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SYNTHESIS AND STUDY OF IMIDAZOLE DERIVATIVES OF ARYL SUBSTITUTED 1,3-THIAZOLES AND THEIR NANOPARTICLES ON PHYTOTIC GROWTH OF SOME VEGETABLE CROPS

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ABSTRACT
The synthesis, spectral analysis and biological activities of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole ($8d_2$) (J") have been carried out. In this case 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(heptan-1-one)-2- amino-1,3-thiazole (8d) (J), 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[(2-hydroxy-3,5-dichlorophenyl)ethanonylamino]-1,3-thiazole ($8d_1$) (J') & 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one- 2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole ($8d_2$) (J") have been screened. The compound (J) was synthesized from 1-(2'-Hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4) by the action of thiourea, while (J") was synthesized from (J) by reaction with α-bromo,2-hydroxy-3,5 dichloroacetophenone to get 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[(2-hydroxy-3,5-dichlorophenyl)ethanonylamino]-1,3-thiazole ($8d_1$) (J'). Further (J') on treatment with KSCN was dissolved in acetic acid gave (J''). The nanoparticles of the compounds J, J'and J'' have been prepared by using ultrasonic technique. The titled compounds and their nanoparticles were screened for their growth promoting activity on some vegetable crop plants viz. *Momordica charantia-L-Bitter guard (Karela), Lagneria siceraria-snake guard (Lavki), Luffa cylindrica L-sponge guard (Gilke) and Benincasa hispida-Pumpkin (Kohle).*

KEYWORDS: Chalcone, thiazine, thiourea, α-bromo,2-hydroxy-3,5 dichloroacetophenone, KSCN was dissolved in acetic, growth promoting activities.

INTRODUCTION

Heterocyclic nucleus plays an important role in medicinal chemistry and it is a key template for the growth of var ious therapeutic agents. Thiazole is a heterocyclic compound featuring both a nitrogen atom and sulfur atom as part of the aromatic f ive-membered ring. Thiazoles and re lated compounds are called1,3-azoles (nitr ogen and one other hetero atom in a f ive-membered ring). They are isomeric with the 1,2- azoles, the nitrogen and sulphur containing compound be in g called isothiazoles. Thiazoles are found naturally in the essential vitamins. Molecules that possess sulfur atoms are important in living organisms. Chalcones and their analogues having α, β -unsaturated carbonyl system are very versatile substrates for the evolution of var ious reactions and phys iologically active compounds. Plant Pathology or Phytopathology deals with the cause, etiology, resulting losses and control or management of the plant diseases.

It is the scientific study of diseases in plants caused by pathogens (infectious organisms) and environmental conditions (physiological factors). Organisms that cause infectious disease include *fungi*, *oomycetes*, *bacteria*, *viruses*, *phytoplasmas*, *protozoa*, *nematodes* and *parasitic plants.*

The researchers[1-6] have reported the synthesis of several thiazoles and also their potent biological activities such as antimicrobial[7], antibacterial[8], antifungal[9], fungicidal[10] and insecticidal agent.[11]

Now a days nanotechnology is a promising field of interdisciplinary research. It opens up a wide array of opportunities in various fields like medicine, pharmaceuticals, electronics and agriculture. Since the physiochemical properties of nanoforms vary greatly, it becomes important to examine the effect of nanoparticles on microorganisms to harness the benefit of this technology in the plant protection especially against phytopathogens. Previous studies confirmed that metal nanoparticles are effective against pathogens, insects and pests. Hence nanoparticles can be used in the preparation of new formulations like nanomedicines for the diseases

like diagnosing & treating cancer[12], enhancing outer membrane of living cells[13], inhibiting tumour growth in human being[14], brain cancer.[15] Nanotechnology has the potential to revolutionize the different sectors of agriculture and food industry with modern tools for the treatment of diseases by providing the medicines for rapid diseases like malaria[16], cancer & HIV[17], breast cancer[18], localized diseases.[19]

In the present study, the chlorosubstituted 1,3-thiazoles & their imidazole derivatives (J, J', & J") have been prepared along with their nanoparticles and screened them for their growth promoting activity on some vegetable crop plants viz. *Momordica charantia-L-Bitter guard (Karela), Lagneria siceraria-snake guard (Lavki), Luffa cylindrica L-sponge guard (Gilke) and Benincasa hispida-Pumpkin (Kohle).*

EXPERIMENTAL

All the glasswares used in the present work were of pyrex qua lity. Melting points were determined in hot paraffin bath and are uncorrected. The purity of compounds was monitored on s ilica gel coated TLC plate. IR spectra were recorded on Perkin-Elmer spectrophotometer in KBr pelletes, H1 NMR spectra on spectrophotometer in CDCl3 with TMS as internal standard. UV spectra were recorded in nujol med ium. The analytical data of the titled compounds was highly satisfactory. A ll the chemicals used were of analytical grade. All the solvents used were purified by standard methods. Physical characterisation data of all the compounds is given in Table 1.

2'-Hydroxy 3',5'-Dichloroacetophenone

2-Hydroxy- 5-chloroacetophenone was dissolved in acetic acid (5 ml), Sodium acetate (3g) was added to the reaction mixture and then chlor ine in acetic acid reagent (40 ml; 7.5 w/v) was added dropwise with stirr ing. The temperature of the reaction mixture was maintained be low 200C. The mixture was allowed to stand for 30 minutes. It was poured into cold water with stirr ing. A pale yellow solid then obta ined was filtered, dr ied and crystallized from ethanol to get the compound 2'-hydroxy 3',5'-dichloroacetophenone.

Preparation of 2'-hydroxy-3',5'-dichloro-4-hexylchalcone

2-Hydroxy-3,5-dichloroacetophenone (0.01 mol) dissolved in ethanol (50 ml) treated with heptanaldehyde (0.1 M) at its boiling temperature. Aqueous sodium hydroxide solution [40%, 40 ml] was added dropwise and the the mixture was stirred mechanically at room temperature for about 1 hour. It is then kept for 6 to 8 hours followed by decomposition with ice cold HCl [1:1]. The yellow granules thus obtained were filtered, washed with 10% $NaHCO_3$ solution and finally crystallized from ethanol-acetic acid solvent mixture to get the compound.

Preparation of 1-(2'-hydroxy-3'-5'-dichlorophenyl)-2,3-dibromononan-1-one (a_1)

2'-Hydroxy-3',5'-dichloro-4-hexylchalcone (0.01 M) was suspended in bromine–glacial acid reagent [25% w/v] [6.4 ml]. The reagent was added dropwise with constant stirring. After complete addition of reagent the reaction mixture was kept at room temperature for about 30 minutes. The solid product, thus separated, was filtered and washed with a little petroleum ether to get the compound (a_1).

Preparation of 2-(4"-hexyl)- 6,8-dichloroflavone (a_2)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2,3-dibromo-nonan-1-one (0.01 mol) was dissolved in ethanol (25 ml). To this, aqueous solution of KOH (25 ml) was added. The reaction mixture was refluxed for 1 hour, cooled and diluted with water. The product, thus separated, was filtered and crystallized from ethanol to get the compound (a_2).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-1,3-nonanedione (a_3)

2-(4"-Hexyl)-6,8-dichloroflavone (0.01 mol) was dissolved in ethanol (25 ml). To this, aqueous solution of HCl (25 ml) was added. The reaction mixture was then refluxed for one hour, cooled and diluted with water. The solid product, thus obtained, filtered and crystallized from ethanol to get the compound (a_3).

Preparation of 1-(2'-hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-1,3-nonanedione (0.01 mol) was dissolved in a mixture of ethanol (10 ml) and dioxane (10 ml). To this, calculated amount of liquid bromine (0.5 ml) was added. The product was not separated even after standing for one hour. It was then diluted with water and washed with water several times and extracted with ether. The solvent was removed under reduced pressure to get the white solid of the compound (a_4).

Preparation of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(heptan-1-one)-2- amino-1,3-thiazole (J):

1-(2'-Hydroxy-3',5'-dichlorophenyl)-2-bromo-1,3-nonanedione (a_4) (0.01 mol) and thiourea (0.01 mol) were dissolved in ethanol (25 ml). To this, aqueous KOH solution (0.01 mol) was added. The reaction mixture was then refluxed for three hours, cooled, diluted with water and acidified with conc HCl. The product, thus separated, was filtered and crystallized from ethanol to get the compound (J).

Preparation of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[(2-hydroxy-3,5-dichlorophenyl)ethanonylamino]-1,3-thiazole (J')

A stoichiometeric mixture of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(heptan-1-one)-2- amino-1,3-thiazole (J) and α-bromo-2-hydroxy-3,5-dichloro acetophenone was dissolved in ethanol and refluxed for one hour. It

was then cooled, diluted with water and crystallized from ethanol to get the compound (J').

Preparation of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one- 2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole (J")

A stoichiometeric mixture of 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[(2-hydroxy-3,5-dichlorophenyl)ethanonylamino]-1,3-thiazole(J') and KSCN was dissolved in acetic acid, refluxed for 4.5 hours, cooled, diluted with water, and solid product, thus obtained crystallized from ethanol to get the compound (J")**.**

The UV, IR, and NMR spectral data

Compound (J)

UV: Spectrum No. 1

The UV-Vis spectrum of the compound (J) reported in dioxane showed λ_{max} value 410 nm corresponding to n→π* transition.

IR (KBr):- Spectrum No. 2

3036.60 cm^{-1} (-OH phenolic), 2955.55cm^{-1} (aliphatic -C-H stretching), 3036.60cm^{-1} (aromatic -C-H stretching), 3797.72 cm^{-1} (-NH_2 stretching), 1538.48 cm^{-1} (-C=N stretching), 1228.56 cm^{-1} [(C-N=) stretching], 756.57 cm^{-1} (C-Cl stretching in aliphatic), 1073.66 cm^{-1} (C-Cl) stretching in aromatic).

PMR :- Spectrum No. 3

∂ 5.2 (hump, 2H, -N-**H_2**); ∂ 6.7 (d, 1H, -CH=C-**H**); ∂ 6.8 (d, 1H, -C**H**=C-H); ∂ 7 to 7.8 (m, 6H, Ar-**H**); offset (region not observed, observed, O-**H**)

Compound (J'')

UV : Spectrum No. 4

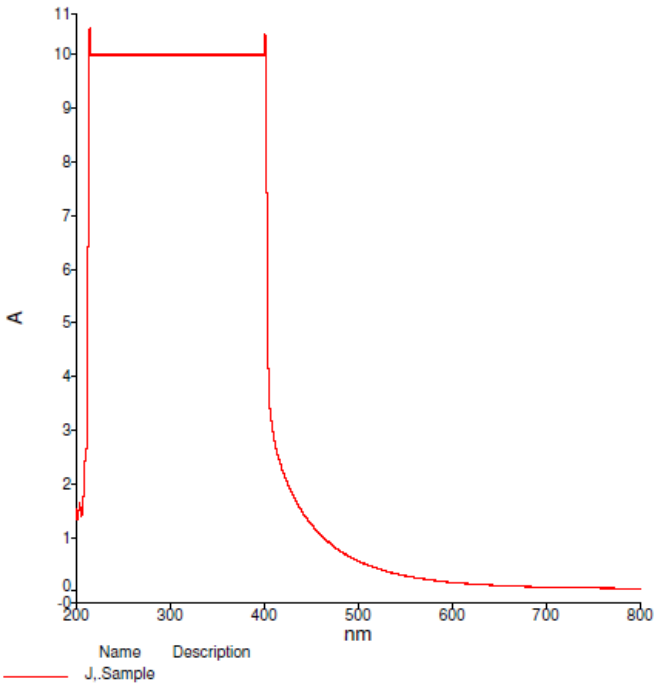
The UV-Vis spectrum of the compound J" reported in dioxane showed λ_{max} value 399 nm corresponding to n→π* transition.

IR (KBr) :- Spectrum No. 5

1649 cm^{-1} (=C=O stretching), 3391 cm^{-1} (-OH phenolic), 2925 cm^{-1} (aliphatic -C-H stretching), 3068 cm^{-1} (aromatic -C-H stretching), 1435.8 cm^{-1} (-C=N stretching), 1305 cm^{-1} [(C-N) (C-NO_2) stretching], 738 cm^{-1} (C-Cl stretching in aliphatic), 2547 cm^{-1} (-S-H stretching).

PMR :- Spectrum No. 6

∂ 7.4 to 8.25 (m, 4H, Ar-**H**); ∂ 0.80 (t, 3H, -CH2-C**H**3, ∂ 1.064 (envelope of CH2, **10H,** -(CH2)-C**H3).**



Spectrum No. 01

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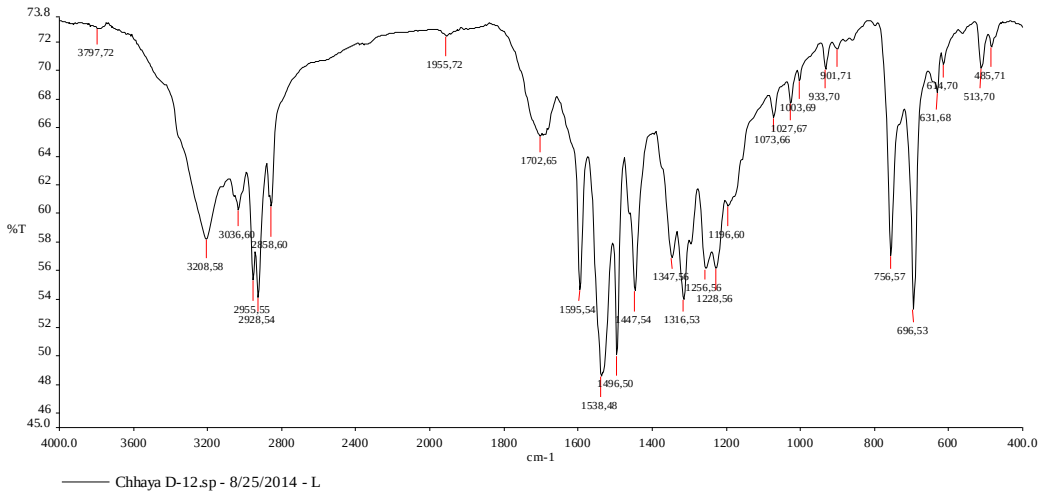

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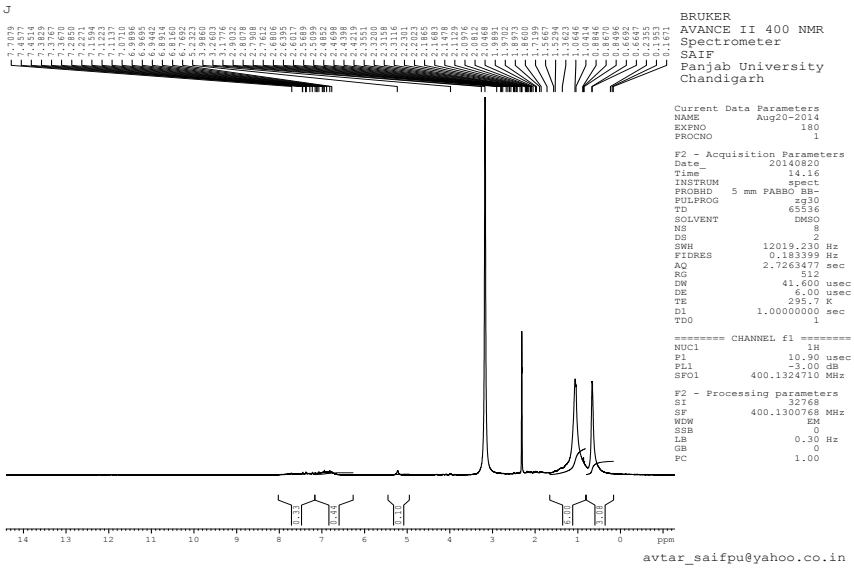

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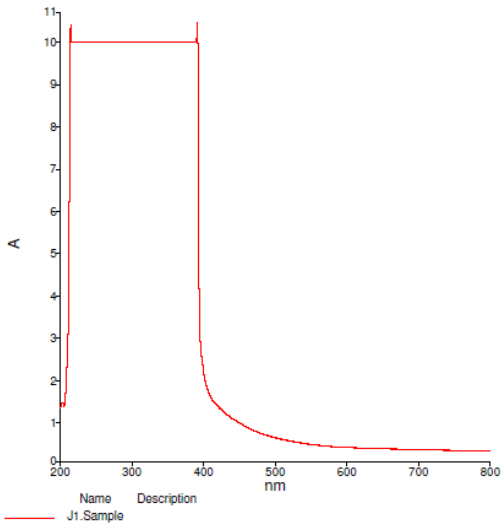

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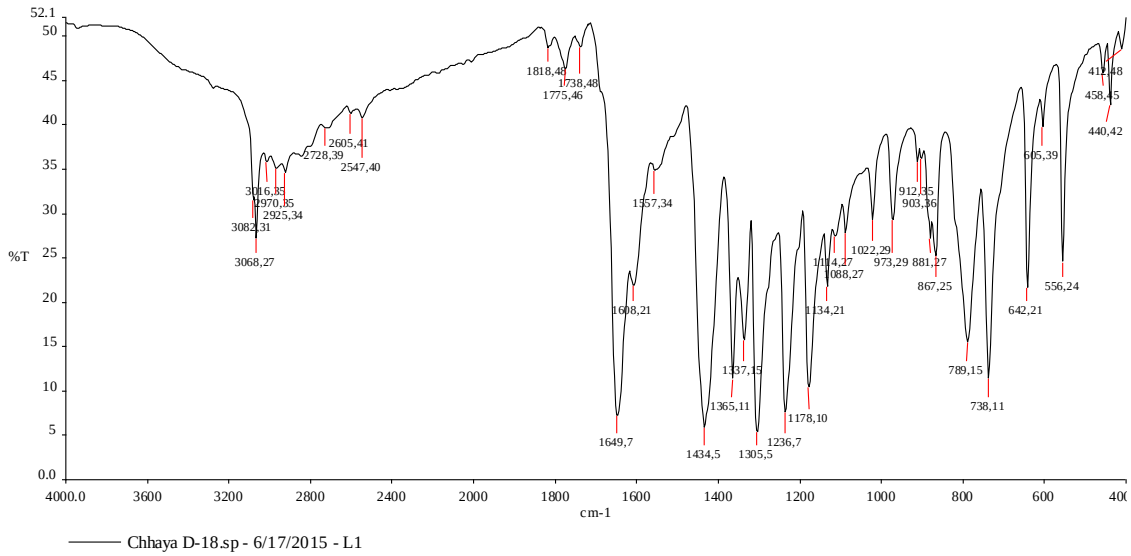

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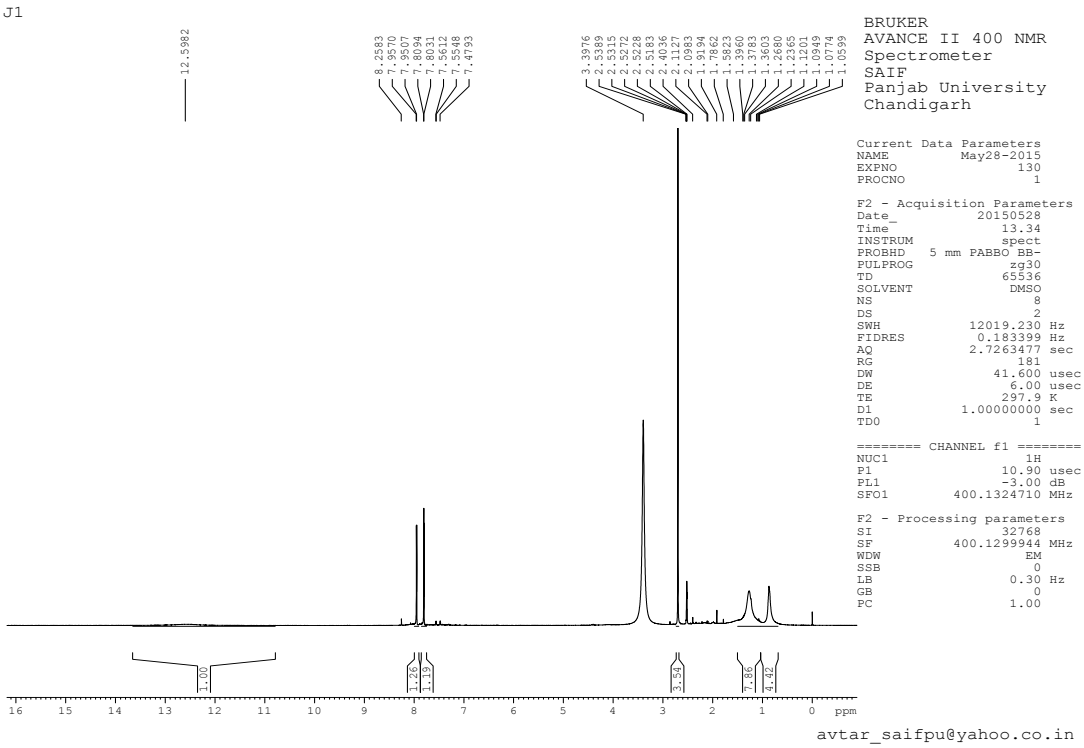
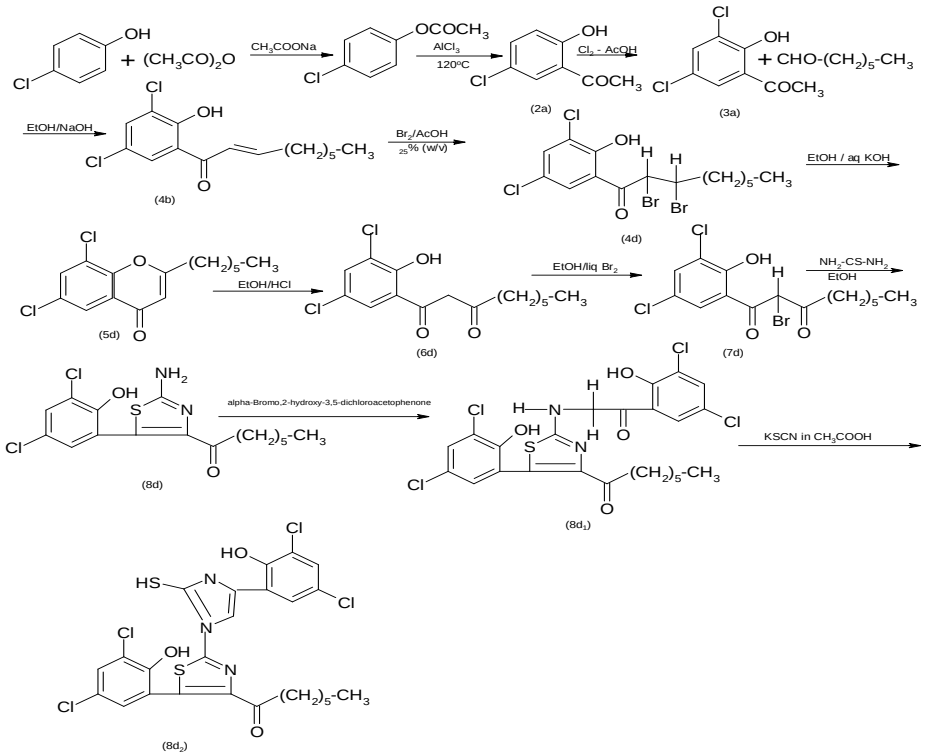


Spectrum No. 06.

Table 1: Characterisation data of newly synthesized compounds.

Compounds	Molecular formula	M.P. in ^{0}C	% of yield	% of element					
				C	H	N	S	Cl	Br
	$C_8H_6O_2Cl_2$	54	80	47.90/48	2.95/3			34.15/34.58	
a	$C_{15}H_9O_4NCl_2$	250	70	53.10/53.25	2.40/2.66	3.98/4.18		21/21.77	
a_1	$C_{15}H_9O_4NCl_2Br_2$	72	70	36.01/36.14	1.78/1.80	2.78/2.81		14.20/14.25	32.08/32.12
a_2	$C_{15}H_7O_4NCl_2$	132	60	53.14/53.57	2.07/2.08	4.13/4.16		21.03/21.13	
a_3	$C_{15}H_9O_5NCl_2$	117	50	50.74/50.84	2.45/2.54	3.90/3.95		20.03/20.05	
a_4	$C_{15}H_8O_5NCl_2Br$	78	60	41.12/41.57	1.78/1.84	3.20/3.23		16.08/16.39	18.34/18.47
J	$C_{16}H_{20}O_2N_2Cl_2S$	96	60	51.10/51.20	5.30/5.33	7.40/7.46	7.67/7.76	17.20/17.23	
J’	$C_{24}H_{22}O_4N_2Cl_4S$	94	70	49.85/50.00	3.78/3.81	4.78/4.86	5.50/5.55	24.50/24.65	
J”	$C_{25}H_{21}O_3N_3Cl_4S_2$	108	70	48.60/48.62	3.38/3.40	6.75/6.80	10.35/10.37	23.00/23.01	



Scheme

Growth Promoting Effect on some Vegetable crop Plants

The experimental set up of the study was devided into two parts:
(i) Seed treatment (ii) Field experiment.

(i) Seed treatment

With a view to safeguard dormant seed's potential from harmful external agencies, the seeds of the test plants were treated by test compounds before sowing.

(ii) Field experiment

Pregerminated quality seeds of *Momordica charantia L-Bitter guard (Karela), Lagneria siceraria -snake guard (Lavki), Luffa cylindrica L-Sponge guard-(Gilke) and Benincasa hispida -Pumpkin (Kohle*) were procured from Department of Horticulture, Dr. PDKV, Akola.

The beds of cotton soil, 2.5 x 2.5 m size were prepared in an open field. The sowing of seeds of all four test vegetable crop plants were done in separate beds and irrigated periodically.

The plants from each bed were devided into two groups i.e. A and B and designated as "Control" and "Treated" group plants respectively.

The plants from group B were sprayed with the solution of test compounds at weekly intervals. The field experiments were conducted to compare the treated plants of group B with untreated plants of controlled group A. In this context, the observations were recorded on 7, 14, 21, 28, 35, 42, 45, 56, 63, 70, 77, 84, 91 days after sowing corresponding to early vegetative, late vegetative, flowering, pod filing and pod maturation, with special reference to number of leaves and height of shoots.

The results of field's experiments are tabulated in the tables 2, 3 and 4.

Table (2): Activity of the test compounds J , J’ and J”.

Table No. (02): 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-(heptan-1-one)-2- amino-1,3-thiazole (J).

Periodicity of Observations [in days]	*Momordica charantia* (Bitter guard) (Karela)				*Lageneria siceraria* (Snake guard) (Lavki)				*Luffa cylindrica* (Sponge guard) (Gilke)				*Benincasa hispida* (Pumpkin) (Kohle)			
	Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves	
	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
7	2.5	1.5	2	2	2.5	1.5	2	2	4.5	6	2	2	20	21	2	3
14	7	2.7	2	2	7.5	10	2	2	10	8	2	2	20	23	2	3
21	25	28	7	9	8	11.2	2	2	15	10	3	5	23	24.5	3	5
28	35	60	9	12	9	15	3	4	16	18	4	6	25	27	4	6
35	47	69	10	16	11	20	4	5	20	24.5	5	8	27	35	5	8
42	51	75	12	14	17	34	5	6	25	32	7	9	30	37	6	9
49	55	81	14	16	25	37	6	7	30	35	8	11	35	40	8	12
56	60	104	16	21	28	47	7	8	35	42	10	13	38	50	10	14
63	67	112	18	24	31	51	8	10	40	46	12	14	42	54	12	16
70	72	120	20	28	34	55	9	11	45	50	14	16	46	60	14	18
77	75	127	22	30	36	58	10	13	50	54	16	20	49	65	16	22
84	80	132	24	32	38	61	11	14	55	59	18	20	53	79	18	24
91	82	175	26	47	40	72	12	17	57	72	20	24	56	83	20	26

Table No. (03): 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one-2-[(2-hydroxy-3,5-dichlorophenyl)ethanonylamino]-1,3-thiazole (J').

Periodicity of Observations [in days]	*Momordica charantia* (Bitter guard) (Karela)				*Lageneria siceraria* (Snake guard) (Lavki)				*Luffa cylindrica* (Sponge guard) (Gilke)				*Benincasa hispida* (Pumpkin) (Kohle)			
	Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves	
	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
7	2.5	1.5	2	2	2.5	1.5	2	2	4.5	4	2	2	20	20	2	3
14	7	1.7	2	2	7.5	5	2	2	10	5	2	2	20	22	2	3
21	25	15	7	6	8	8	2	3	15	12	3	7	23	23	3	4
28	35	33	9	10	9	9.5	3	4	16	23	4	7	25	27	4	6
35	47	40	10	12	11	12	4	5	20	30	5	8	27	32	5	8
42	51	60	12	15	17	14	5	6	25	40	7	11	30	37	6	9
49	55	72	14	17	25	17	6	6	30	44	8	13	35	39	8	10
56	60	90	16	21	28	30	7	8	35	52	10	15	38	52	10	14
63	67	96	18	25	31	35	8	9	40	57	12	17	42	60	12	16
70	72	102	20	32	34	38	9	11	45	62	14	19	46	64	14	18
77	75	108	22	34	36	39	10	14	50	66	16	28	49	70	16	19
84	80	123	24	35	38	47	11	17	55	69	18	30	53	76	18	20
91	82	127	26	38	40	49	12	19	57	72	20	32	56	78	20	24

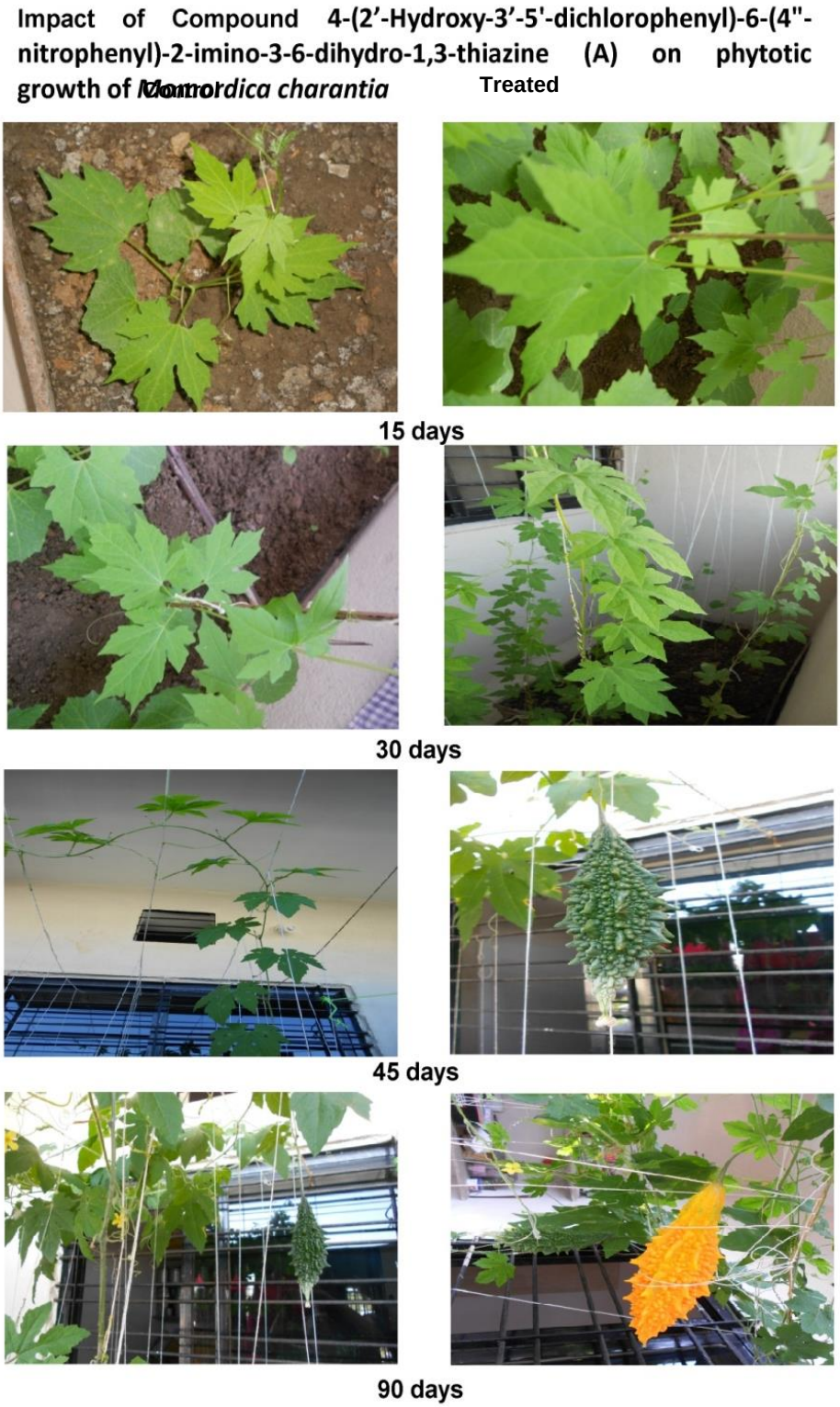
Table No. (04): 5-(2'-hydroxy-3',5'-dichlorophenyl)-4-heptan-1-one- 2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole (J").

Periodicity of Observations [in days]	*Momordica charantia* (Bitter guard) (Karela)				*Lageneria siceraria* (Snake guard) (Lavki)				*Luffa cylindrica* (Sponge guard) (Gilke)				*Benincasa hispida* (Pumpkin) (Kohle)			
	Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves		Shoot height		No. of leaves	
	C	T	C	T	C	T	C	T	C	T	C	T	C	T	C	T
7	2.5	1.5	2	2	2.5	1.5	2	2	4.4	4	2	2	20	20.5	2	3
14	7	2.7	2	2	7.5	7	2	2	10	8	2	2	20	22.5	2	3
21	25	28	7	10	8	12	2	4	15	11	3	5	23	23.5	3	4
28	35	40	9	11	9	19	3	6	16	25	4	6	25	25	4	5
35	47	47	10	12	11	26	4	7	20	38	5	9	27	30	5	7
42	51	52	12	15	17	42	5	8	25	49	7	12	30	34	6	8
49	55	60	14	18	25	48	6	8	30	53	8	14	35	39	8	9
56	60	81	16	22	28	52	7	9	35	62	10	17	38	45	10	12
63	67	96	18	24	31	55	8	10	40	65	12	18	42	50	12	14
70	72	104	20	28	34	60	9	11	45	70	14	20	46	54	14	16
77	75	108	22	30	36	63	10	13	50	73	16	23	49	59	16	18
84	80	115	24	32	38	65	11	15	55	78	18	25	53	65	18	20
91	82	119	26	36	40	68	12	17	57	82	20	27	56	68	20	22

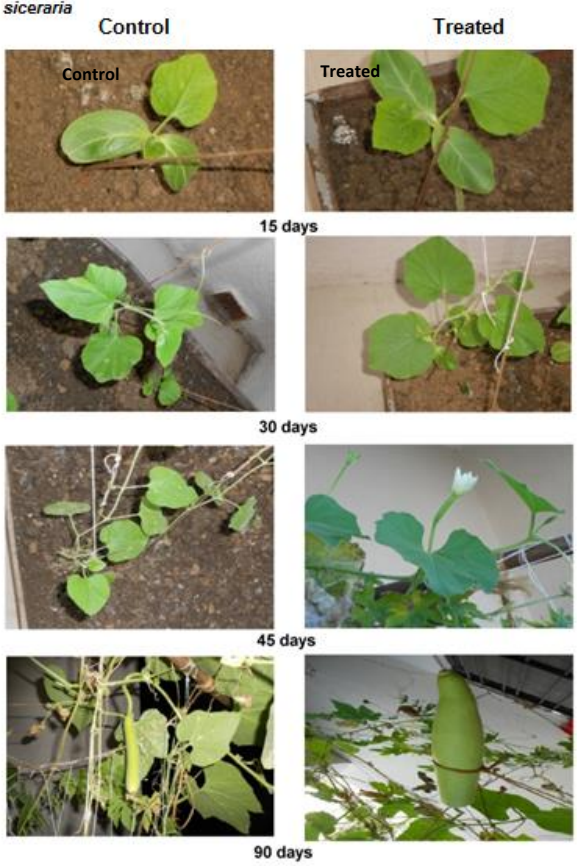
RESULT AND DISCUSSION

The titled compounds and their nanoparticles were screened for their growth promoting activity on test vegetable crop plants viz, *Momordica charantia-L-Bitter guard (Karela), Lagneria siceraria-snake guard (Lavki), Luffa cylindrica L-sponge guard (Gilke) and Benincasa hispida-Pumpkin (Kohle).*

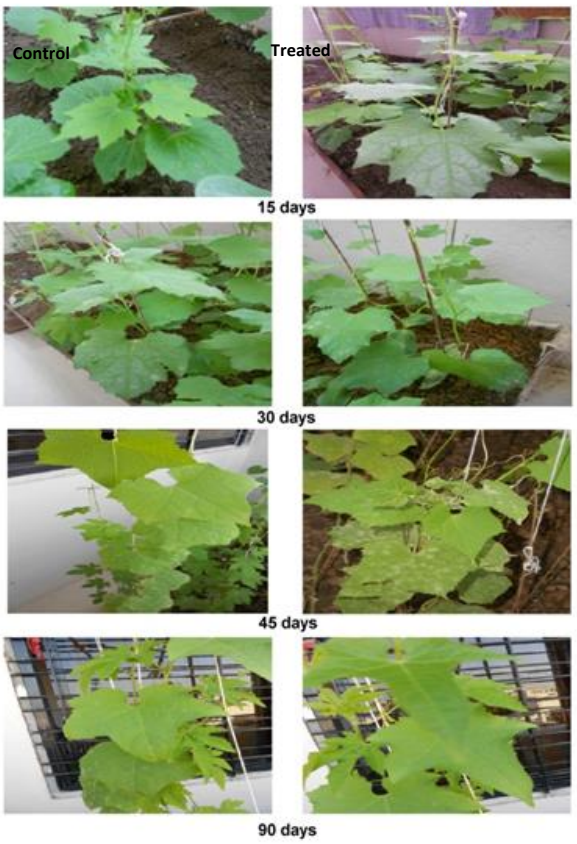
When a comparison of morphological characters was made between those of treated and control group plants, it was interesting to note that all the treated plants exhibited significant shoot growth and considerable increase in the number of leaves as compared to those of untreated ones.



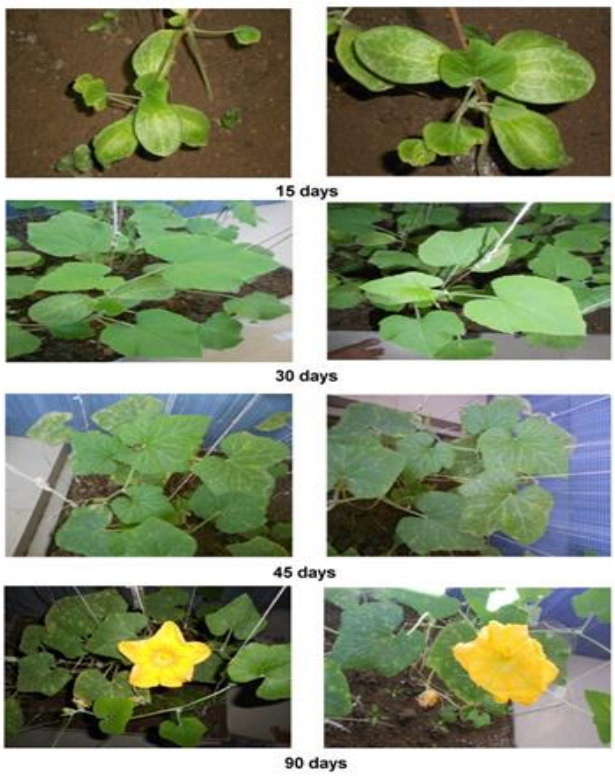
Impact of Compound 5-(2'-Hydroxy-3',5'-dichlorophenyl)-4-(4''-nitrobenzoyl)-2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole (D'') on phytotic growth of *Lageneria siceraria*



Impact of Compound 5-(2'-Hydroxy-3',5'-dichlorophenyl)-4-(4''-nitrobenzoyl)-2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole (D'') on phytotic growth of *Luffa cylindrica*



Impact of Compound 5-(2'-Hydroxy-3',5'-dichlorophenyl)-4-(4''-nitrobenzoyl)-2-[4-(2-hydroxy-3,5-dichlorophenyl)-2-mercapto-imidazolo]-1,3-thiazole (D'') on phytotic growth of *Benincasa hispida*



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