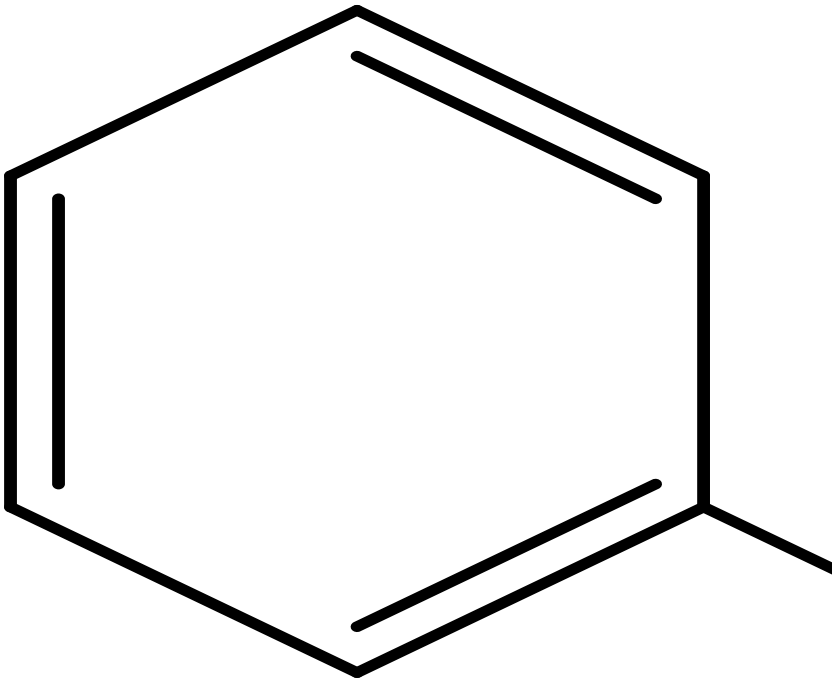
symptoms that heavier infections can produce. Extremely strong infections can result in intestinal blockage, which needs to be surgically repaired. [3]

Strongloides stercoralis is known to be connected to chronic malnutrition in children and may induce gastro-intestinal and dermatological morbidity.

II. MATERIAL AND METHODS

PLAN OF WORK



Synthesis

Step1.

General procedure for Synthesis of (E)-1-(1-phenylethylidene)-2-(2-(trifluoromethyl) phenyl) hydrazine (3a)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydazine and 2'-(Trifluoromethyl) Acetophenone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

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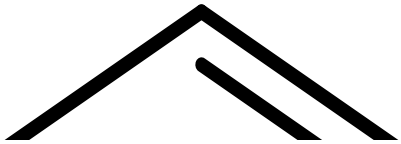

General procedure forSynthesis of (E)-1-(4-chlorophenyl)-2-(1-phenylethylidene) hydrazine (3b)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydrazine and (4-chloro methyl) Acetophenone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

General procedure for Synthesis of (E)-1-(4-(methylthio) phenyl)-2-(1-phenylethylidene) hydrazine (3c)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydrazine and 4'-(Methylthio) phenyl) Ethanone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

General procedure for Synthesis of (E)-1-(4-methoxyphenyl)-2-(1-phenylethylidene) hydrazine (4d)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydrazine and 4'-Methoxyacetophenone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

International Journal of Pharmaceutical Research and Applications
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General procedure forSynthesis of (E)-1-(3-nitrophenyl)-2-(1-phenylethylidene) hydrazine (3e)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydrazine and 3'-Nitroacetophenone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

General procedure for Synthesis of (E)-4-(2-(1-phenylethylidene) hydrazine) phenol (3f)

Using glacial acetic acid as catalysis, an (0.08 mol) mixture of phenyl hydrazine and 1-(4-hydroxyphenyl) Ethanone into pure ethanol will be refluxed over a water bath for two hours. From only alcohol, the raw material will be separated and crystallized.

Step 2

General procedure for Synthesis of 1-phenyl-3-(2-(trifluoromethyl) phenyl)-1H-pyrazole-4-carbaldehyde (4a)

After adding (3a) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been ice-cooled, it will reflux for five hours. After adding the reaction mixture to the ice, sodium bicarbonate will be used to neutralize it. From the ethanol, the solid form will be separated and crystallized.

International Journal of Pharmaceutical Research and Applications
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General procedure for Synthesis of 3-(4-chlorophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4b)

After adding (3b) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been ice-cooled, it will reflux for five hours. After adding the reaction mixture to the ice, sodium bicarbonate will be used to neutralize it. From the ethanol, the solid form will be separated and crystallized.

General procedure for Synthesisof 3-(4-(methylthio) phenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4c)

After adding (3c) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been ice-cooled, it will reflux for five hours. After adding the reaction mixture to the ice, sodium bicarbonate will be used to neutralize it. From the ethanol, the original substance will be separated and crystallized.

General procedure for Synthesis of 3-(4-methoxyphenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4d)

After adding (3d) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been ice-cooled, it will reflux for five hours. The reaction

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mixture will then be added to ice, and sodium bicarbonate will be used to neutralize the mixture. After being separated from the ethanol, the crude product will crystallize.

General procedure for Synthesis of 3-(2-nitrophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4e)

After adding (3e) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been ice-cooled, it will reflux for five hours. After adding the reaction mixture to the ice, sodium bicarbonate will be used to neutralize it. From the ethanol, the original substance will be separated and crystallized.

General procedure for Synthesisof 3-(4-hydroxyphenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (4f)

After adding (3f) (0.01M) to the Vilsmayer-Haack reagent, which was made by adding 3 ml $POCl_3$dropwise to 25 ml DMF that had been cooled on ice. It will reflux for five hours. After adding the reaction mixture to the ice, sodium bicarbonate will be used to neutralize it. From the ethanol, the original substance will be separated and crystallized.

International Journal of Pharmaceutical Research and Applications
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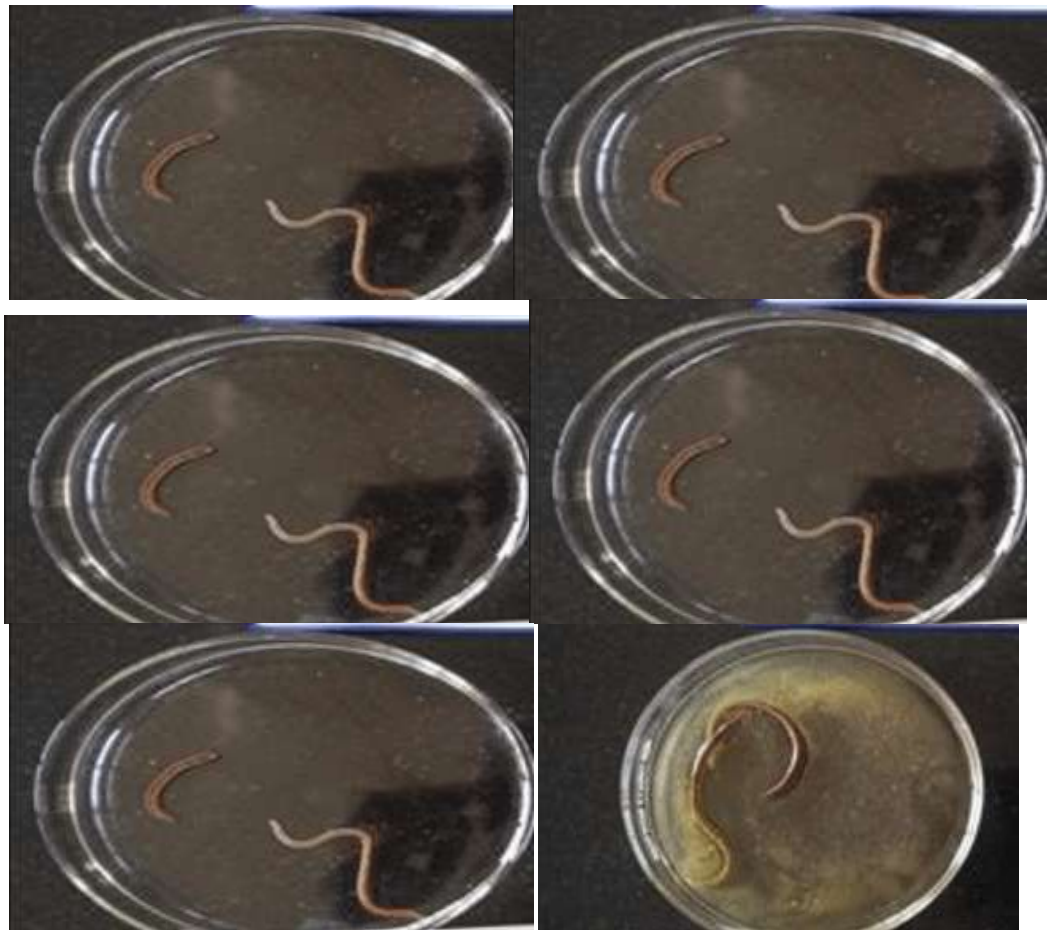
Biological activity (in-vitro)

The active component, was identified in 1908. From the 1920s through the 1970s, halogenated hydrocarbons were used in a growing number of more potent anthelmintic, until the underlying toxicity to hosts was found. Anthelmintic are drugs used to treat warm parasitic infections like nematodes and flatworms (tapeworms and flukes), which usually infect people, cattle, and crops and lower food production. They are also referred to as parasitic ides, and nematodes.

Collection of earthworms

The earthworms of 4-6 cm in length were collected from ground. They were washed with normal saline of 0.9% concentration



International Journal of Pharmaceutical Research and Applications
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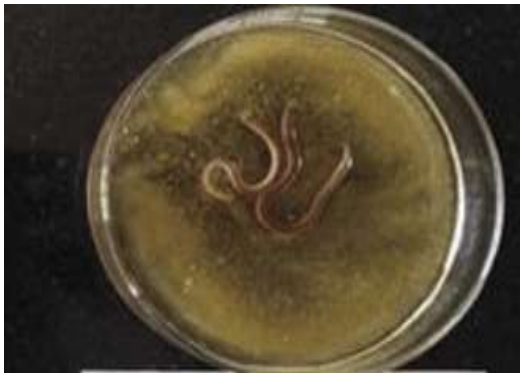

Test organisms
Ascarislumbricoides

Requirements: Albendazole (Glaxo Smitthkline Pharmaceuticals Ltd.), petri dish, normal saline, earthworm.

Study protocol

The anthelmintic action of all the recently compounds **(4a-f)** was evaluated using earth warms in comparison to Albendazole. The earth warms were divided into three groups, each of which had two earth warms that are almost identical in size. The tests were conducted at ambient temperature throughout. A very little amount of DMSO was used to dissolve the test and standard compounds, and the volume was subsequently adjusted to 10 milliliters using regular saline. The concentrations of the test and standard solutions were 0.25%, and 0.50% w/v. Normal saline was used for the control group. The time was recorded for both the phases of study i.e. paralysis and Death of earth warms.

All the earthworms are divided into three main groups

s.no.	**Drug**	**Time of Paralysis (in minutes)**		**Time of Death (in minutes)**	
		Concentration		**Concentration**	
		0.25ug/ml	**0.50ug/ml**	**0.25ug/ml**	**0.50ug/ml**
1	Control (Normal Saline)	-	-	-	-
2	Albendazole (standard)	31.27±0.44	26.04±0.12	34.25±0.65	29.27±0.31
3	4a	50.04±0.78	45.21±0.36	55.14±0.65	51.45±0.57
4	4b	36.13±0.84	30.32±0.45	38.29±0.32	34.25±0.56
5	4c	37.35±0.65	31.35±0.47	39.57±0.58	33.17±0.36
6	**4d**	**33.54±0.27**	**29.32±0.54**	**36.45±0.21**	**32.23±0.65**
7	4e	42.23±0.54	45.37±0.50	45.35±0.36	51.27±0.45
9	**4f**	**34.55±0.22**	**28.33±0.01**	**37.07±0.44**	**32.47±0.12**

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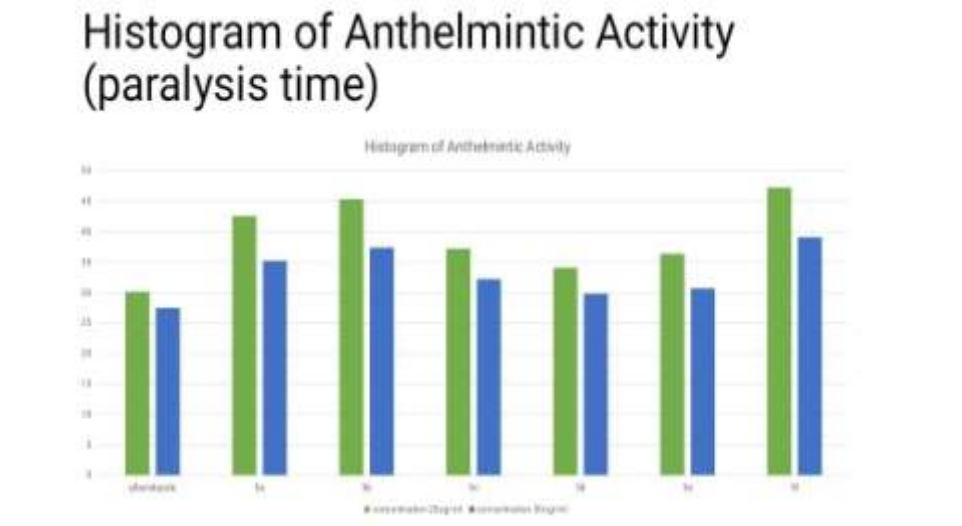

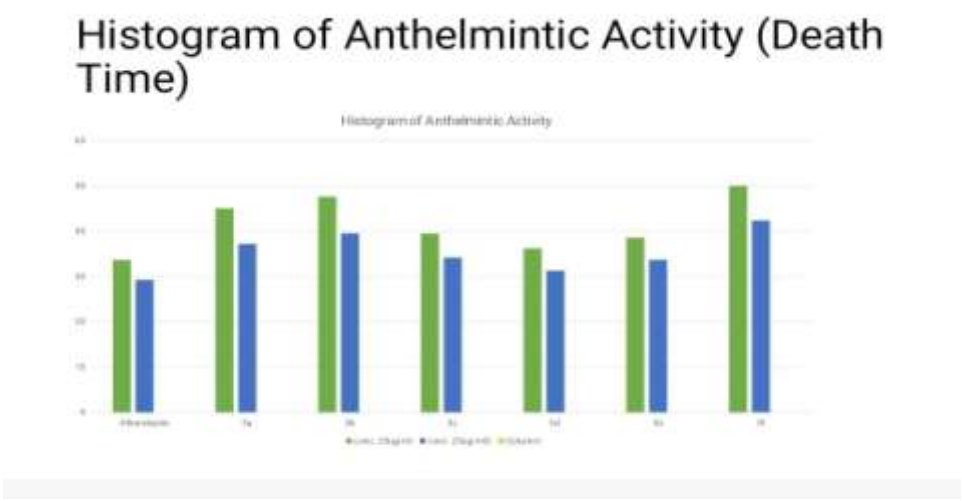

III. RESULT

Spectral characterization IR(4a)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H (Aromatic)	3168.0
3	C=C	1652.9
4	C-N stretching	1328.0
5	C=O	1733.1
6	C-F	1132.6

Observed values of IR (4b)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H (Aromatic)	3115.9
3	C=C	1653.6
4	C-N stretching	1303.5
5	C=O	1733.5
6	C-Cl	647

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Volume 10, Issue 1 Jan - Feb 2025, pp: 469-480 www.ijprajournal.com ISSN: 2456-4494

Observed values of IR (4c)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H	3168.8
3	C=C	1652.1
4	C-N stretching	1302.3
5	C=O	1733.4
6	C-S	3448.4

Observed values of IR (4d)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H (Aromatic)	3168.8
3	C=C	1652.1
4	C-N stretching	1302.3
5	C=O	1733.4
6	C-O-C	1255.5

Observed values of IR (4e)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H (Aromatic)	3115.7
3	C=C	1651.4
4	C-N stretching	1303.6
5	C=O	1732.9
6	NO_2	1474.4

Observed values of IR (4f)

S.NO.	Functional group	IR (cm^{-1}) observed
1	C-H (Aromatic)	3167.6
3	C=C	1654.1
4	C-N stretching	1297.1
5	C=O	1733.9

^{1}H NMR Observed values **(4a)**

S.NO.	Type and number of hydrogen	Observed value
1	10H (Aromatic hydrogen)	6.898-8.038
2	1H (Aldehyde Hydrogen)	9.809

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^{1}H NMR Observed values **(4b)**

S.NO.	Type and number of hydrogen	Observed value
1	10H (Aromatic hydrogen)	7.315-8.096
2	1H (Aldehyde Hydrogen)	9.717

^{1}H NMR Observed values **(4c)**

S.NO.	Type and number of hydrogen	Observed value
1	10H, m, (Aromatic)	7.315-8.096
2	1H,s, (Aldehyde)	9.717
3	3H,m, (Aliphatic)	3.359

^{1}H NMR Observed values **(4d)**

S.NO.	Type and number of hydrogen	Observed value
1	10H, m, (Aromatic)	8.503-8.326
2	1H,s, (Aldehyde)	9.533
3	3H,m, (Aliphatic)	3.363

^{1}H NMR Observed values **(4e)**

S.NO.	Type and number of hydrogen	Observed value
1	10H, m, (Aromatic)	70716-7.354
2	1H,s, (Aldehyde)	9.043

13 ^{1}H NMR Observed values **(4f)**

S.NO.	Type and number of hydrogen	Observed value
1	10H, m, (Aromatic)	7.918-7.496
2	1H,s, (Aldehyde)	9.696
3	1H,s, (Alcoholic)	8.027

IV. CONCLUSION

In the current research work, 1H-(4a-f) were synthesized and examined for their anthelmintic Activity. IR, 1H NMR, and UV spectroscopy were used to characterize every molecule that was produced. The structures of all the synthesized compounds were supported by their physiochemical characteristics and spectral characterization, which were performed using FT-IR, 1H NMR, and UV spectroscopic techniques. According to the results of the anthelmintic activity tests, compounds (4d and 4f) with electron withdrawing groups at Para positions (4-OCH3, 4-OH) substituted at phenyl rings exhibited the highest activities against Ascarislumbricoides. It was discovered that a compound having the methoxy group at the para position to the phenyl ring was considerably efficient against the Ascarislumbricoides.

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