Phytocidal Properties of Hydrazide, Thiosemicarbazide and Thiadiazole Derivatives of Benzylic, Cinnamic, O-nitrobenzoic and Resorcylic Acids

Part I: Effect on Wheat Seedlings

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ABSTRACT

Twelve hydrazide, thiosemicarbazide and thiadiazole derivatives of benzylic, cinnamic, O-nitrobenzoic and resorcylic acids were synthesized, purified and analysed. The prepared compounds were tested for their phytocidal activities against shoot and root systems of wheat seedlings using plain agar technique. However, a few compounds only exhibited strong phytocidal activity against these seedlings, while most of the compounds were completely inactive and showed no effect. Generally the root system was more sensitive than the shoot to the tested compounds. The hydrazide derivative of resorcylic acid was less toxic to wheat seedlings than the thiosemicarbazide or thiadiazole ones of the same acid. The highest phytocidal effect was obtained from the hydrazide derivatives of O-nitrobenzoic acid. All hydrazide derivatives were active compounds and caused a strong phytocidal action, except the hydrazide derivative of resorcylic acid. However, the thiosemicarbazide and thiadiazole derivatives of resorcylic acid were the most effective derivatives in this respect and the results were consistent for all shoot and root systems of seedlings. Conversely, the hydrazide derivative of the same acid caused a slight phytocidal effect.

INTRODUCTION

This work was conducted to synthesize and study the phytocidal properties of hydrazide, thiosemicarbazide and thiadiazole derivatives against shoot and root systems of wheat seedlings using plain agar techniques. The phytocidal properties of these compounds, that is, the relationship between chemical structure and their phytocidal activities, have been carried out by many investigators[1-10]. This kind of work has also been studied since 1954 in our lab by El-Nawawy and his co-workers[11-13].

MATERIALS AND METHODS

Chemical Work

The following compounds were prepared and analysed according to conventional methods[14]. The analysis of these compounds included sulphur, nitrogen determination and infra-red spectra. The tested compounds and symbols used in this paper are:

Symbol	Compound
1H	Diphenyl, hydroxy acetyl hydrazide
1TSC	1-(diphenyl hydroxyacetyl) thiosemicarbazide
1TD	2-amino-5-(diphenyl hydroxymethyl) 1,3,4-thiadiazole
2H	p.phenyl propenoyl hydrazide
2TSC	1-(p.phenyl propenoyl) thiosemicarbazide
2TD	2-amino 5-(2-phenyl ethenyl)-1,3,4 thiadiazole
3H	O-nitrobenzoyl hydrazide
3TSC	1-(O-nitrobenzoyl)-thiosemicarbazide

3TD 2-amino-5-(O-nitrophenyl)-1,3,4-thiadiazole

4H 2,4-dihydroxybenzoyl hydrazide

4TSC 1-(2,4-dihydroxybenzoyl) thiosemicarbazide

4TD 2-amino-5-(2,4-dihydroxyphenyl)

-1,3,4 -1,3,4 thiadiazole

Biological Work

Seedling Growth Test

This test was carried out by using plain agar solution (1.5% agar) containing the required concentration of the compound under investigation. This solution, while hot, was poured into test tubes (1.5% 20 ml) and left to solidify. The seeds of wheat (*Triticum aestivum* L.) were soaked in water at 25°C for 24 hrs, then the water was drained off and the seeds were left at about 25°C for another 24 hrs. Homogenous seedlings were selected and placed on the agar surface with their roots slightly immersed in it. Three replicates were made for every single treatement. The control tubes did not receive any of the tested compounds. The growth of each of the root and shoot systems were measured (in cm), as well as the dry weights (in mg) at the end of the experiments. The concentration of each tested compound that caused 50% reduction in the growth of either the root or the shoot lengths (GR_{50}) was calculated according to the method of Gligox and Burnside[15] and Steinert and Stritzke[16] by the aid of regression line drawn on log-probit paper and hence correlating the inhibition percentage in length with the concentration.

The inhibition percentages of the dry weight of the root and shoot systems were calculated also according to this equation:

$$I\% = \frac{A - B}{A} \times 100$$

Where A = the dry weight of untreated seedlings
B = the dry weight of treated seedlings

The concentration of each tested compound that caused 50% reduction in the dry weight of either the roots or shoots (GR_{50}) was also calculated.

RESULTS AND DISCUSSION

The phytocidal activity of the tested compounds has been assayed against wheat seedlings. The length and dry weight of shoot and root systems were taken as parameters for this study. The results of phytocidal activity of the tested compounds are shown as percentage of inhibition (I%) and the GR_{50} values which is the concentration which caused 50% inhibition in either length or dry weight of the studied system for each tested compound. The GR_{50} values are also derived from the regression lines of the molar concentrations/inhibition percentages relationship, drawn on log-probit papers. The results are recorded as GR_{50} values shown in Table 1 and illustrated in Figures 1 to 4.

Effect on Lengths of Wheat Shoot Systems

The most effective compounds against the shoot lengths of the wheat seedlings were the resorcylic acid derivatives. However, the strongest compound was 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole which gave the lowest GR_{50} value (4×10^{-4} M) followed by the thiosemicarbazide derivative of the same acid where the GR_{50} value was still lower than the GR_{50} values of all tested compounds. In addition, the GR_{50} values of the thiosemicarbazide of benzylic, cinnamic, and O-nitrobenzoic acids were higher than the highest concentration used ($2x10^{-3}$ M), while the GR_{50} value of 1-(2,4-dihydroxybenzoyl)-thiosemicarbazide was $6x10^{-4}$ M.

The least effective compounds were the hydrazide, thiosemicarbazide and the thiadiazole derivatives of cinnamic acid, where the GR_{50} values of all three compounds were more than the highest concentration used ($2x10^{-3}$ M).

Diphenylhydroxyacetyl hydrazide was the most effective compound among the benzylic acid derivatives which the GR_{50} value was $1.45x10^{-3}$ M. The GR_{50} values for the thiosemicarbazide, and the hydrazide derivatives of the same acid were higher than $2x10^{-3}$ M. The same phenomena appeared in the case of O-nitrobenzoic acid in which the hydrazide derivative was more effective against the shootlengths of the wheat seedlings than the other derivatives tested. The GR_{50} value of O-nitrobenzoyl hydrazide was $1.05x10^{-3}$, for 1-(O-nitrobenzoyl)-thiosemicarbazide was $2x10^{-3}$, and for 2-amino-5-(O_nitrophenyl)-1,3,4-thiadiazole was $1.9x10^{-3}$ M.

Ex+ <u>Effect on the Lengths of Wheat Root Systems</u>

The phytocidal activity of the tested compounds on the root system of wheat seedlings was higher than the shoot system. This fact was expected as the root is in contact with the tested chemicals, and in addition the root system is more sensitive than the shoot one.

Hydrazide, thiosemicarbazide and 1,3,4-thiadiazole derivatives of resorcylic acid were the most effective compounds against the root system of wheat seedlings, but the hydrazide derivative was the least effective in this respect. The GR_{50}

values for 2,4-dihydroxy-benzoyl hydrazide, 1-(2,4-dihydroxybenzoyl)-thiosemicarbazide, and 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole were $1.15x10^{-3}$ M, less than $5x10^{-5}$ M and $1.5x10^{-4}$ M, respectively. It was obvious that cyclization of thiosemicarbazide of resorcylic acid to form 1,3,4-thiadiazole decreased the activity.

While hydrazide and 1,3,4-thiadiazole derivatives of O-nitrobenzoic acid exhibited a high degree of toxicity against the root system of wheat seedlings, the thiosemicarbazide one showed a very low degree of toxicity in the same concern. The GR_{50} value of 1-(O-nitrobenzoyl)-thiosemicarbazide was more than $2x10^{-3}$ M (the highest concentration used). The GR_{50} was less than $5x10^{-5}$ M for O-nitrobenzoyl hydrazide and 2-amino-5-(O-nitrophenyl)-1,3,4-thiadiazole, respectively.

The hydrazide and 1,3,4-thiadiazole derivatives of cinnamic acid were nearly equal in their phytocidal activity and the GR_{50} values were $5x10^{-4}$ M. The thiosemicarbazide derivative of the same acid was less active against the root system than other derivatives, whereas its toxicity was nearly half of hydrazide or thiadiazole ones. The GR_{50} value of 1-(B-phenylpropenoyl)-thiosemicarbazide was $1.075x10^{-3}$ M.

Comparing the inhibition percentage for the compounds showed GR_{50} values less than $5x10^{-5}$ M. It was clear that the hydrazide derivative of benzylic acid was the most effective compound among all tested compounds. Also, thiosemicarbazide and 1,3,4-thiadiazole derivatives of the same benzylic acid caused a marked degree of phytocidal activity against the root system of wheat seedlings. The GR_{50} values of 1-(diphenylhydroxyacetyl)-1,3,4-thiadiazole were $9x10^{-4}$ and $1.25x10^{-3}$ M, respectively.

Effect on Dry Weight of Wheat Shoot Systems

Hydrazide, thiosemicarbazide, and 1,3,4-thiadiazole derivatives of resorcylic acid were the most effective compounds against the dry weight of wheat shoot systems and caused the highest inhibition in this respect. The strongest compound was 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole with a GR_{50} value less than the lowest concentration used ($5x10^{-5}$), followed by the compound 2,4-dihydroxybenzoyl hydrazide which showed a high degree of dry weight inhibition for the shoot system. Its GR_{50} value was almost equal to $5x10^{-5}$ M. However, the GR_{50} value of 1-(2,4-dihydroxybenzoyl)-thiosemicarbazide was$2.7x10^{-4}$ M, which means that cyclization of thiosemicarbazide to form thiadiazole analogue significantly increased the toxicity.

The hydrazide derivative of O-nitrobenzoic acid was the strongest compound among this group. The GR_{50} value of O-nitrobenzoyl hydrazide was less than $5x10^{-5}$ M, while the GR_{50} value of 1-(O-nitrobenzoyl)-thiosemicarbazide was $3x10^{-4}$ M. However, when the thiosemicarbazide was transformed chemically to a thiadiazole one, the inhibition potency increased for the resultant with about 4.2 folds, compared with the parent one. So, the GR_{50} of 2-amino-5-(O-nitrophenyl)-1,3,4-thiadiazole was $7x10^{04}$ M. The same trend appeared when the hydrazide, thiosemicarbazide, and thiadiazole derivatives of O-nitrobenzoic acid were tested against the lengths of wheat shoot systems.

The hydrazide and 1,3,4-thiadiazole derivatives of cinnamic acid exhibited a small degree of dry weight inhibition on the wheat shoot system, with the GR_{50} values of B-phenylpropenoyl hydrazide and 2-amino-5-(2-phenylethenyl)-1,3,4-thiadiazole were $1.4x10^{-3}$ and $1.1x10^{-3}$ M, respectively. The thiosemicarbazide of the same acid caused a moderate inhibition of the same system. The GR_{50} value of 1-(B-phenylpropenoyl)thiosemicarbazide was $6x10^{-4}$ M.

Although the effect of benzylic acid derivatives on the dry weight was higher than the lengths of the shoot system, the hydrazide derivative was the only compound which exerted a moderate phytocidal effect among this group. The thiosemicarbazide and thiadiazole derivatives caused a small inhibition effect against the dry weight of wheat shoot system. The GR_{50} values of diphenylacetyl hydrazide, 1-(diphenyl hydroxyacetyl)-thiosemicarbazide, and 2-amino-5-diphenyl hydroxymethyl)-1,3,4-thiadiazole were $2x10^{-4}$, $1.2x10^{-3}$, and $5x10^{-3}$ M, respectively.

Effect on Dry Weight of Wheat Root System

The effect of tested compounds on the dry weight of wheat root system was less than their effect on the lengths of the same system. Most of the tested compounds exerted GR_{50} values higher than $2x10^{-3}$ M, which is the highest concentration used. In addition, the hydrazide, thiosemicarbazide and thiadiazole derivatives of benzylic and cinnamic acids caused a slight stimulation of the dry weight of wheat root systems, especially at low concentrations, except the thiadiazole derivative of the cinnamic acid which exhibited a slight inhibition of the dry weight of wheat root system.

The O-nitrobenzoic acid derivatives were the most effective compounds against the dry weight of wheat shoot systems, especially the compounds 1-(B-phenylpropenoyl)-thiosemicarbazide and 2-amino-5-(O-nitropehnyl)-1,3,4-thiadiazole, which exerted GR_{50} values of $4.2x10^{-4}$ M and $6.2x10^{-4}$ M, respectively. The O-nitrobenzoylhydrazide exhibited a slight effect and its GR_{50} value was more

Table 1: GR_{50} values (in M x 10^{-3}) of tested compounds on the length and dry weight of wheat seedlings.

Tested Compounds	Lengths		Dry Weight	
	Shoot	Root	Shoot	Root
1. Derivatives of Cinnamic Acid				
Hydrazide	1.45	0.05	0.30	2.00
Thiosemicarbazide	2.00	0.90	1.20	–
Thiadiazole	2.00	1.25	1.50	2.00
2. Derivatives of Benzylic Acid				
Hydrazide	2.00	0.50	1.40	2.00
Thiosemicarbazide	2.00	1.075	0.60	2.00
Thiadiazole	2.00	0.42	1.10	2.00
3. Derivatives of O-nitrobenzoic Acid				
Hydrazide	1.05	0.05	0.05	2.00
Thiosemicarbazide	2.00	2.00	0.30	0.42
Thiadiazole	1.90	1.80	0.07	0.62
4. Derivatives of Resorcylic Acid				
Hydrazide	2.00	1.15	0.05	2.00
Thiosemicarbazide	0.65	0.05	0.27	2.00
Thiadiazole	0.40	0.15	0.07	0.20

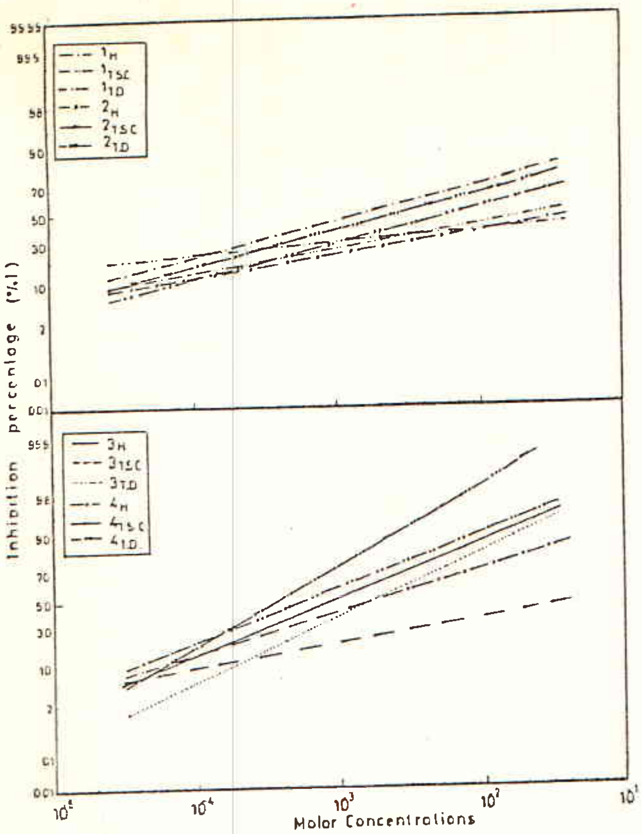

Figure 1 : Regression lines of the effect of hydrazide, thiosemicarbazide and thiadiazole derivatives on wheat seedlings shoot length (6 days old)

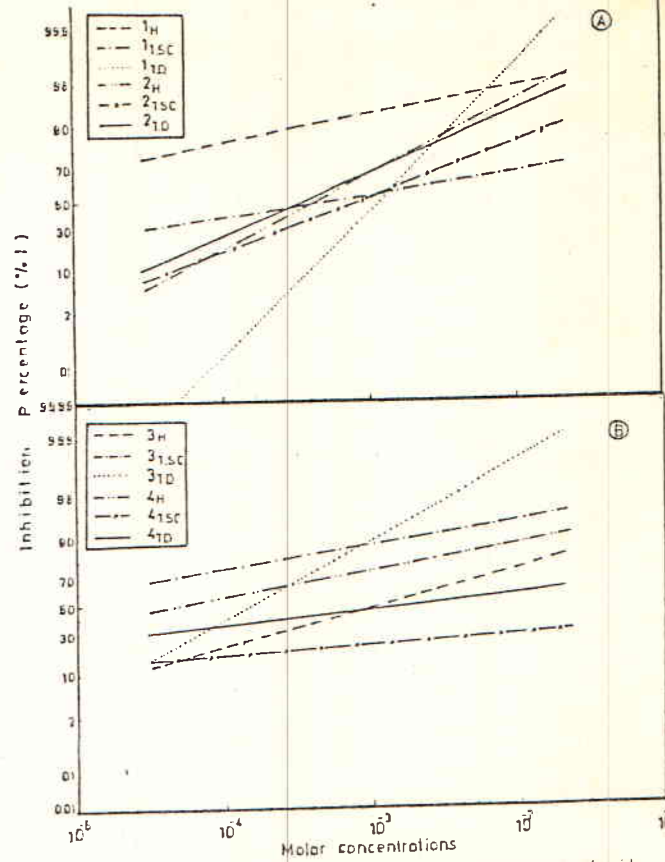

Figure 2 Regression lines of the effect of hydrazide, thiosemicarbazide and thiadiazole derivatives on wheat seedlings root length (6 day old)

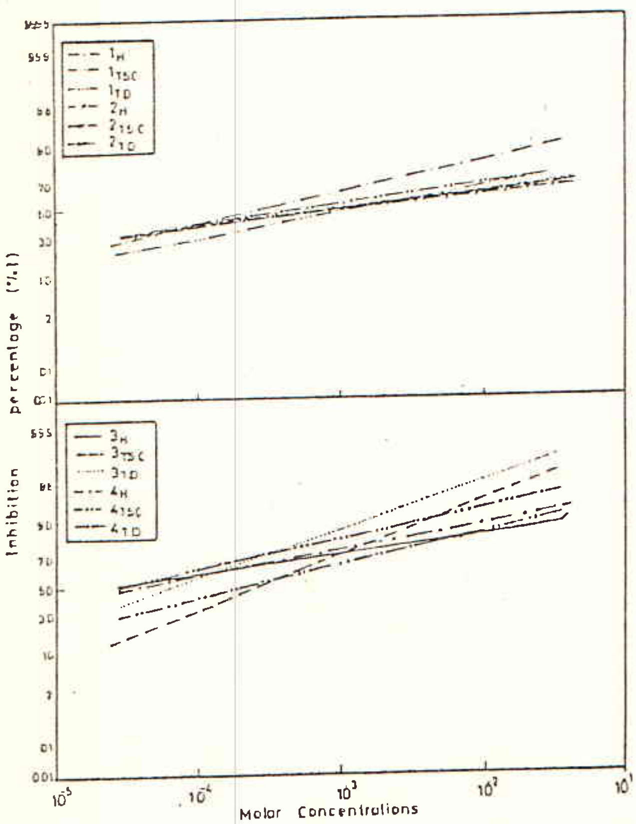

Figure 3 : Regression lines of the effect of hydrazide, thiosemicarbazide and thiadiazole derivatives on dry weight of the wheat seedlings (shoot system, 6 days old)

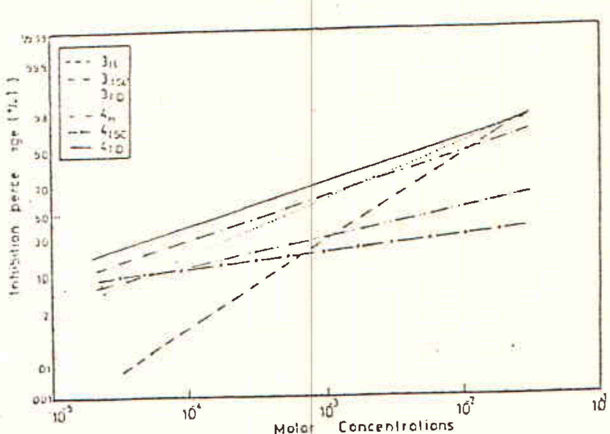

Figure 4A Regression lines of the effect of the hydrazide, thiosemicarbazide, thiadiazole derivatives on the dry weight of the wheat seedlings (root system, 6 days old)

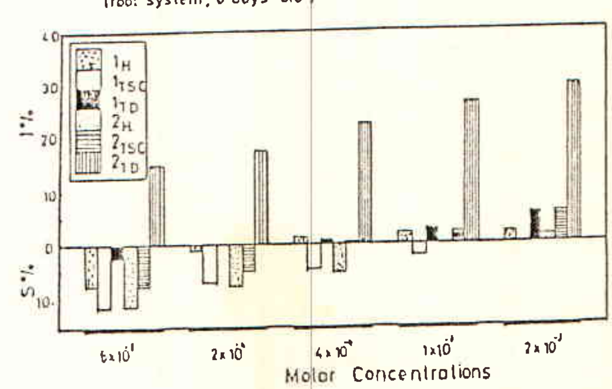

Figure 4 B : Effect of hydrazide, thiosemicarbazide, and thiadiazole derivatives on the dry weight of the wheat seedlings (root system, 6 days old)

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than 2×10^{-3} M, the highest concentration used.

The 1,3,4-thiadiazole derivative of resorcylic acid was the most effective compound among all tested compounds against the dry weight of wheat root systems. The GR_{50} value of 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole was 2×10^{-4} M, the least GR_{50} value obtained in this respect. The hydrazide and thiosemicarbazide derivatives of the smae acid were completely ineffective against the same parameter. This assures us of the inconsistency between the chemical structure and the phytocidal activity of these compounds.

REFERENCES

1. Ahmed, H.A. 1980. Synthesis, Fungitoxicity and Phytoxicity of 2-amino-5-phenyl-1,3,4-thiadiazole. Proc. IV Conf. Egyptian Soc. Applied Microbiology., Cairo. Vol. II: Plant Pathology.

2. Amer, Soheir M. 1973. Effect of some drugs on the meiosis of <u>Vicia faba</u> nucleus (calcutte) 16 (1): 26-28. (BA, 1974, 58 (2): 6818).

3. El-Gibali, A.A.; S. El-Serogy and W.I. Mesiha. 1974. Effect of growth retardants on drought tolerance and growth of cotton plants. Egypt J. Bot., 17 (1): 85-88. (BA, 1974, 61 (3): 11672).

4. Guseinov, D.M.; T.N. Dzhalilov; F.G. Isaeva and T.G. Gasanov. 1977. Plant growth stimulant. USSR 549, 124 (C). AOIN4(00), 05 Mar., 1977, App. 2, 120, 550, 04 Apr. 1975. From Otkrytiya, Izobret., Prom. Obraztsy Tovornye Znak, 1977, 54 (9):9. (CA, 1977, 87 (1): 11872).

5. Hagimato, H.; T. Arai; H. Yoshikawa; M. Watanabe; Y. Okada. 1973. Herbicidal 2-(benzylthio-1,3,4-oxa (or thia) diazoles. Brit. 1,307, 283 (Cl.A01n), 14 Feb. (CA, 1973, 79 (5), 28395 m).

6. Hagimato, H.; T. Arai; H. Yoshikawa; M. Watanabe; and Y. Okada. 1974. Herbicidal compositions containing benzylthiadiazoles and trizens. US 3, 787, 198. (Cl. I1/93; A01n), (Japan). (CA, 1974, 80 (23):129271 v).

7. Hsuh, W.; Yuling Liu; and Tie Fan. 1985. A sensitive method for the determination of residues of N, N'-bis-(1,3,4-thiadiazol-2-yl) methanediamine in rice. Pestic. Sci., 16: 59-64.

8. Ishida, M.; K. Kawakubs; T. Henma; T. Yamazaki; H. Yoshitake; T. Honda; F. Kimura and Y. Kawaguchi. 1973. Herbicides containing 3,4-thiadiazole derivatives. Kokai 73, 23, 935. (Cl. 30 F 371. 222, 30 F 932) (Japan). (CA, 1973, 79 (13), 74937 p).

9. Mazzone, G.G.; G. Puglisi; F. Bonina and A. Corsaro. 1983. A new synthesis of symetrical 2,4-di-aryl-1,3,4-thiadiazoles. J. Heterocyclic Chem., 20: 1399.

10. Vassilev, G.N. and N.P.Maschev. 1974. Chemical structure and cytokinin activity of some new derivatives of N-alkyl-N-arylthiourea and their effect on the uptake of amino acids into plant seedlings. Biochem. Physiol. Pflanz (BPP) 165 (1/2): 49-60. (BA, 1974, 58 (12): 68916.)

11. El-Nawawy, A.S.; S. Al-Deeb; A. Tag El-Din;

M.S. Khalifa and E.A. Kadous. 1974. Relation between chemical and biological activity of pesticides. XXXV. Relation bewteen structure of alkyl group and fungitoxicity of several compounds. Proc. 1st Congress of Egyptian Phytopathological Soc. CAiro.

12. El-Nawawy, A.S.; E.A. Kadous; A.S. Abdel-Fattah; M.S. Khalifa and S.T. El-Deeb. 1977. Relation between chemical structure and biological activity. Part XXX VIII. Fungicidal proportions of certain arylthioronium arylarsonates. Proc. 2nd Arab Pest. Conf. Tanta Univ., 11: 878-87.

13. El-Nawawy, A.S. and S.A. El-Kheshin. 1960. The relation between chemical structure and biological activity. Part I. The principle of covelenelectrovalent organic molecule. Alex. J. Agric. Research, 8 (1): 277.

14. Abd El-Naby, L.M.A. 1986. Biological activity of some new organic compounds. Ph.D. thesis, Fac. of Agric. Alexandria Univ. Egypt.

15. Gligox, O.R. and O.C. Burnside. 1977. Herbicide phytotoxicity, movement and persistence in asphalt. Weed Science, 25 (5) 426.

16. Steinert, W.G. and J.F. Stritzke. 1977. Uptake and phytotoxicity of tebuthiuron. Weed Science, 25 (5): 390.