JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Synthesis and Study of Impact of p-Chloro-m-cresol Incorporated Pyrazole and Isoxazole Derivatives on Phytotic Growth of Some Food Grain & Vegetable Crop Plants

[1]Sushil K. Pagariya, [2]Pravin S. Bodkhe

[1]Research Scholar, Department of Chemistry, Vidya Bharati Mahavidyalaya, Amravati-444602 (M.S.), India

[2]Associate Professor, Department of Chemistry, Vidya Bharati Mahavidyalaya, Amravati-444602 (M.S.), India

Abstract: A series of 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) incorporating 4-chloro-3-methylphenol viz. p-chloro-m-cresol moiety have been effectively synthesized and studied their impact on phytotic growth of some food grain and vegetable crop plants. Initially, 5-chloro-2-hydroxy-4-methylacetophenone (2) has been prepared by an acetylation of p-chloro-m-cresol followed by Fries rearrangement with anhydrous $AlCl_3$. The acetophenone (2) on treatment with substituted aromatic carboxylic acids in dry pyridine with $POCl_3$ affords substituted 2-benzoyloxy acetophenones (3a-d) which on Baker-Venkatraman transformation (BVT) in dry pyridine with pulverized KOH yielded corresponding 1-(5'-chloro-2'-hydroxy-4'-methylphenyl)-3-(substituted phenyl) propane-1,3-diones (4a-d) i.e. β-diketones. All the newly synthesized β-diketones underwent dehydrative cyclization in acidic media affords the respective 2-(substituted phenyl)-6-chloro-7-methyl-4*H*-chromen-4-ones (5a-d) as key intermediates which were refluxed with phenyl hydrazine hydrochloride and hydroxylamine hydrochloride in DMF solvent with small amount of piperidine yielded novel 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) respectively. All the newly synthesized titled compounds were screened for their impact on phytotic growth of some food grain crop plants viz. *Cicer arientinum*, *Glycine max*, *Vigna radiata*, *Vigna mungo* and some vegetable crop plants viz. *Solanum lycopersicum*, *Trigonella foenum-graecum* and *Capsicum annuum* with reference to their shoot height and number of leaves at definite periodicity and found to have remarkable growth promoting, antifungal and antimicrobial activity on plants.

IndexTerms **- Pyrazoles, isoxazoles, p-chloro-m-cresol, phytotic growth, food grain and vegetable crop plants.**

1. INTRODUCTION

Heterocyclic compounds are very widely distributed in nature and are essential for the sustainable of life in various ways. Pyrazoles and isoxazoles are well known and important class of nitrogen containing five membered heterocycles widely found as the core structure in a large variety of compounds those possess important pharmacological and agrochemical activities. The azoles containing two nitrogen atoms at 1,2-positions are designated as pyrazoles while azoles with one oxygen and one nitrogen atoms at 1,2-positions are designated as isoxazoles. They are one of the most studied groups of compounds among the azole family. Various methods have been worked out for their synthesis[1-9]. Pyrazole derivatives exhibits a broad spectrum of pharmacological and biological activities such as inhibitors of protein glycation, antimicrobial, antibacterial, antifungal, anti-inflammatory and analgesic, anti-obesity drug rimonabant, anticancer, antitumor, anti-tubercular, antioxidant, anticonvulsant and antidepressant, antidiabetic, antipyretic, antiarrhythmic, antiviral, anti-AIDS, antiproliferative, anti-hyperglycemic, anti-anxiety, anti-enzymatic, anti-FAAH, etc[10-17]. As well, a good number of isoxazole derivatives have also been reported to have promising anti-inflammatory, antibacterial, antifungal, antimicrobial, analgesic, anticancer, antitumor, anticonvulsant, antileishmanial, anti-tubercular, ulcerogenic, anti-HIV, antioxidant, antiplatelet, anxiolytic, antiepileptic, antiarthritic, anesthetic, antiviral, anti-nociceptive, immunological and CNS (central nervous system) activity and miscellaneous activities like GABA (γ-amino butyric acid) agonistic activity, inhibitory activity, antihypertensive activity and glutamate transporter activity[18-21]. A survey of literature reveals that several pyrazoles and isoxazoles derivatives have been reported to have promising insecticidal, pesticidal, fungicidal, herbicidal, acaricidal activity which render them valuable active ingredients of plant protecting agents[22-30]. We know the grains, fruits and vegetables have huge importance in human nutrition as these are the rich sources of vitamins and minerals. Today the India is almost self-sufficient to produce food grains, vegetables and fruits. Our greatest achievement is self-sufficient in cereals, foods and vegetables. Yet researchers are continuously working for improvement of quality as well as yield of agricultural products due to continuous increase in population. Now-a-days scientists across the globe are emphasizing more on an interdisciplinary approach to control plant disease, to enhance vegetative growth and to increase the yield of various crops. Pyrazoles and isoxazoles have played a crucial role in the history of heterocyclic chemistry and have been extensively instrumental as pharmacophores and synthons in the field of organic chemistry and drug designing**.** Recently in the field of agricultural sciences they have attracted considerable attention due to their phytotic growth promoting and hormonal activities. Nimbalkar[31] synthesized and studied dichlorosubstituted

4-aroyl-1-substituted pyrazoles for their impact on the phytotic growth of some vegetable crop plants and showed that pyrazoles have remarkable effects on some plants growth and protect the plant from fungal and microbial infections. Deotalu[32] *et al* also synthesized some chlorosubstituted 4-aroyl/alkoyl pyrazoles and isoxazoles and studied their impact on phytotic growth of some vegetable crop plants. Bhade[33] *et al* and Hushare[34] *et al* have reported the growth promoting hormonal activity of chlorosubstituted pyrazoles and isoxazoles on some flowering plants. Keeping in view the phytochemical profile of pyrazoles and isoxazoles, we have decided to study the impact of our newly synthesized p-chloro-m-cresol incorporated pyrazole and isoxazole derivatives on the phytotic growth of some food grain viz. *Cicer arientinum* (Chana), *Glycine max* (Soyabean), *Vigna radiata* (Mung), *Vigna mungo* (Udid) and some vegetable viz. *Solanum lycopersicum* (Tomato), *Trigonella foenum-graecum* (Methi) and *Capsicum annuum* (Mirchi) crop plants particularly with reference to their height of shoots and number of leaves at definite periodicity.

2. MATERIALS AND METHODS

All the chemicals used were of synthetic grade. Melting points were determined in open glass capillaries and were uncorrected. The purity of compounds was monitored on silica gel-G coated TLC plate. Elemental analyses were carried out with a Thermo Scientific FLASH 2000 instrument. IR spectra were recorded on Shimadzu IR Afinity-1 CE spectrophotometer in KBr matrix. ^{1}H NMR spectra were recorded on Bruker Avance Neo 500 MHz spectrometer in DMSO-d_6 with TMS as internal standard. Meanwhile, LC-MS mass spectra were recorded on Waters Micromass Alliance 2795 Q-TOF micromass spectrometer.

2.1 General procedure for the synthesis of pyrazole (6a-d) and isoxazole (7a-d) derivatives[35]

The synthesis of titled compounds involves the following synthetic steps:

2.1.1 Synthesis of p-Chloro-m-cresyl acetate (1): A p-chloro-m-cresol (50g) was mixed with acetic anhydride (60 ml) and anhydrous sodium acetate (5g). The reaction mixture was refluxed for about 1½ hrs. The reaction mixture was allowed to cool followed by their decomposition in ice-cold water. Two layers aqueous and acetate were formed out of which lower acetate layer was separated by means of separating funnel and purified by distillation to obtained a p-chloro-m-cresyl acetate viz. 4-chloro-3-methylphenyl acetate (1).

2.1.2 Synthesis of 5-Chloro-2-hydroxy-4-methylacetophenone (2): A mixture of p-chloro-m-cresyl acetate (1) (50 ml) and anhydrous aluminium chloride (120g) in Kjeldal's flask were heated at about 120 ^{0}C for about 1 hr in an oil bath (Fries migration). The reaction mixture was cooled and decomposed with ice-cold water containing a little HCl (10%) to get crude ketone. It was purified by dissolving it in an acetic acid and allowing the solution to fall drop wise into ice-cold water with continuous stirring to get 5-chloro-2-hydroxy-4-methylacetophenone viz. 1-(5'-chloro-2'-hydroxy-4'-methylphenyl) ethanone (2).

2.1.3 Synthesis of 2-(Substituted benzoyloxy)-4-methyl-5-chloroacetophenones (3a-d): 5-chloro-2-hydroxy-4-methylaceto-phenone (2) (0.04 mol) and appropriate aromatic carboxylic acids (i.e. substituted benzoic acids) (0.05 mol) were dissolved in dry pyridine and $POCl_3$ was added dropwise with stirring and cooling simultaneously till the viscous mass was obtained. Temperature was maintained below 10 ^{0}C during the addition of $POCl_3$. The reaction mixture was allowed to stand for overnight at room temperature and then decomposed by dil. HCl (10%) in an ice bath. The solid product thus separated was filtered, washed with water followed by 10% sodium bicarbonate ($NaHCO_3$) solution and then several times with water. Finally, it was purified by recrystallization from hot ethanol to afford corresponding 2-(substituted benzoyloxy)-4-methyl-5-chloroacetophenones (3a-d).

2.1.4 Synthesis of 1-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-3-(substituted phenyl) propane-1, 3-diones (4a-d) i.e. β-diketones: 2-(substituted benzoyloxy)-4-methyl-5-chloroacetophenones (3a-d) (0.05 mol) was dissolved in dry pyridine (40 ml). The solution was warmed up to 60 ^{0}C and pulverized KOH was added slowly with constant stirring (Baker-Venkataraman rearrangement). Vigorous reaction took place and mixture began to thicken when yellowish-brown mass was obtained. The reaction mixture was kept overnight and then worked up by the dilution and acidification with ice-cold dil. HCl (1:1). The yellowish-brown solid thus obtained was filtered, washed with water followed by 10% sodium bicarbonate ($NaHCO_3$) solution to remove unhydrolysed acid and then again with excess of water. The dried product was purified by recrystallization from ethanol-acetic acid mixture to get yellow crystals of respective 1-(5'-chloro-2'-hydroxy-4'-methylphenyl)-3-(substituted phenyl) propane-1,3-diones (4a-d) i.e. β-diketones with good yield.

2.1.5 Synthesis of 2-(Substituted phenyl)-6-chloro-7-methyl-4*H*-chromen-4-ones (5a-d) i.e. substituted flavones: To a solution of 1-(5'-chloro-2'-hydroxy-4'-methylphenyl)-3-(substituted phenyl) propane-1,3-diones (4a-d) (0.025 mol) in glacial acetic acid (30 ml), sulphuric acid (5 ml) was added. The content of reaction mixture was refluxed on water bath for 2 hrs. followed with occasional stirring. The reaction mixture was allowed to cooled at room temperature and poured into crushed ice to precipitate the product. The separated product was filtered, washed with water followed by 10% sodium bicarbonate ($NaHCO_3$) solution and then with sufficient cold water until the washings were neutral to litmus. The dried product was purified by recrystallization from hot ethanol to get shiny yellow crystals of corresponding 2-(substituted phenyl)-6-chloro-7-methyl-4*H*-chromen-4-ones (5a-d) i.e. substituted flavones with satisfactory yield.

2.1.6 Synthesis of 3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(substituted phenyl)-1-phenyl pyrazoles (6a-d): A mixture of 2-(substituted phenyl)-6-chloro-7-methyl-4*H*-chromen-4-ones (5a-d) (0.01 mol) and phenylhydrazine hydrochloride (0.02 mol) was refluxed in DMF solvent with few drops of piperidine for about 1½ hrs. The reaction mixture was cooled and then acidified with ice-cold dil. HCl (1:1). The product thus separated was filtered, washed with water followed by 10% sodium bicarbonate ($NaHCO_3$) solution and then again with plenty of water. It was dried and purified by recrystallization from ethanol-acetic acid mixture to get shiny coloured crystals of corresponding 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(substituted phenyl)-1-phenyl pyrazoles (6a-d) as desired products with excellent yield.

2.1.7 Synthesis of 3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(substituted phenyl) isoxazoles (7a-d): A mixture of 2-(substituted phenyl)-6-chloro-7-methyl-4*H*-chromen-4-ones (5a-d) (0.01 mol) and hydroxylamine hydrochloride (0.02 mol) was refluxed in DMF solvent with few drops of piperidine for about 1½ hrs. The reaction mixture was cooled and then acidified with ice cold dil. HCl (1:1). The product thus separated was filtered, washed with water followed by 10% sodium bicarbonate ($NaHCO_3$) solution and then again with plenty of water. It was dried and purified by recrystallization from ethanol-acetic acid mixture to get shiny coloured crystals of corresponding 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(substituted phenyl) isoxazoles (7a-d) as desired products with excellent yield. The general reaction scheme outlined for the synthesis of 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) is depicted below in **Figure 1** and their physical characterization data is shown in **Table 1**.

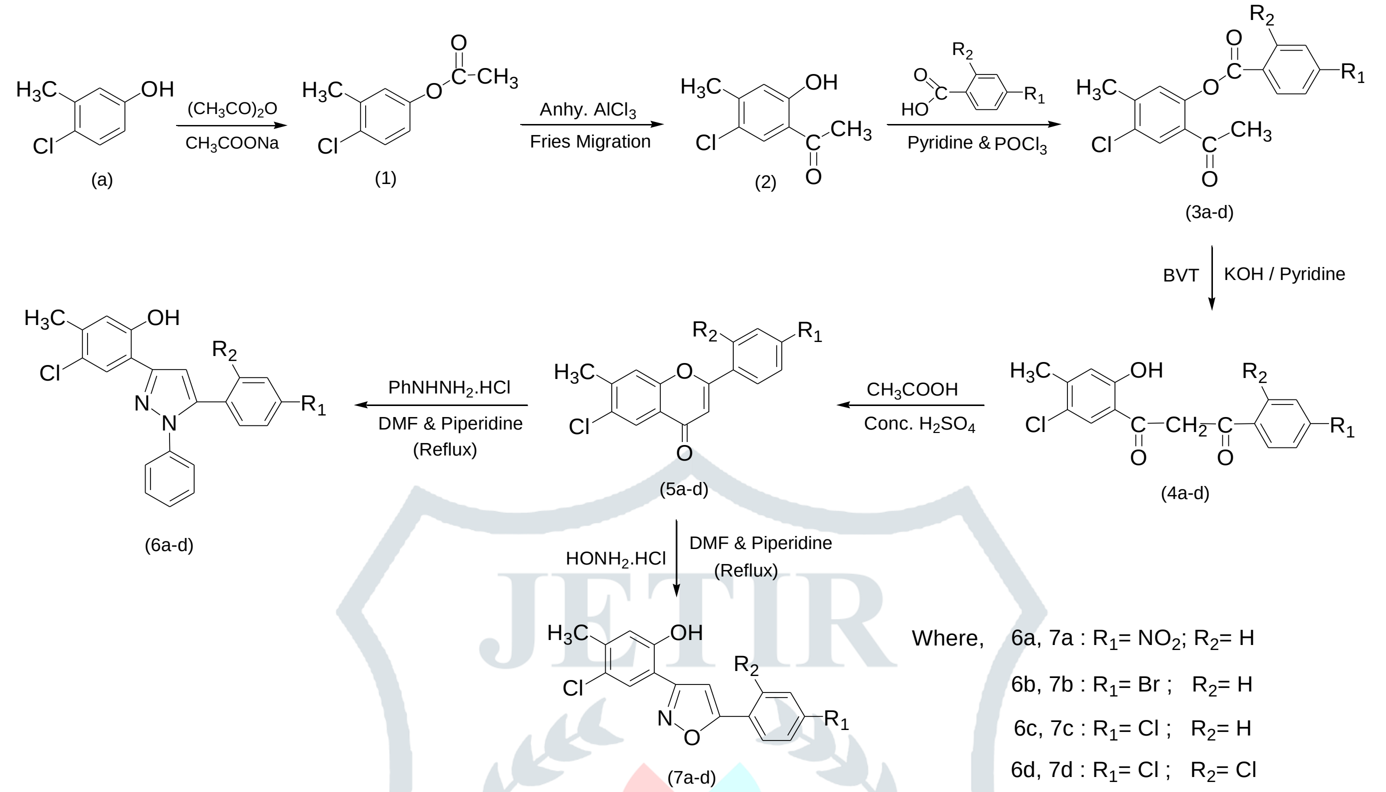

Figure 1: The general reaction scheme for the synthesis of novel pyrazole (6a-d) and isoxazole (7a-d) derivatives

Table 1: Physical characterization data of newly synthesized pyrazole (6a-d) and isoxazole (7a-d) derivatives

Compound Code	Compound Name	Mol. Formula	Mol.Wt. (g/mol)	M.P. (^{0}C)	Yield (%)	R_f value
6a	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-nitrophenyl)-1-phenyl pyrazole*	$C_{22}H_{16}ClN_3O_3$	405.83	220-222	79	0.70
6b	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-bromophenyl)-1-phenyl pyrazole*	$C_{22}H_{16}BrClN_2O$	439.73	218-222	86	0.67
6c	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-chlorophenyl)-1-phenyl pyrazole*	$C_{22}H_{16}Cl_2N_2O$	395.28	218-224	84	0.82
6d	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(2',4'-dichlorophenyl)-1-phenyl pyrazole*	$C_{22}H_{15}Cl_3N_2O$	429.73	238-240	90	0.80
7a	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-nitrophenyl) isoxazole*	$C_{16}H_{11}ClN_2O_4$	330.72	228-230	85	0.65
7b	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-bromophenyl) isoxazole*	$C_{16}H_{11}BrClNO_2$	364.62	254-258	87	0.76
7c	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-chlorophenyl) isoxazole*	$C_{16}H_{11}Cl_2NO_2$	320.17	218-222	88	0.82
7d	*3-(5'-Chloro-2'-hydroxy-4'-methylphenyl)-5-(2', 4'-dichlorophenyl) isoxazole*	$C_{16}H_{10}Cl_3NO_2$	354.62	240-244	90	0.70

2.2 Phytotic growth effects of the titled compounds on some food grain and vegetable crops plants[31-34]

The experimental set up of the present study was divided into two segments:

2.2.1 Seed treatment: Pregerminated quality seeds of some food grains viz. *Cicer arientinum* (Chana/Chana), *Glycine max* (Soyabean), *Vigna radiata* (Mung), *Vigna mungo* (Udid) and vegetables viz. *Solanum lycopersicum* (Tomato), *Trigonella foenum-graecum* (Methi/Fenugreek) and *Capsicum annuum* (Mirchi/Chilli) have been procured from authorized agroagency. With a view to safeguard dormant seed potential from harmful external agencies, the seeds of all the grain and vegetable crops were treated before sowing with test compounds 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-nitrophenyl)-1-phenyl pyrazole (6a), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-bromophenyl)-1-phenyl pyrazole (6b), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-chlorophenyl)-1-phenyl pyrazole (6c), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(2', 4'-dichlorophenyl)-1-phenyl pyrazole (6d), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-nitrophenyl) isoxazole (7a), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-bromophenyl) isoxazole (7b), 3-(5'-chloro-2'-hydroxy-4'-methylphenyl)-5-(4'-chlorophenyl) isoxazole (7c), and 3-(5'-

chloro-2'-hydroxy-4'-methylphenyl)-5-(2', 4'-dichlorophenyl) isoxazole (7d) by immersing dry seeds in their solutions prepared by 1,4-dioxane solvent having concentration (0.01 mg/ml) at room temperature for 6-8 hrs by soaking method i.e. treated.

2.2.2 Field experiment: The pots of black cotton soil were prepared on an open field by using 8 x 12-inch size high density polythene (HDPE) nursery bags and labelled it. The sowing of seeds of all seven species under examination were done in these pots separately by conventional sowing method and irrigated it by water whenever required. The plants from these pots were divided into two groups i.e. A and B. The plants from group A were kept untreated and unsprayed which were termed as 'Control' group whereas plants from group B were treated with test compounds as well as sprayed and designated as 'Treated' group plants. The spraying solutions of newly synthesized 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) containing p-chloro-m-cresol moiety have been prepared in 1,4-dioxane (0.01 M) separately and the plants from group B were sprayed with these test compounds solutions at fortnightly intervals after germination to screen their impact on test plants. The field experiments were conducted to compare the treated plants of group B with untreated plants of controlled group A. In this context, the plants were carefully examined and the observations were recorded on 7^{th}, 14^{th}, 21^{th}, 28^{th}, 35^{th} and 42^{th} days after sowing stage with special reference to their number of leaves and height of their shoots. The results obtained subjected to analysis of phytotic growth parameters during the field experiments with test compounds are tabularized in the following tables:

Table 2: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Cicer arientinum* (Chana/Gram) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants								
	Compd. code →	**Control (C)**	**(6a)**	**(6b)**	**(6c)**	**(6d)**	**(7a)**	**(7b)**	**(7c)**	**(7d)**
7^{th} Days	Shoot height	6	8	7	7	7	7	8	8	8
	No. of leaves	18	25	24	25	25	26	26	26	20
14^{th} Days	Shoot height	8	9.5	10	9.5	9	9	10.5	10	11
	No. of leaves	47	56	66	55	66	63	58	58	52
21^{th} Days	Shoot height	10	11	14	14	15	14	14	15	15
	No. of leaves	81	97	99	95	90	98	105	96	92
28^{th} Days	Shoot height	13	13.5	17	16.5	17	15	15.5	17	17
	No. of leaves	125	136	146	144	172	136	139	139	143
35^{th} Days	Shoot height	16	17	18	18	18	19	20	19	18.5
	No. of leaves	188	199	190	219	209	224	215	220	216
42^{th} Days	Shoot height	20	19	22	24	20	20	22	22	21
	No. of leaves	204	210	220	229	218	239	227	232	228

Table 3: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Glycine max* (Soyabean) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants								
	Compd. code →	**Control (C)**	**(6a)**	**(6b)**	**(6c)**	**(6d)**	**(7a)**	**(7b)**	**(7c)**	**(7d)**
7^{th} Days	Shoot height	5	6	7	5	6	7	7	5.5	5
	No. of leaves	4	4	4	4	4	4	4	4	4
14^{th} Days	Shoot height	6	7	8	6	7	8	8	7	6
	No. of leaves	4	4	5	4	4	4	4	4	4
21^{th} Days	Shoot height	8	9	10	9	9	10	10	9	9
	No. of leaves	7	7	8	9	9	8	8	8	9
28^{th} Days	Shoot height	10	12	12	12	11	14	13	11	10.5
	No. of leaves	8	10	12	11	11	10	10	10	10
35^{th} Days	Shoot height	15	22	21	16	20	20	21	20	20
	No. of leaves	15	17	25	20	13	20	17	19	16
42^{th} Days	Shoot height	17	22	22	23	22	22	22	22	22
	No. of leaves	17	20	28	26	22	24	26	22	21

Table 4: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Vigna radiata* (Mung) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants								
	Compd. code →	**Control (C)**	**(6a)**	**(6b)**	**(6c)**	**(6d)**	**(7a)**	**(7b)**	**(7c)**	**(7d)**
7^{th} Days	Shoot height	1.8	4.5	2.5	5	4.5	5	3.5	4	3
	No. of leaves	2	2	2	2	2	2	2	2	2
14^{th} Days	Shoot height	5	10.5	5	13	10	12	11	12	11
	No. of leaves	2	2	2	2	2	2	2	2	2
21^{th} Days	Shoot height	12	15	8.5	18	19	16	15	17.5	17.5
	No. of leaves	5	5	5	8	5	5	5	8	5

28th Days	Shoot height	13	16	11	20	20	18	18.5	19	19
	No. of leaves	8	8	9	8	8	8	8	8	6
35th Days	Shoot height	14	16.5	15	22	20.5	19	22	20	20
	No. of leaves	9	8	12	9	8	10	11	10	8
42th Days	Shoot height	15	18	16	23	23	22	24	22	21
	No. of leaves	14	10	15	14	9	12	14	13	9

Table 5: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Vigna mungo* (Udid) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants									
	Compd. code →	Control (C)	(6a)	(6b)	(6c)	(6d)	(7a)	(7b)	(7c)	(7d)
7th Days	Shoot height	0.5	1.2	2.5	1.2	1.5	1	1.5	1.5	2
	No. of leaves	2	2	2	2	2	2	2	2	2
14th Days	Shoot height	5	5	6.5	4	7	5	2.5	4	4.5
	No. of leaves	2	2	2	2	2	2	2	2	2
21th Days	Shoot height	9	9	10	5	12	9	4	8	10
	No. of leaves	5	8	5	5	8	5	5	5	8
28th Days	Shoot height	10.5	10	11	6	13	11	6	8.5	11.5
	No. of leaves	11	14	8	8	14	11	8	8	14
35th Days	Shoot height	12	10.5	11	8	15	12	8	9	13
	No. of leaves	14	20	9	9	29	17	11	11	17
42th Days	Shoot height	16	12	11.5	9	19	16	10	11	18
	No. of leaves	18	21	10	15	47	19	13	14	20

Table 6: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Solanum lycopersicum* (Tomato) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants									
	Compd. code →	Control (C)	(6a)	(6b)	(6c)	(6d)	(7a)	(7b)	(7c)	(7d)
7th Days	Shoot height	2	2.3	2.2	2.4	2.4	2.6	2.9	2.5	2.5
	No. of leaves	2	2	2	2	2	2	2	2	2
14th Days	Shoot height	3	3.4	3.3	3.5	3.5	3.5	3.3	2.8	3.5
	No. of leaves	4	4	4	4	4	4	4	4	4
21th Days	Shoot height	4.5	7	7	7	7	5	7	7	7
	No. of leaves	7	12	11	17	13	10	12	9	11
28th Days	Shoot height	7	9.5	9.5	9	8.5	9	9	9.2	9.4
	No. of leaves	17	20	22	21	19	18	20	21	18
35th Days	Shoot height	11	12	12	12	12	12	13	12	12
	No. of leaves	22	24	24	25	23	22	25	26	25
42th Days	Shoot height	14	16	19	16	18	18	18	18	20
	No. of leaves	29	34	43	36	47	39	37	42	39

Table 7: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Trigonella foenum-graecum* (Methi/Fenugreek) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants									
	Compd. code →	Control (C)	(6a)	(6b)	(6c)	(6d)	(7a)	(7b)	(7c)	(7d)
7th Days	Shoot height	2	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
	No. of leaves	2	2	2	2	2	2	2	2	2
14th Days	Shoot height	2.5	3	3	3	3	3.3	3.2	3	3
	No. of leaves	3	3	3	3	3	3	3	3	3
21th Days	Shoot height	9	11	11	12	13	10	10	13	14
	No. of leaves	10	12	11	11	12	6	8	11	14
28th Days	Shoot height	12	17	17	18	18	10.5	11	15	16.5
	No. of leaves	10	15	17	16	20	10	11	16	19

35th Days	Shoot height	20	26	28	28	29	14	17	24	25
	No. of leaves	16	26	25	22	28	15	20	22	24
42th Days	Shoot height	27	36	38	35	40	24	25	36	36
	No. of leaves	27	30	36	40	38	28	29	37	40

Table 8: Effects of newly synthesized substituted pyrazoles (6a-d) and isoxazoles (7a-d) derivatives on phytotic growth of *Capsicum annuum* (Mirchi/Chilli) crop plants

Periodicity of observation in Days	Observation of shoot height (in cm) and number of leaves of control (C) and treated (T) crop plants									
	Compd. code →	Control (C)	(6a)	(6b)	(6c)	(6d)	(7a)	(7b)	(7c)	(7d)
7th Days	Shoot height	1.5	2.3	2.4	2.4	2.5	2.5	2.5	2.5	2.5
	No. of leaves	4	5	5	4	4	4	4	4	4
14th Days	Shoot height	2	2.8	2.8	2.8	3	3	3	3	3
	No. of leaves	4	5	5	5	5	5	5	5	5
21th Days	Shoot height	3	3.5	6.5	6	6.5	7.5	11	5.5	5.5
	No. of leaves	5	5	6	5	8	8	10	5	8
28th Days	Shoot height	3.8	8	8.5	7.5	9	13	17	7.5	8
	No. of leaves	5	8	7	6	10	10	15	8	8
35th Days	Shoot height	4.4	11	12	8.5	11	17	22	9	9
	No. of leaves	6	10	10	7	16	17	22	10	10
42th Days	Shoot height	6	13	16	11	14	23	25	11.5	12
	No. of leaves	8	14	16	9	22	27	29	12	15

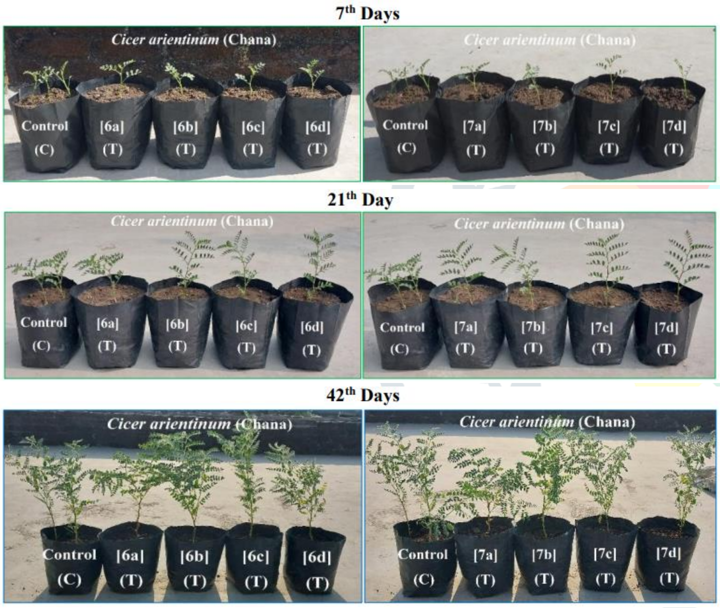

Figure 2: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Cicer arientinum* (Chana/Gram) plants

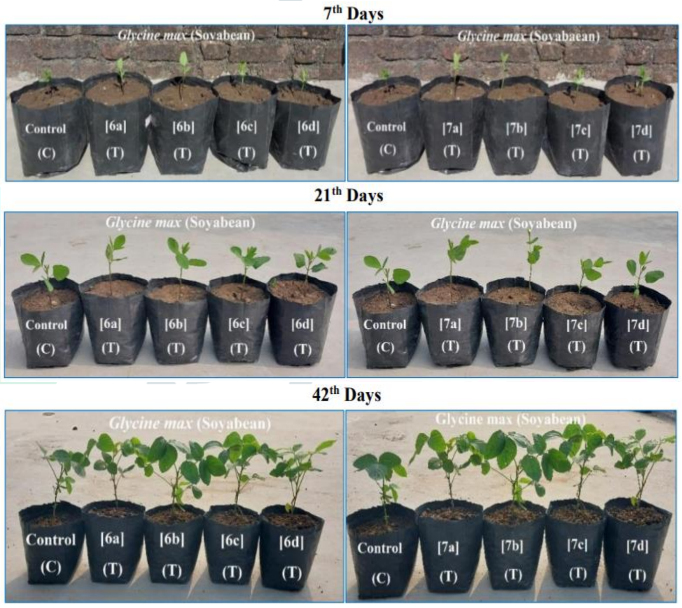

Figure 3: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Glycine max* (Soyabean) plants

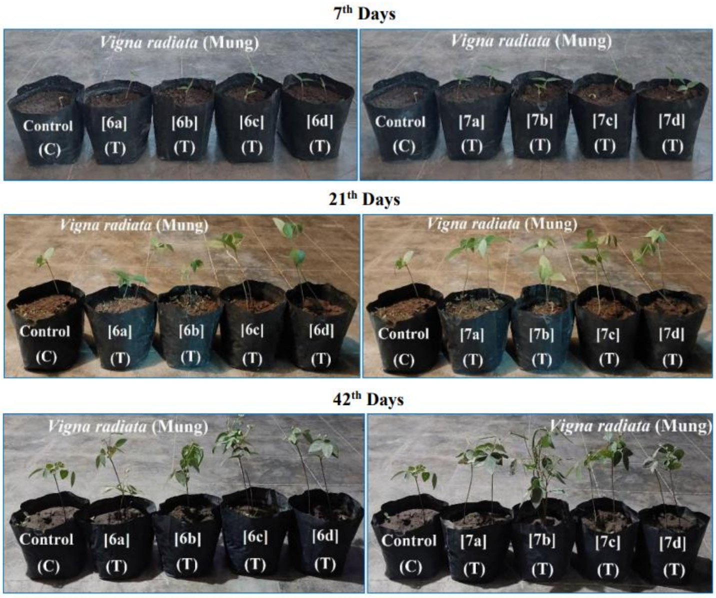

Figure 4: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Vigna radiata* (Mung) plants

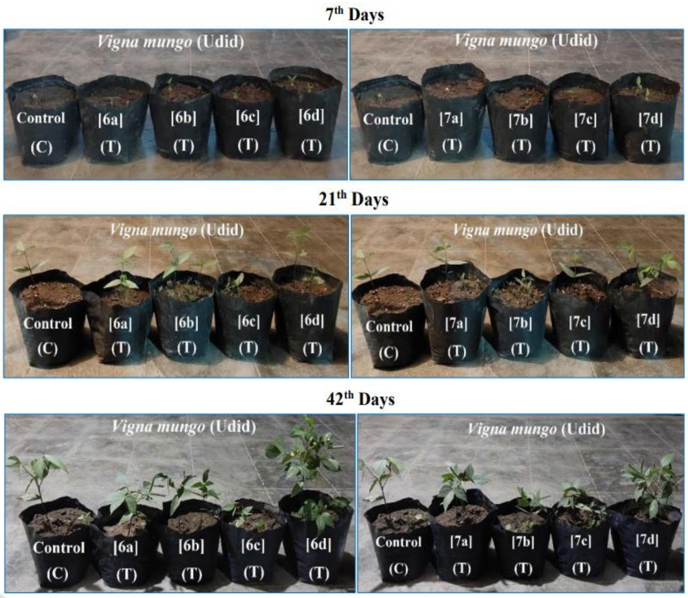

Figure 5: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Vigna mungo* (Udid) plants

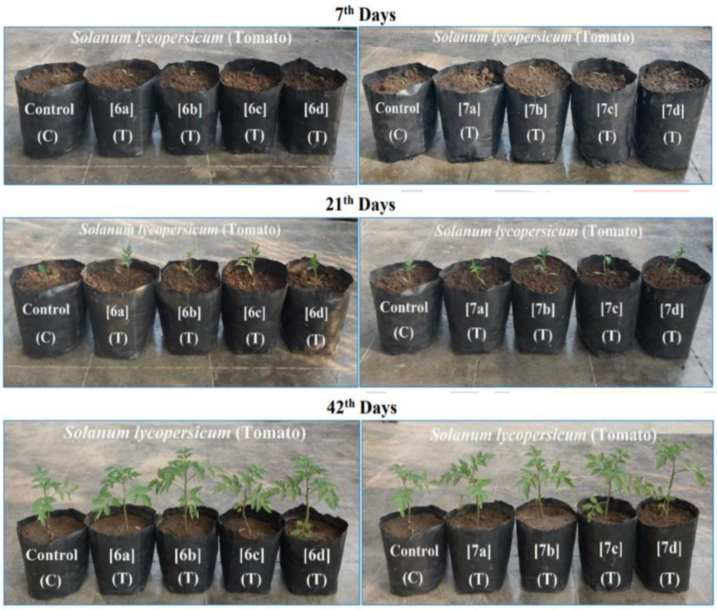

Figure 6: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Solanum lycopersicum* (Tomato) plants

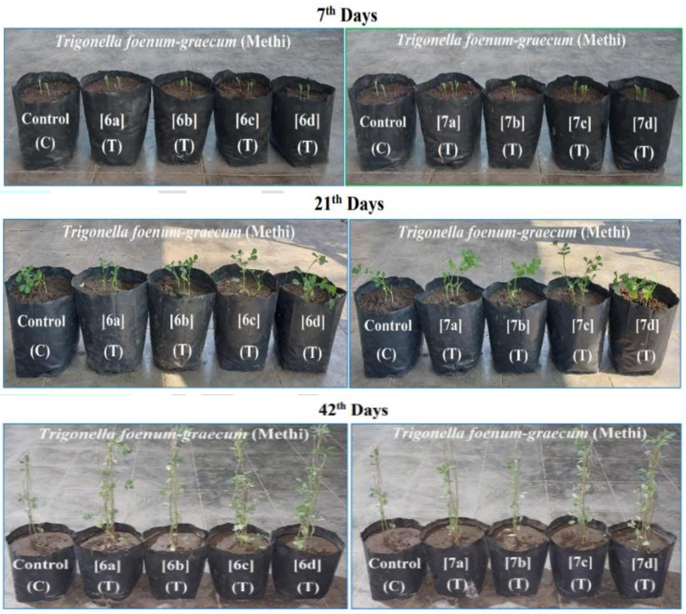

Figure 7: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Trigonella foenum-graecum* (Methi/ Fenugreek) plants

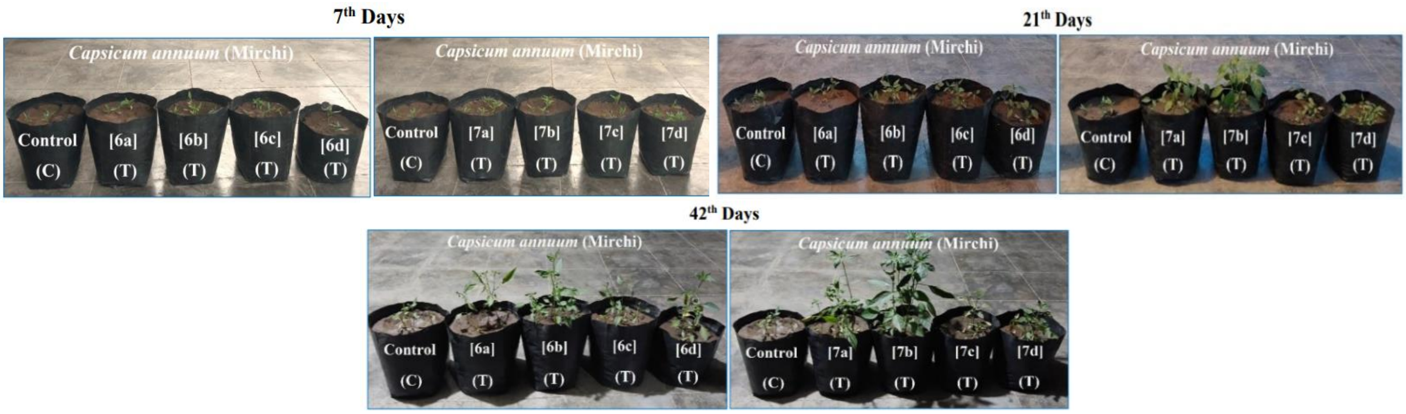

Figure 8: Impact of newly synthesized pyrazoles (6a-d) & isoxazoles (7a-d) derivatives on phytotic growth of *Capsicum annuum* (Mirchi/Chilli) plants

3. RESULTS AND DISCUSSION

The present study was aimed at impact of newly synthesized p-chloro-m-cresol incorporating 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) on phytotic growth of *Cicer arientinum* (Chana), *Glycine max* (Soyabean), *Vigna radiata* (Mung), *Vigna mungo* (Udid), *Solanum lycopersicum* (Tomato), *Trigonella foenum-graecum* (Methi) and *Capsicum annuum* (Mirchi) crop plants. The seeds of all these plants under investigation fall into the category of dicots. The choice of these crops was made on the basis of their enormously vast utility, distinctive features, and indispensability for the survival of the human race across the globe. The efforts have been made to investigate and analyse the convergence and divergence of the effects of test compounds on morphology of plants under investigation. When the first comparison of morphological character was made between those of controlled (C) and treated (T) group plants, it was interesting to note that all the treated plants exhibited remarkable shoot growth and considerable increase in the number of leaves as compared with the controlled crop plants. When all the treated plants were compared among themselves, it was distinctly observed that the plants of *Cicer arientinum* (Chana), *Glycine max* (Soyabean), *Vigna radiata* (Mung), *Solanum lycopersicum* (Tomato), *Trigonella foenum-graecum* (Methi) and *Capsicum annuum* (Mirchi) showed pronounced and dominant vegetative growth in shoot height and number of leaves. It was noticed that, all the newly synthesized pyrazoles (6a-d) and isoxazoles (7a-d) derivatives showed excellent growth promoting effects on *Cicer arientinum* (Chana), *Glycine max* (Soyabean), *Vigna radiata* (Mung) and *Solanum lycopersicum* (Tomato) plants. In case of *Trigonella foenum-graecum* (Methi), the compounds 6a, 6b, 6c, 6d, 7c and 7d showed excellent growth promoting impact whereas compound 7a, 7b exhibit less to moderate effects on shoot height and number of leaves. In case of treated crop plants of *Capsicum annuum* (Mirchi), the compounds 6a, 6b, 6d, 7a, 7b and 7d showed excellent growth promoting effects while compound 6c and 7c shows less to moderate effects on vegetative growth. As far as *Vigna mungo* (Udid) plants is concern, the compounds 6d, 7a and 7d showed good vegetative growth than compounds 6a, 6b, 6c, 7b, 7c which showed moderate growth. This observation may be attributed to the presence of nitrogen containing heterocyclic rings in the test compounds, which might have encouraged the nitrogen fixation in plant roots. In the first 3-week intervals the growth of treated plants gradually increases but after 21 and 28 days it shows a rapid increase in height of shoots and number of leaves and shows good results. Another fact which was observed during field experiment is that, all the tested plants were free from any pathogenic microbial or fungal infections. This might be due to the presence of p-chloro-m-cresol phenolic moiety in the test compounds.

4. CONCLUSION

From above discussion it is concluded that all the newly synthesized nitrogen containing 3,5-disubstituted-1-phenyl pyrazoles (6a-d) and 3,5-disubstituted isoxazoles (7a-d) compounds incorporating p-chloro-m-cresol moiety shows remarkable effects on phytotic growth of tested grain and vegetable crop plants as compared to controlled ones and they have protected the plants from fungal and microbial infections. However further detailed study in the light of agricultural sciences especially for their pathogenic disease controlling activities in crops would certainly prove to be beneficial tool for service to the mankind and society.

5. ACKNOWLEDGEMENT

The authors are thankful to the Principal, Vidya Bharati Mahavidyalaya, Amravati for providing research facilities to carry out synthetic part of research work. The authors are also thankful to Prof. Dr. C. N. Deshmukh, Department of Horticulture, Shri. Shivaji Agriculture College, Amravati for his guidance for the completion of interdisciplinary part of the present work.

6. REFERENCES

1. Ajay Kumar K, Jayaroopa P. Pyrazoles: Synthetic strategies and their pharmaceutical applications-An overview. Int J PharmTech Res 2013; 5(4):1473-1486.
2. Jyoti M, Merugu R. A review on synthesis and biological significance of pyrazoles. Int J PharmTech Res 2015; 8(1):80-87.
3. Dar AM, Shamsuzzaman. A concise review on the synthesis of pyrazole heterocycles. J Nucl Med Radiat Ther 2015; 6(5): 250.
4. Sisodiya V, Pandya A, Patel R, Patel M, Patel H, Lakshmi SR. A short review on synthesis of pyrazole derivatives & their properties. Int J Crea Res Thoug 2022; 10(4): c104-113.
5. Denmark SE, Kallemeyn JM. Synthesis of 3,4,5-trisubstituted isoxazoles via sequential [3+2] cycloaddition/silicon-based cross-coupling reactions. J Org Chem 2005; 70:2839-2842.
6. Kumar KS, Reddy KT, Vamsikanth A, Dubey PK. Synthesis and characterization of some novel isoxazoles via chalcone intermediates. Der Pharma Chemica 2011; 3(5):113-122.
7. Chauhan SS, Joshi YC. Solid phase synthesis of isoxazole derivatives from diaryl 1,3-diketones under microwave irradiation. Rasayan J Chem 2008; 1(3):475-480.
8. Musad EA, Lokanatha Rai KM, Byrappa K. Synthesis of some new 3,5-bis (substituted) pyrazoles and isoxazoles based on ($N'^{1}E$, $N'^{3}E$)-N'^{1}, N'^{3}-bis (3,4,5-substitutedbenzlidene) malonohydrazide under solvothermal conditions. Int J Biomed Sci 2010; 6(1):45-48.
9. Ratan Y, Kishore D. Novel pyrazole and isoxazole derivatives from deoxybenzoin as intermediates for the synthesis of new chemical entities. Int J Adv Res Pharma Bio Sci 2013; 3(2):95-101.
10. Reddy SP, Yamini G, Sowmya DV, Padmavathi V, Padmaja A. Synthesis and antimicrobial activity of some new 3,5-disubstituted pyrazoles and isoxazoles. Med Chem (Los Angeles) 2017; 7(12):371-380.
11. Nagaraj D, Nagamallu R, Kariyappa AK. Design, synthesis, spectroscopic characterization of new pyrazole carbothiomides as antifungal and antibacterial candidates. Lett Appl NanoBioSci 2022; 11(3):3689-3699.
12. Pande KK, Jain AP, Nayak A. Synthesis, characterization and pharmacological evaluation of novel isoxazole bearing pyrazole derivatives for antibacterial activity. Indo Amer J Pharma Sci 2022; 9(7):56-64.
13. Poudyal B, Bharghav G. A review of pyrazole and its derivative. Nat J Pharma Sci 2021; 1(1):34-41.
14. Mahesh P, Akshinthala P, Katari NK, Gupta LK, Panwar D, Sharma MK, Jonnalagadda SB, Gundla R. Antiproliferative activity of new pyrazole-4-sulfonamide derivatives: Synthesis and biological evaluation. ACS Omega 2023; 8(29):25698-25709.

15. Naim MJ, Alam O, Nawaz F, Alam MJ, Alam P. Current status of pyrazole and its biological activities. J Pharm Bioall Sci 2016; 8(1):2-17.
16. Maddineni AK, Chunduri VR. A review on recent trends in the bioactive studies of pyrazole derivatives. Asian J Res Chem 2020; 13(5):383-394.
17. Aziz H, Zahoor AF, Ahmad S. Pyrazole bearing molecules as bioactive scaffolds: A review. J Chil Chem Soc 2020; 65(1):4746-4753.
18. Rajput PR, Hushare VJ. Synthesis, characterization and antimicrobial activity of some novel isoxazoles. Rasayan J Chem 2012; 5(1):121-126.
19. Ajay Jumar K, Jayaroopa P. Isoxazoles: Molecules with potential medicinal properties. Int J Pharma Chem Bio Sci 2013; 3(2):294-304.
20. Raja S, Chikkula KV. Isoxazole: A potent pharmacophore. Int J Pharm Pharma Sci 2017; 9(7):13-24.
21. Antal S, Kumar D, Saini K, Poonam, Pannu S, Rajni, Kumar S. A review of recent scientific strategies and biological activities of isoxazole. Eur Chem Bull 2023; 12(Special Issue 4):444-459.
22. Verma RK, Nayal SS. Study of insecticidal activity of some pyrazole derivatives against American cockroaches. Ind J Chem Tech 2003; 10:347-349.
23. Heller ST, Natrajan SR. 1,3-Diketones from acid chlorides and ketones: A rapid and general one-pot synthesis of pyrazoles. Org Lett 2006; 8(13):2675-2678.
24. Wang W, Wang LP, Ning BK, Mao MZ, Xue C, Wang HY. Synthesis and insecticidal activities of O, O-dialkyl-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carbonyloxy] (aryl) methylphosphonates. Phosp Sulp, Sil Rela Elem 2016; 191(10): 1362-1367.
25. Luo J, Ding W, Zhang Y, Yang Z, Li Y, Ding L. Semisynthesis and acaricidal activities of isoxazole and pyrazole derivatives of a natural product bisdemethoxycurcumin. J Pestic Sci 2013; 38(4):214-219.
26. Fu Y, Wang M-X, Zhang D, Hou Y-W, Gao S, Zhao L-X, Ye F. Design, synthesis and herbicidal activity of pyrazole benzophenone derivatives. RSC Adv 2017; 7:46858-46865.
27. Upadhyay A, Gopal M, Shrivastava C, Pandey ND. Isoxazole derivatives as a potential insecticide for managing *Callosobruchus chinensis.* J Pest Sci 2010; 35(4):464-469.
28. Yang Z, Zhao Y, Li P, He Y. Design, synthesis and insecticidal activity of novel isoxazole derivatives containing bisamide moiety. J Hetero Chem 2019; 56(11):3042-3047.
29. Zhou Y, Chen Y, Miao W, Qu J. Synthesis, structures, and herbicidal activity of isoxazole derivatives. J Hetero Chem 2010; 47(6):1310-1316.
30. Du K, Mei YJ, Cao XT, Zhang PF, Zheng H. The synthesis of pyrazole derivatives based on glucose. Int J Chem Engg Appl 2013; 4(4):238-40.
31. Nimbalkar SD. Synthesis and study of dichlorosubstituted 4-aroyl-1-substituted pyrazoles and their impact on phytotic growth of some vegetable crop plants. Bionano Frontier 2012; 5(2-III):93-95.
32. Deotalu CL, Rajput PR. Synthesis and study of chlorosubstituted 4-aroyl/alkoyl pyrazoles and isoxazoles and their impact on phytotic growth of some vegetable crop plants. Der Pharma Chemica 2011; 3(5):318-323.
33. Badnakhe CD, Bhade MW. Novel synthesis and study of impact of chlorosubstituted 4-aroyl/alkoyl pyrazoles and its nanoparticles on phytotic growth of some flowering plants. Eur J Biomed Pharma Sci 2023; 10(9):235-239.
34. Hushare VJ, Rajput PR, Malpani MO, Ghodile NG. Synthesis, characterization of some novel pyrazoles and their growth promoting activity on some flowering plants. Int Res J Pharm 2013; 4(1):205-208.
35. Pagariya SK, Bodkhe PS. Synthesis, characterization and pharmacological evaluation of some novel pyrazole and isoxazole derivatives carrying 4-chloro-3-methyl phenol (p-chloro-m-cresol) moiety. Eur J Biomed Pharma Sci 2024; 11(5):399-409.