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SYNTHESIS AND BIOLOGICAL ACTIVITY OF THIOSEMICARBAZIDES

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Abstract: The thiosemicarbazaides synthesized from different acid hydrazides with some thiocynates in alcohalic medium. The products of these are found to possess significant pesticidal as well as antifungal activities.

Keywords: Derivatives of 1,2,4-triazoles, Thiosemicarbazides, Biological activities.

Introduction: Work on biologically actives heterocycles and related compounds was undertake with a view to synthesize mostly potential pesticides like herbicides, fungicides, weedicides and bactericides, Indian masses reside in village and major population depends on agriculture and only recently enough food grains are produced to food entire population. It has been a continuous endeavor to seek suitable measures to protect our plants and grains from pests. The famine which took millions of lives is well recorded around the world. Being tropical country and where breeding capacity of pests is very high. It is necessary to find out chemicals which can protect our crops from pests and are less hazardous to man. In early stage Burgundy Mixture[1], Bordeaux mixture[2], salts of mercury[3], Paris green etc were used as pesticides but these were toxic and hazardous to human beings. Only recently organic pesticides especially which are derived from aromatic and heterocyclic compounds such as Gammaxene, Chlorodane[4], Heptachlor[5], Toxaphane[6], D.D.T. and its analogous organphosphorus compounds-Dithane[7], Malathion[8] etc. have seen developed. The late blight of potato destroys the potato crop and in Ireland. This caused a famine and many people died of starvation. In India worth of millions of food grains is lost due to mice, locusts and other pests.

The livelihood of whole communities in certain parts of Middle East and in the northern parts of Africa are periodically threatened by the invasion of locusts. The pioneer farmers in the middle west of America in the early Nineteen century were forced to leave their farms and returned to east when invading swarms of grasshopper devoured the grass and crops denuding country sides in Missoure, Italian Town and neighboring states[9].

The term pesticides includes all the chemicals used as pest controlling agent repellants fungicides, seed protectants, weed killers and rodenticides.

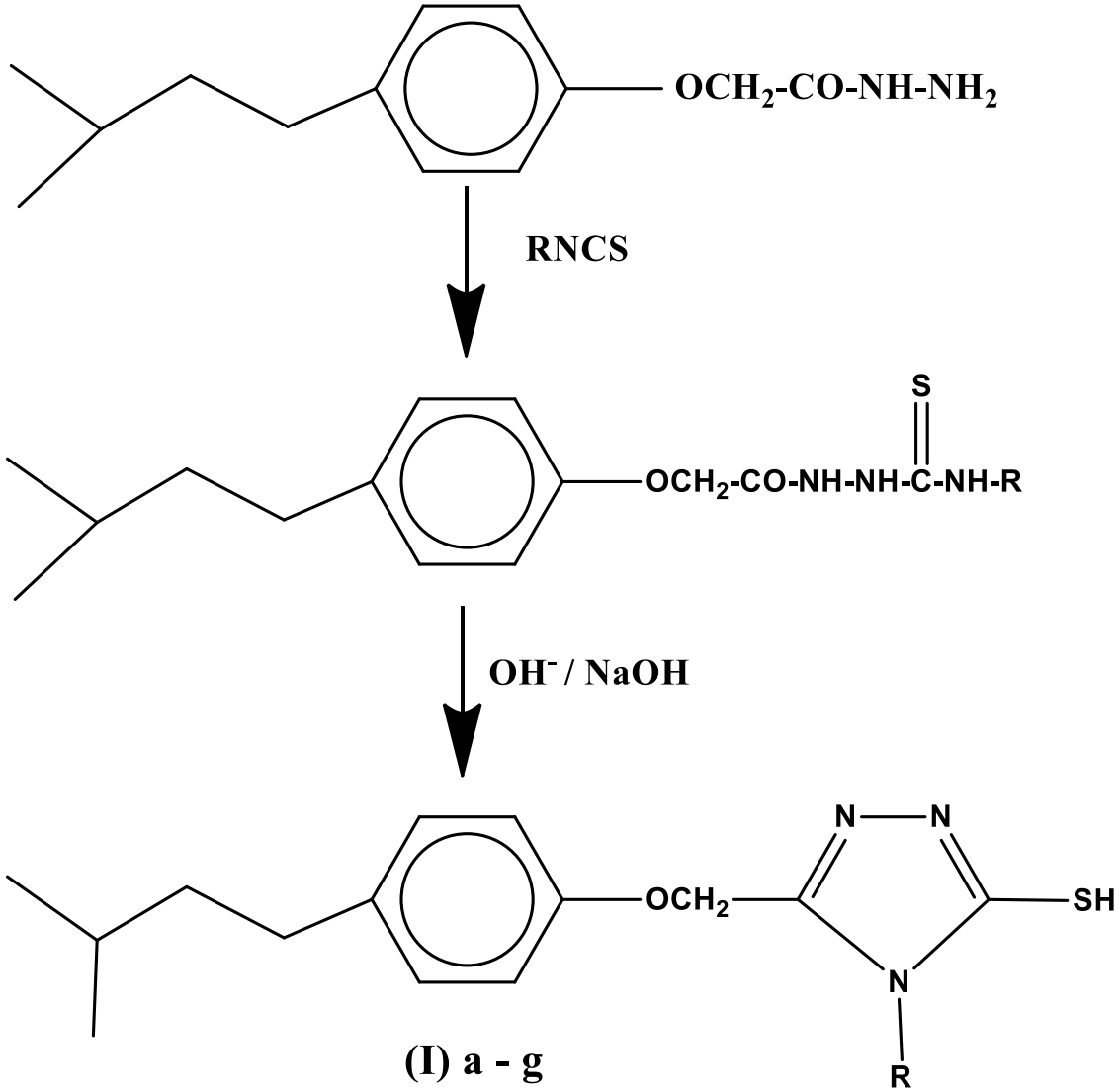
The heterocyclic compounds and their derivatives have proved to be better pesticides and are less hazardous to the operator. They have proved C.N.S.- depression agent, analgesics[1], fungicides[2], herbicides[4], viruscides[5] and bacteriocides[6]. This is due to certain toxopheric groups present heterocyclic compounds. Harsfall and Rice[7] have studies a large number of heterocyclic compounds and reported that pure heterocyclic compounds have no pesticidal activities[8] and certain groups are responsible for their pesticidal action. These groups are $-NH_2$, -SH, and $-NO_2$, etc. Quaternary ammonium salts showed increased pesticidal action.

Keeping view on the above facts, we have synthesized a series of new heterocyclic compounds such as Triazoles, Oxadiazloes, Thaidiazoles and Pyrazoles and tested them as weedicides[9], fungicides[10] and bacteriocides[11]. The compounds have been analyzed by modern methods. Their purity is established by spectroscopic and analytical means. The work can

summarized as follow. Thiosemicarbazide and its derivatives are well studied for their vast biological activities[12,13,14]. In present work some derivatives of thiosemicarbazide are studied for their biological strudies.

1. Synthesis of thiosemicarbazides:

Preparation of thiosemicarbazides: The thiosemicarbazides were prepared by reaction of different acid hydrazides with different isothiocyanates in equimolecular quantities in alcoholic medium. Their purification was done by crystallization with ethanol and tested by TLC. The thiosemicarbazides thus prepared as reported in **Table I** and **II**.



(I) a - g

Table: 1

Physical data of thiosemicarbazide derivatives (I_{a-g})

Compounds	Side Chain (R)	M.P. °C	Molecular Formula	Reqd. N%	Found
I_a	2-Chlorophenyl	160	$C_{20}H_{24}ClN_3O_2S$	10.36	10.53
I_b	3-Methoxylphenyl	175	$C_{21}H_{27}N_3O_3S$	10.47	10.95
I_c	4-Methoxyphenyl	210	$C_{21}H_{27}N_3O_3S$	10.47	10.10
I_d	Benzyl	162	$C_{21}H_{27}N_3O_2S$	10.91	10.90
I_e	Cyclohexyl	190	$C_{20}H_{31}N_3O_2S$	10.41	11.35
I_f	2-Ethylphenyl	148	$C_{29}H_{29}N_3O_3S$	10.52	10.47
I_g	4-Ethoxyphenyl	213-14	$C_{22}H_{29}N_3O_3S$	10.12	10.37

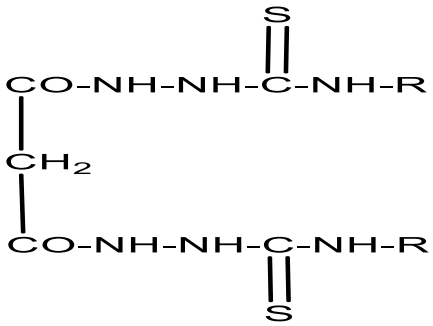


Table: 2

S. No.	Side Chain (R)	M.P. °C	Molecular Formula	Analysis Reqd.	N% Found
1.	H	223	$C_5H_{10}O_2N_6S_2$	33.58	33.4
2.	Benzyl	205	$C_{10}H_{22}O_2N_6S_2$	19.52	19.8
3.	m-Tolyl	190	$C_5H_{10}O_2N_6S_2$	19.52	19.6
4.	p-Tolyl	215	$C_5H_{10}O_2N_6S_2$	19.52	19.6
5.	p-Chlorophenyl	200	$C_{17}H_{16}O_2N_6S_2Cl_2$	17.83	18.1
6.	p-Bromophenyl	206	$C_{17}H_{16}O_2N_6S_2Br_2$	14.82	15.4
7.	p-Ethoxyphenyl	205	$C_5H_{26}O_4N_6S_2$	17.13	16.9

Growth Technique: The moulds selected for evolution of antifungal activities were *Aspergillus flavus* and *Candida albicans*.

Aspergillus flavus grows as saprophyte on various decaying substrates. It causes important diseases *e.g.* Aspergillosia allergy and toxicosis. It is the causing organism of several plant diseases. Aspergillus flavous causes appreciable lipolytic activity while growing on sunflower seeds, caster beans coconut mends. It liberates sufficient amount of folic acid causes destruction of fats.

Candida (Camonilia albicans) is yeast living fungi, occurs in throat and other part of the body of normal, individuals, apparently existing as saprophyte. It is frequently manifested in the intestinal mucosa and may cause diarrhea and burning. This is commonly caused by moniliasis of mouth and throat. Monilial infections of the lungs and angina are more serious thoracic disorders.

Method: *Asperyillus flavus* and *Candida albicans* were used the moulds were ten days old.

The following synthetic Czapek's agar medium was used.

Agar-ager	15.00 g
Sucrose	30.00 g
Sodium citrate	3.00 g
Dipotassium hydrtogen phosphate	1.00 g
Magnessium sulphate	0.50 g
Potassium chloride	0.50 g
Ferrous sulphate	0.01 g
Distilled water	1000 mL

The antifungal activity of each compound was evaluated at 100 ppm and 10 ppm, concentrations. The compounds were tested either as a solution or suspension in acetone water (25-30%) mixture. For each compound two standard solution of concentration 1:1000 (1000 μml^{-1}) were prepared.

Several test tubes containing 9 ml of the agar-medium, were properly plugged with cotton and autoclaved for half an hour at 2 Ibs pressure. To this 1 ml of a solution or suspensions of the test compound was added thus now the concentration of solution or suspension becomes one-tenth of the original concentration. The medium was made homogeneous and subsequently poured in to sterilized petri-dishes. In the centre of the petri-dishes, the test fungus (ten days old) was inoculated and incubated for 96 hrs.

The experiments were reported generally in triplicate for each concentration of the compound investigation, and a fair number of replicates of the controls (six) were provided. A commercial fungicide, Griseofulvin was also tested under similar condition, with a view to compare the results.

At the interval of 48, 72 and 96 hours, three diameters of the fungus colony were measured by means of a millimeters scale. The diameters were marked by different coloured grease pencils for subsequent identifications. The inhibition of the fungus growth was determined as the difference in growth between control plates and those treated with test compounds. The percentage inhibition was expressed as:

$$\text{Percentage inhibition} = \frac{(C-T)\times 100}{C}$$

where, C = Diameter of fungus colony (in mm) in control plates after 96 h.

T = Diameter of fungus colony (in mm) in tested plates after 96 hr.

The antifungal activity in terms of percentage inhibition shown by various compounds has been listed in **Table 3**.

Antifungal activity of thiosemicarbazides:

The antifungal activity of thiosemicarbazides of seven such compounds was valuated and the screening results have been reported in the **Table 3**. It is evident from the fungicidal screening that compounds (l_a - I_g) have fungicidal activities against both higher and lower concentrations. Compound I_f has shown highest inhibition activities at higher as well as lower concentration against both the taken fungal stains. Compound I_a has shown lowest activity amongst all compounds. Rest prepared compounds has shown moderate antifungal activities against both the fungal strains at lower as well as higher concentrations.

Table - 3

Number of Replication of AVERAGE PERCENTAGE INHIBITION AFTER 96 HOURS

Fungi strain ⟶	***C. albicans***		***A. flavus***	
Compound No.	**100 µgml^{-1}**	**10 µgml^{-1}**	**100 µgml^{-1}**	**10 µgml^{-1}**
I_a	39.5	17.8	40.0	18.5
I_b	40.5	18.3	41.2	19.3
I_c	41.2	19.4	43.1	20.5
I_d	41.3	20.1	43.2	20.6
I_e	42.5	20.4	43.4	21.6
I_f	46.3	21.4	47.1	22.3
I_g	41.5	20.0	43.1	20.5

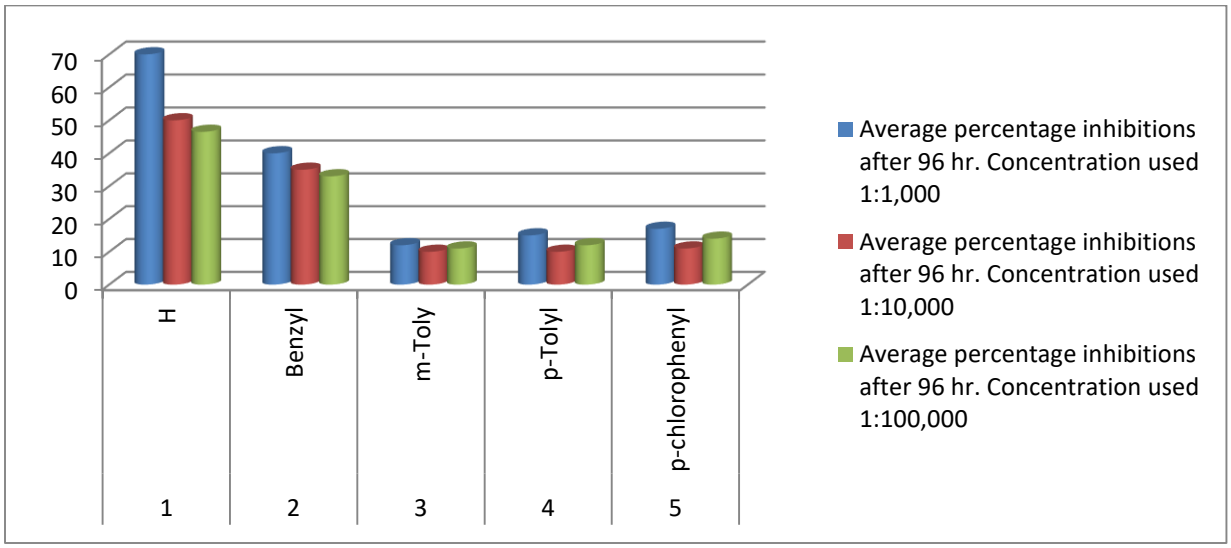
Seed Germination Activity: All the targeted compounds are screened for their activities on seed germination. The seed germination activity was observed on *Pisum sativum* at 22.3ºC and 1.00 ppm concentration at diffused day light and there effects were recorded. It is evident from **Table: 4** & **Graph 1**.

Table: 4

Activities of Thiosemicarbazides on Seed Germination

S. No.	**Compounds**	**Average percentage inhibitions after 96 hr. Concentration used**	**Seed germination activity Germination percentage after 10 days at 100 ppm concentration**

		1:1,000	1:10,000	1:100,000	Seeds soaked in solution of chemicals for 24 hr.	Seeds soaked in solution of chemicals for 24 hr. (Control)
1	**H**	70	50	46.5	0	95
2	**Benzyl**	40	35	33.0	0	95
3	**m-Toly**	12	10	11.0	18	95
4	**p-Tolyl**	15	10	12.0	20	95
5	**p-chlorophenyl**	17	11	14.0	22	95



Graph: 1

Conclusion about Biological Activities:

The compounds reported above are found to exhibit pesticidal activities. Unsubstituted thiosemicarbazides were found to be more active in comparison to m-Tolyl and p-Tolyl substituted thiosemicarbazides derivatives against the seed germination activities and shown highest activity amongst all derivatives taken for 96 hrs at concentration level 1:1000, 1:10000 and 1:100000 level. Benzyl substituted compounds shown moderate activity and rest were of lower activities.

References:

1. Jin G.Y., Ren. J., Zhao G.F. Chin. J. Org. Chem. 17,349
2. Rollas S., Karakus S., Purgun B.B., 19896. Farmaco, 51 (12), 811.
3. Mliczar Ska B., Foks H., SklolowaskaJ, 1999. Acta Pol., Pharm. 56(2), 21.
4. Mazzaa A.A.B. Laboula .M. Kassem M.G. 1983. Arch. Pharm. Chem. Sci. Ed. 11, 43.
5. Rollas S. Bulyuktin Kin, s., Cevikbas A 1960. Arch. Pharm. Venheim 1991, 324, 189.
6. Vanden Box, B.G. Rec. Trav. Chim. 79, 1129
7. Sahin G., Phaska E., Kizoglu M.E. Ozalp M. 2002, II Farmaco 57.
8. Turan G., Zitouni, Z.A. Kaplancikli, M.T. Yildiz, P. Chevallet, D. Kaya, 2005. Eur. J.Med. Chem. 40, 607-613.
9. Narayana B., Vijaya Roy K.K., Ashalatha B.V., Kuamr N.S. 2005. Arch Pharm (Weinheim) 338, 373-377.

10. Amar M., Shikla K. 2004. II Farmaco 39, 535-445.
11. V.J. Ram And H.N. Pandey Ind. J. Chem. Conm. 1972, U.S.D.A. circular No. 198, 1931.
12. S. Singhal *et al* World J.Pharm.Sci. 2013.
13. Saroush S., Somesh F., Ali H.R., Parisa A., Seyyed Moh. S. and Azizullah Habibi, Iran J. Pharm.Res. (2017) Summer, 16 (**3**); 1128-1140.
14. Prachi T. Acharya, Zeel A. Bhavsar, Divya J. Jethava, Dhaval B. Patel, Hitesh D. Patel; *Journal of Molecular Structure Vol. **1226**, Part A, 2021, 129268.*