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REVIEW ON ANTICONVULSANT ACTIVITY OF SEMICARBAZONES

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ABSTRACT

Semicarbazone derivatives are one of most potent anticonvulsant agent. It has display potent anticonvulsant effect in a wide variety of preclinical anticonvulsant models. Till date various semicarbazone derivatives have been synthesized and evaluated for anticonvulsant activity. This review is an attempt to compile the medicinal chemistry of various synthesized semicarbazone analogs. Semicarbazones and its analogs are versatile substrates, which can be used for the synthesis of numerous heterocyclic compounds. Semicarbazone derivatives are used in organic synthesis and they are used in evaluating new product that possesses different biological activities. This review covers updated information on the most active Semicarbazone derivatives that have been reported to show considerable pharmacological actions such as, anticonvulsant, antidepressant and other biological activity. From these results, ideas for future molecular modifications leading to compounds with greater favorable pharmacological properties may be derived.

Key words: Semicarbazone derivatives, Chemistry, Anticonvulsant.

INTRODUCTION

Semicarbazones are a class of compounds having the structure [R_2C=NNHC(=O)NH_2] formally derived by condensation of aldehydes or ketones with semicarbazide [$NH_2NHC(=O)NH_2$] [1]. This class of compounds that have been evaluated for various biological activities. Literature survey revealed that compounds from this class posses various pharmacological activities including anticonvulsant [2a], antitumor [3-5], antimicrobial activity [6-9]. Semicarbazones have emerged as a class of interest for the scientific community looking for the newer anticonvulsant agents.

CHEMISTRY

According to the IUPAC recommendations for the nomenclature of organic compounds, derivatives of semicarbazide of the types R-CH=N-NH-CO-NH_2 and R^1R^2C=N-NH-CO-NH_2 which are usually obtained by condensation of semicarbazide with suitable aldehydes and ketones, may be named by adding the class name 'semicarbazone' after the name of the condensed aldehyde or ketone. It is usual also to include in this class derivatives with substituents on the amide [10]. The basic structure of semicarbazone compounds and IUPAC numbering scheme is shown in Fig. (1).

Semicarbazone is formed when ammonia related a compound (nucleophile) such as semicarbazide is added to the carbonyl group of aldehyde or ketone, a unstable intermediate forms. This intermediate immediately lose a molecule of water and form respective condensation product semicarbazone. The reaction between ammonia derivatives and carbonyl compounds are acid catalyzed. The first step in the mechanism is the protonation of the carbonyl group. The protonated species is then attacked

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by the ammonia derivative which acts as a nucleophile since it has a lone pair of electrons on the nitrogen atom. The adduct then rapidly loses a proton and a water molecule to give the final product [11].

Semicarbazones in the solid state, predominantly exist in the keto form, whereas in solution state they exhibit a keto-enol tautomerism [12]. Keto form acts as a neutral bidentate ligand and the enol form can deprotonate and serve as monoanionic bidentate ligand in metal complexes. Thus semicarbazones are versatile ligands in both neutral and anionic forms. semicarbazones behave as chelating ligands when react with metallic cations and form complexes. A review of semicarbazone structures shows that in free unsubstituted semicarbazones in solid state are usually almost planar, with the oxygen atom atom *trans* to the azomethine nitrogen atom (configuration E). Although there are several electronic and steric factors that may contribute to the adoption of this arrangement, the most important is probably that the trans arrangement places the amine (4N) and azomethine (1N) nitrogen atoms in relative positions suitable for intramolecular hydrogen bonding. The coordination capacity of semicarbazones can be further increased, if substituents R^1 and:or R^2 include additional donor atoms [13].

LITRATURE REVIEW

Anticonvulsant Activity

Dimmock *et al.* [2b], synthesized various aryl semicarbazones (Fig .3) and evaluated for anticonvulsant activity using MES and scPTZ test models. All compounds were administered intraperitonealy to mice at doses of 30, 100, 300 mg/kg. in MES test 70% of the compounds found active while 54% of the compounds were active in scPTZ test. Authors found compound 2-(4fluorobenzylidene) hydrazinecarboxamide (3.3a) and 2-[1-(4fluorophenyl)ethylidene] hydrazinecarboxamide (3.3b) most active in both screens.

Dimmock *et al.* [14], synthesized various semicarbazones (Fig. 4) from corresponding arylalicyclic ketones. All the compounds evaluated for anticonvulsant activity using MES and scPTZ test models after intraperitoneal administration to mice. All of the semicarbazones and thiosemicarbazones found active in MES screen while 70% of these compounds were active in scPTZ screen. Semicarbazones named 2-(2,3-dihydro-1*H*-inden-1-ylidene) hydrazinecarbox- amide (4.4a), 2-(3,4-dihydronaphthalen-1(2*H*)-ylidene)hydrazine carboxamide (4.4b) and 2-(6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-ylidene) hydrazinecarboxamide (4.4c) exhibited higher activity in MES screen than valproate.

Dimmock *et al.*[15], synthesized various (aryloxy) aryl semicarbazones (Fig. 5). All compounds were evaluated for anticonvulsant activity using MES and scPTZ screens after intraperitoneal administration in mice using doses of 30, 100 and 300 mg/kg. In MES screen 74% of the compounds found active and compound named 2-[3-(4-propylphenoxy)benzylidene] hydrazine carboxamide (5.5a) exhibited highest PI value 22.0. Most of the compounds also found active in MES screen after oral administration accompanied by very high protection indices.

Puthucode *et al.* [16], synthesized various aryl, arylidene and aryloxyaryl semicarbazones (Fig. 6.1– 6.2). All the compounds evaluated for anticonvulsant activity using MES and scPTZ test models after intraperitoneal administration to mice. Compound named 2-[(2*Z*)-2-bromo-3-phenylprop-2-en-1-ylidene] hydrazine carboxamide (6.1a) and 2-{(2*E*)-3-[4-(4-fluorophenoxy) phenyl]prop-2-en-1-ylidene}hydrazinecarboxamide (6.1b) found most protective in MES and scPTZ screen after i.p. administration. Compound named 2-[3-(2,6-dimethylphenoxy) benzylidene]hydrazinecarboxamide (6.2a) and 2-{1-[3-(4-methylphenoxy) phenyl] ethylidene} hydrazinecarboxamide (6.2b) exhibited highest activity in MES screen after oral administration.

Dimmock *et al.* [17], synthesized various acetylhydrazones (Fig. 7), oxamoylhydrazones (Fig. 8) and semicarbazones (Fig. 9). All compounds evaluated for anticonvulsant activity using MES and scPTZ test models after intraperitoneal administration of doses 30, 100, 300 mg/kg to mice. Compound named 2-[(2*Z*)-undec-2-en-1-ylidene] hydrazine carboxamide (3.9a) emerged as lead compound as activity showed in both screens.

Pandeya *et al.* [18], synthesized a group of 4-bromo-phenyl substituted aryl semicarbazones (Fig. 10) and screened for anticonvulsant and sedative-hypnotic activities. Anticonvulsant activities of compounds were tested using MES, scPTZ, scSTY test models. All the compounds exhibited anticonvulsant activity in one or more test models. Compound named *N*-(4-bromophenyl)-2-(propan-2-ylidene)hydrazinecarboxamide (3.12a) emerged as most promising anticonvulsant compound as the activity shown in all screens employed at doses of 30, 100, 300 mg/kg after intraperitoneal administration to mice. Compound (3.12a) also found active in oral MES screen in rats at dose of 30 mg/kg. None of the compound exhibited the promising sedative-hypnotic activity.

Pandeya *et al.* [18], synthesized a group of 4-bromo-phenyl substituted aryl semicarbazones (Fig. 10) and screened for anticonvulsant and sedative-hypnotic activities. Anticonvulsant activities of compounds were tested using MES, scPTZ, scSTY test models. All the compounds exhibited anticonvulsant activity in one or more test models. Compound named *N*-(4-bromophenyl)-2-(propan-2-ylidene)hydrazinecarboxamide (3.12a) emerged as most promising anticonvulsant compound as the activity shown in all screens employed at doses of 30, 100, 300 mg/kg after intraperitoneal administration to mice. Compound (3.12a) also found active in oral MES

screen in rats at dose of 30 mg/kg. None of the compound exhibited the promising sedative-hypnotic activity.

Pandeya *et al.* [20], synthesized various 4-N-substituted aryl semicarbazones (Fig. 13) and evaluated for anticonvulsant activity using MES andscPTZ test model. Authors also measured the neurotoxicity of the compounds by the rota-rod test. Compound named *N*-ethyl-2-[1-(4-hydroxy phenyl)ethylidene]-*N*-phenylhydrazine carboxamide (3.15a) and *N*-(4-chlorophenyl)-2-[1-(4-methoxyphenyl) ethylidene]hydrazinecarboxamide (3.15b) exhibited 100% protection against seizures at a dose of 300 mg/kg after intraperitoneal administration to mice although they found highly toxic at the same dose in neurotoxicity screening.

Yogeeswari *et al.* [21], synthesized a series of 3-chloro-2 methyl phenyl substituted semicarbazones (Fig. 14) and evaluated for anticonvulsant and other CNS activities. Anticonvulsant activity of the compounds tested using MES, scPTZ and scSTY test models after intraperitoneal administration to mice at doses of 30 , 100, 300 mg/kg. Compound named *N*-(3-chloro-4-methylphenyl)-2-(propan-2-ylidene) hydrazinecarboxamide (3.16a) found active in all the aforementioned screens as well as in oral MES screen in rats. Some of the compounds also exhibited weak CNS depressant activity when tested in forced swim pool test.

Yogeeswari *et al.* [21], synthesized a series of 3-chloro-2 methyl phenyl substituted semicarbazones (Fig. 14) and evaluated for anticonvulsant and other CNS activities. Anticonvulsant activity of the compounds tested using MES, scPTZ and scSTY test models after intraperitoneal administration to mice at doses of 30 , 100, 300 mg/kg. Compound named *N*-(3-chloro-4-methylphenyl)-2-(propan-2-ylidene) hydrazinecarboxamide (3.16a) found active in all the aforementioned screens as well as in oral MES screen in rats. Some of the compounds also exhibited weak CNS depressant activity when tested in forced swim pool test.

Aggarwal *et al.* [23], syhtesized various 4-aryl substituted semicarbazones of citral (Fig. 16) and R-(-) carvone (Fig. 17). All the compounds evaluated for anticonvulsant activity using MES and scMET test models after intraperitoneal administration at doses 30, 100 and 300 mg/kg. neurotoxicity of the compounds measured by rotarod test. All of the synthesized compounds found active in MES test, while 72% of the compounds provided protection against seizures in scMET test. The p-flouro aryl substituted semicarbazones named 2-(5-*tert*-butyl-2-methylcyclohex-2-en-1-ylidene)-*N*-(4-fluorophenyl)hydrazinecarboxamide (3.18a) and 2-[(2*Z*)-3,7-dimethylocta-2,6-dien-1-ylidene]-*N*-(4-fluoro phenyl) hydrazine carboxamide (3.19a) emerged as the most active analogue in both cyclic and acyclic terpenes showing broad spectrum of activity at 100 mg/kg with low neurotoxicity. This analogue also found active in oral MES screen in rats at dose of 30 mg/kg without any sign of neurotoxicity.

Aggarwal *et al.* [24], synthesized various 4-aryl substituted semicarbazones of levulinic acid (Fig. 18) and evaluated for anticonvulsant activity using MES ans scMET test models. Neurotoxicity of the synthesized compounds measured by rotarod test. Most of the compounds showed anticonvulsant activity after intraperitoneal administration. Authors observed 4-(4'-flouro phenyl)levulinic acid semicarbazone (3.20a) as most promising compound showing activity in both screens with low neurotoxicity. Compound (3.20a) also found active in oral MES screen in rats at dose of 50 mg/kg without any sign of neurotoxicity.

Yogeeswari *et al.* [25], synthesized a series of N-(2,6-dimethyl phenyl)- substituted semicarbazones (Fig. 19) and screened for anticonvulsant activity. Anticonvulsant activity of synthesized compounds tested using MES, scSTY, scPTZ and scPIC models. All the compounds exhibited anticonvulsant activity in MES screen administered either intraperitonealy or orally. Compound N^1- (2,6 – dimethyl phenyl) – N^4- (2- hydroxy benzaldehyde) semicarbazone (3.21a) found active in all screens employed by the authors for evaluation of anticonvulsant activity without any sign of neurotoxicity and hepatotoxicity. Compound (3.21a) not only inhibited GABA transaminase enzyme both in vitro and ex vivo but also increased the GABA level in whole rat brain by 118%.

Yogeeswari *et al.* [26], synthesized various 2, 4 –dimethyl phenyl substituted semicarbazones (Fig. 20) and evaluated for anticonvulsant activity using MES, scPTZ and scSTY test models. Compound named *N*-(2,4-dimethylphenyl)-2-(propan-2-ylidene) hydrazinecarboxamide (3.22a) found active in aforementioned screens as well as in oral MES screen. In scPTZ screen compound named *N*-(2,4-dimethylphenyl)-2-(4-methylpentan-2-ylidene) hydrazine carboxamide (3.22b) exhibited activity at a dose of 100 mg/kg comparable with carbemazepine and higher potency than sodium valproate.

Siddiqui *et al.* [27], synthesized a series of 1, 3 – benzothiazol – 2- yl semicarbazones (Fig. 21) and evaluated for anticonvulsant activity using MES test model. Compound named *N*-(6-methyl-1,3-benzothiazol-2-yl)-2-[1-(4-nitrophenyl) ethylidene] hydrazine carboxamide (3.23a) and 2-(diphenyl methylidene)-*N*-(6-methoxy-1,3-benzothiazol-2-yl) hydrazine carboxamide (3.23b) exhibited the 100% protection in MES test at 0.5 and 4.0 h after intraperitoneal administration of dose 30 mg/kg without any sign of neurotoxicity .

Raja *et al.* [28], synthesized various semicarbazones of acetophenone mannich base (Fig. 22). All the compounds evaluated for anticonvulsant activity using MES, scMET and scSTY test models. In initial

screening 70% of the synthesized compounds exhibited the anticonvulsant activity. Compound 3- chloro phenyl [β – dimethyl amino propiophenone] semicarbazone (3.24a) emerged as most promising anticonvulsant compound which exhibited superior activity than reference compounds phenytoin and carbemazepine in MES and scMET test models at a dose of 300 mg/kg after intraperitoneal administration to mice. Compound (3.24a) also found active in oral MES screen in rats at dose of 30 mg/kg.

Shaifee *et al.* [29], synthesized a series of 4- (2-phenoxy phenyl) semicarbazones (Fig. 23) and evaluated for anticonvulsant activity in petylenetetrazole induced kindling model in adult male wistar rats. Compound 4- (2-Phenoxy phenyl) -1- [(pyridine-2-yl) methylene] semicarbazide (3.25a) and 4- (2- Phenoxy phenyl) -1- [(pyridine-4-yl) methylene] semicarbazide (3.25b) exhibited greater protection from seizures than sodium valproate at dose of 100 mg/kg on intraperitoneal administration.

Aggarwal *et al.* [30], synthesized various N_4 phenyl substituted pyridyl semicarbazones (Fig. 24) and evaluated for anticonvulsant activity and neurotoxicity. Anticonvulsant activity of the synthesized compounds was determined after intraperitoneal administration to mice using MES and scMET test models, while rotarod test was used for evaluation of neurotoxicity. Most of the compounds provided protection against seizures in anticonvulsant screening. Authors found that compound (Methyl- 4- pyridyl) ketone – N_4-(p- chloro phenyl) substituted semicarbazone (3.26a) provide prolonged protection against seizures at dose of 100 mg/kg in both of the screens. Compound (3.26a) exhibited neurotoxicity at dose 300 mg/kg.

Amir *et al.* [31], synthesized various 3- chloro-4- flouro phenyl substituted semicarbazones (Fig. 25) and evaluated for anticonvulsant activity using MES test. Active compounds from initial screening was also tested for their neurotoxicity and CNS depressant activity using rotarod test and forced swim pool method respectively. Compound N^1- (3- chloro – 4 – flouro phenyl) – N^4- (4-N, N- dimethyl amino benzaldehyde) semicarbazone (3.27a) provided 50 % protection at 30 mg/kg and 100 % protection against seizures at 100 mg/kg after 4.0 h without any sign of neurotoxicity. Compound (45a) also exhibited weak CNS depressant activity as compared to standard drug carbemazepine.

Mozaffari *et al.* [32], synthesized a series of methylene bridged aryl semicarbazones (Fig. 26) and evaluated for anticonvulsant activity against PTZ induced seizures . Neurotoxicity of the compounds was determined by rotarod test. Most of the compounds exhibited anticonvulsant activity. Compound 2- (4- bromo phenyl amino) – N'- (2- hydroxyl benzylidene) acetohydrazide (3.28a) exhibited protection against seizures at all three doses 50, 100 and 300 mg/kg administered intraperitonealy. While compound 2- (4-bromo phenyl amino) – N'- (propan -2-ylidene) acetohydrazide (3.28b) provided 45 % protection against seizures at dose of 300 mg/kg after intraperitoneal administration. None of the (3.28a) and (3.28b) showed any sign of neurotoxicity.

Rajak *et al.* [33], synthesized various semicarbazones containing 1, 3, 4 – thiadiazole and quinazoline ring (Fig. 27). All compounds evaluated for anticonvulsant activity using MES and scPTZ models. Neurotoxicity of compounds measured by rotarod test. Most of the compounds showed anticonvulsant in initial screening. Compound (3.29a) emerged as most promising compound as the activity shown in MES screen at doses 100 mg/kg and 300 mg/kg after intraperitoneal administration. Compound N1-{5-(2-methyl-4-oxo quinazolin-3(4*H*)-yl) amino]methyl}-1,3,4-thiadiazol-2-yl)}-N4-[1-(4-nitro phenyl) (phenyl) methanone]-semicarbazones (3.29a) also found active in scPTZ screen at dose 300 mg/kg . This compound devoid of neurotoxicity in rotarod test.

Banjare *et al.* [34], synthesized a series of novel 1-(3 chloro – 2-methyl phenyl) –[(3- hydroxyzinoloxy carbonyl)] semicarbazone derivatives (Fig. 28). All compounds evaluated for anticonvulsant and antibacterial acvity using MES screen and cup plate agar diffusion method respectively. Neurotoxicity of the compounds measured by rotarod test. In MES screen compound named (2*Z*)-2-(2-chlorobenzylidene)-*N*-[(3-chloro-2-methyl phenyl) carbamoyl] hydrazine carboxamide (3.30a) provided maximum protection against seizures at dose 50 mg/kg after intraperitoneal administration with lesser neurotoxicity.

Siddiqui *et al.* [35], synthesized a series of 3,4 – Disubstituted benzaldehyde – N- (6- substituted – 1,3-benzothiazol – 2- yl) semicarbazones (Fig. 29) and evaluated for anticonvulsant activity using MES test model. Neurotoxicity of the compounds measured using rotarod test. Compounds named (2*Z*)-*N*-(6-fluoro-1,3-benzothiazol-2-yl)-2-(4-hydroxy-3-methoxybenzylidene) hydrazinecarboxamide (3.31a), (2*Z*)-2-benzylidene-*N*-(6-nitro-1,3-benzothiazol-2-yl)hydrazinecarboxamide (3.31b), (2*Z*)-2-(4-hydroxy-3-methoxybenzylidene)-*N*-(6-nitro-1,3-benzothiazol-2-yl)hydrazine carboxamide (3.31c), (2*Z*)-2-(3,4-dimethoxy benzylidene)-*N*-(6-nitro-1,3-benzothiazol-2-yl)hydrazinecarboxamide (3.31d), (2*Z*)-2-benzylidene-*N*-(6-methyl-1,3-benzothiazol-2-yl)hydrazinecarboxamide (3.31e) and (2*Z*)-2-(4-hydroxybenzylidene)-*N*-(6-methyl-1,3-benzothiazol-2-yl)hydrazine carboxamide (3.31f) provided 100 % protection against seizures after intraperitoneal administration to mice at a dose of 30 mg/kg without any sign of neurotoxicity.

Scheme 1. General method for the synthesis of semicarbazone analogues

The general method of synthesis of semicarbazones is given below.

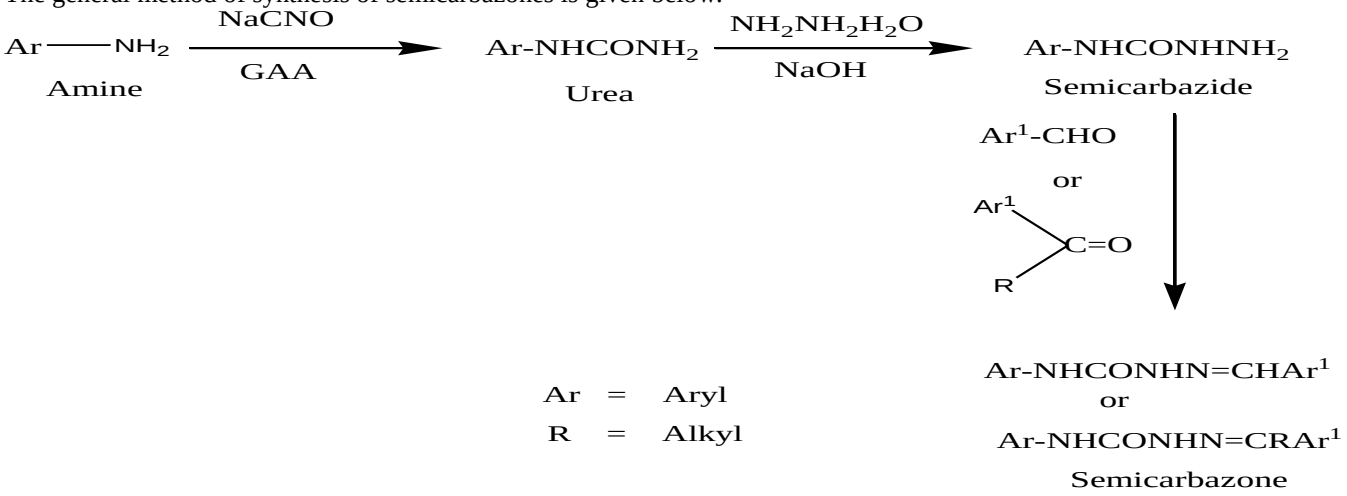
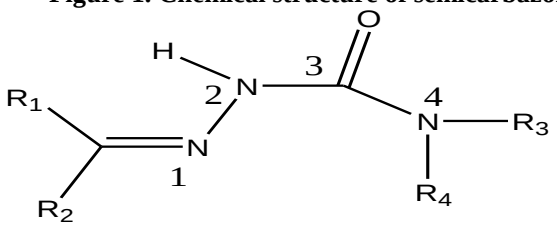


Figure 1. Chemical structure of semicarbazones



R_1, R_2, R_3, R_4 = H, Alkyl or Aryl group

Figure 2. Keto – enol tautomerism of semicarbazones

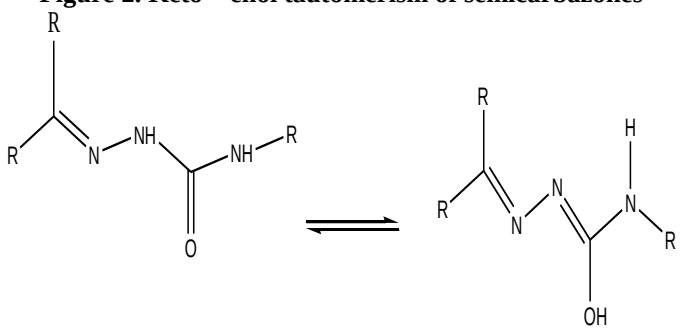
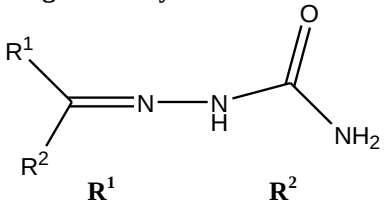
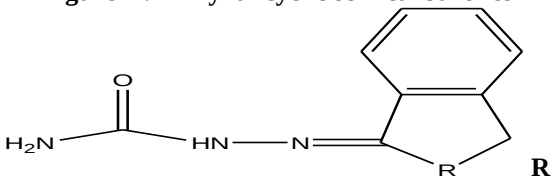


Figure 3. Aryl semicarbazones



R^1	**R^2**
(3.3a) - H	4- Flouro phenyl
(3.3b) - CH3	4- Flouro phenyl

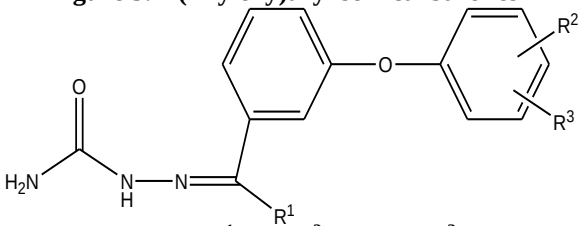
Figure 4. – Aryl alicyclic semicarbazones



R

(4.4a) - CH_2
(4.4b) - $(CH_2)_2$
(4.4c) - $(CH_2)_3$

Figure 5. – (Aryloxy)aryl semicarbazones



R^1	**R^2**	**R^3**
(5.5a) - H	4-$C_3H_7^n$	H

Figure 6. Aryl semicarbazones

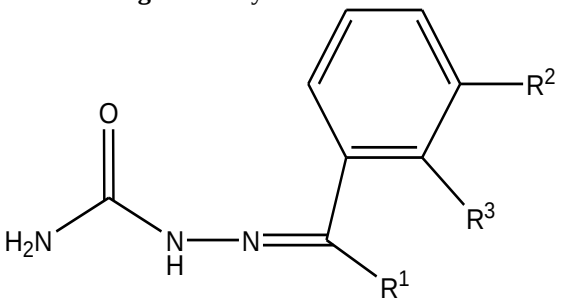
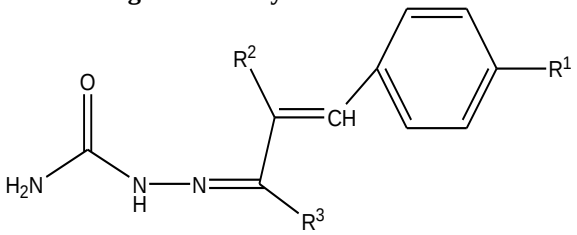
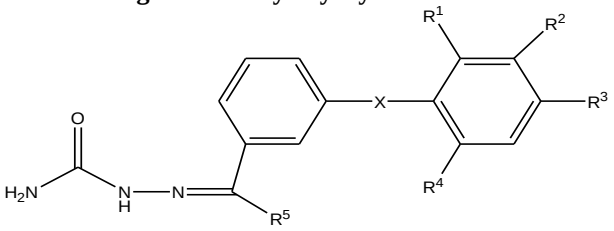


Figure 6.1. Arylidene semicarbazones



	R^1	R^2	R^3
(6.1a) -	H	Br	H
(6.1b)-	OC_6H_4 4F	H	H

Figure 6.2. Aryloxyaryl semicarbazones



	R^1	R^2	R^3	R^4	R^5	X
(6.2a) -	CH_3	H	H	CH_3	H	O
(6.2b) -	H	H	CH_3	H	CH_3	O

Figure 7. Acetylhydrazones

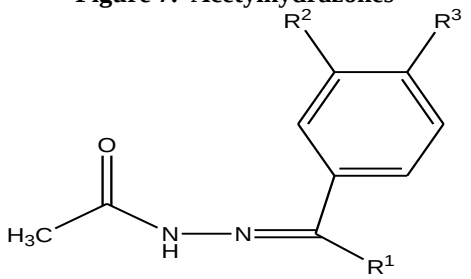


Figure 8. Oxamoylhydrazones

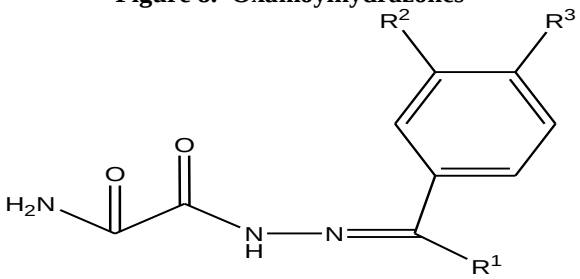
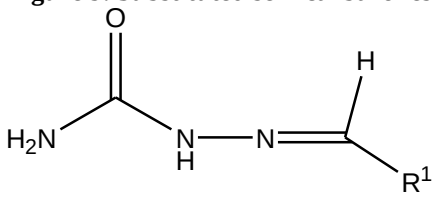
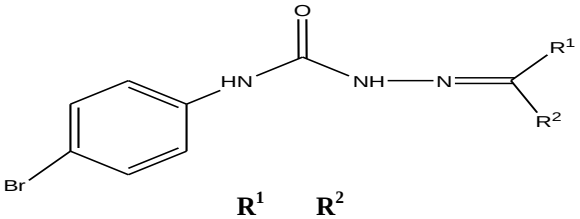


Figure 9. Substituted semicarbazones



	R
(9.1a) -	$CH=CH(CH_2)_7CH_3$

Figure 10. 4-bromo phenyl substituted aryl semicarbazones



	R^1	R^2
(3.12a) -	CH_3	CH_3

Figure 11. p- Nitro phenyl substituted semicarbazone

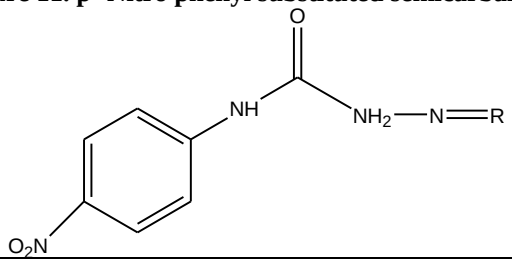


Figure 12. Phenoxy/p –bromophenoxy acetyl hydrazones

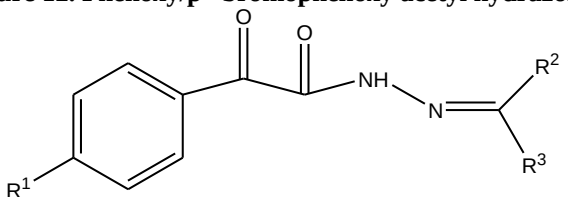
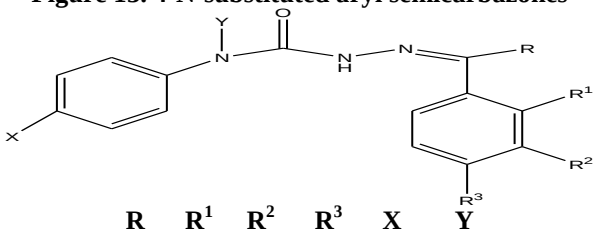
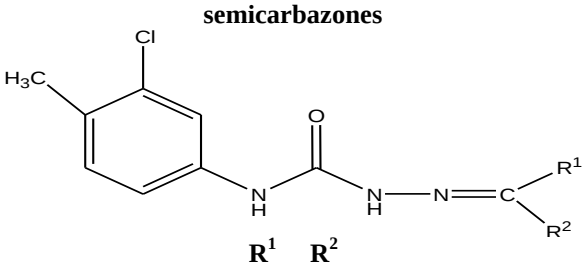


Figure 13. 4-N-substituted aryl semicarbazones



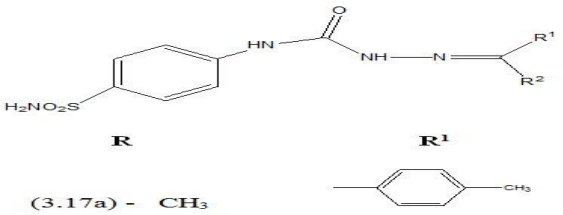
	R	R^1	R^2	R^3	X	Y
(3.15a) -	CH_3	H	H	OH	H	C_2H_5
(3.15b) -	CH_3	H	H	OCH_3	Cl	H

Figure 14. 3-chloro-2 methyl phenyl substituted semicarbazones



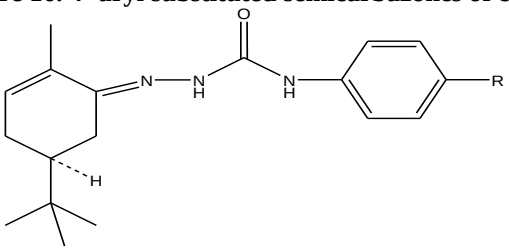
	R^1	R^2
(3.16a) -	CH_3	CH_3

Figure 15. 4-sulphamoylphenyl semicarbazone derivatives



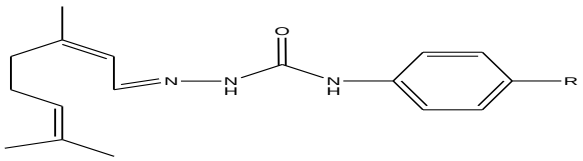
R	R^1
(3.17a) - CH_3	

Figure 16. 4- aryl substituted semicarbazones of citral



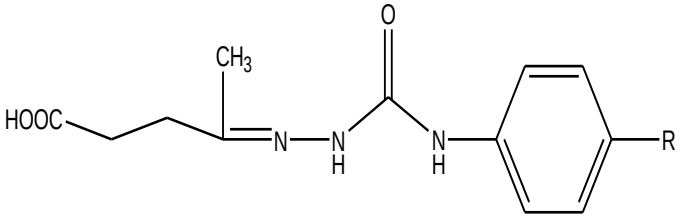
R (3.18a) - F

Figure 17. 4- aryl substituted semicarbazones of R-(-) carvone



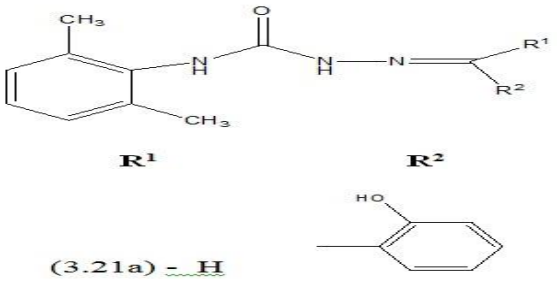
R (3.19a) - F

Figure 18. 4-aryl substituted semicarbazones of levulinic acid



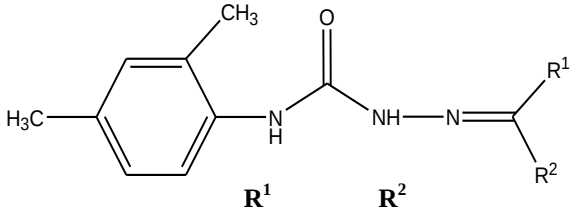
R(3.20a) - F

Figure 19. N-(2, 6-dimethyl phenyl)- substituted semicarbazone



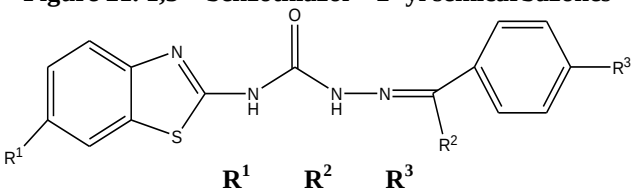
R^1	R^2
(3.21a) - H	

Figure 20. 2, 4 – dimethyl phenyl substituted semicarbazones



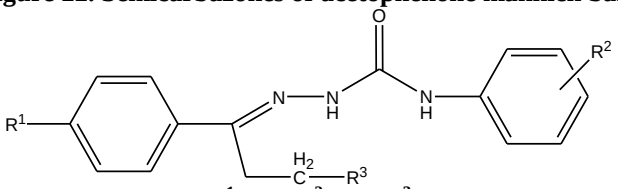
R^1	R^2
(3.22a) - CH_3	CH_3
(3.22b) - CH_3	$CH_2CH(CH_3)_2$

Figure 21. 1,3 – benzothiazol – 2- yl semicarbazones



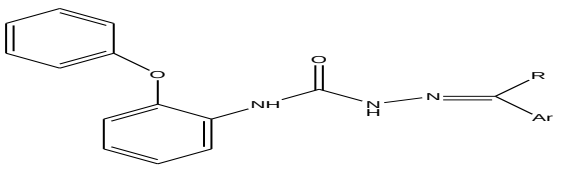
R^1	R^2	R^3
(3.23a) - CH_3	CH_3	NO_2
(3.23b) - CH_3O	C_6H_5	H

Figure 22. Semicarbazones of acetophenone mannich base



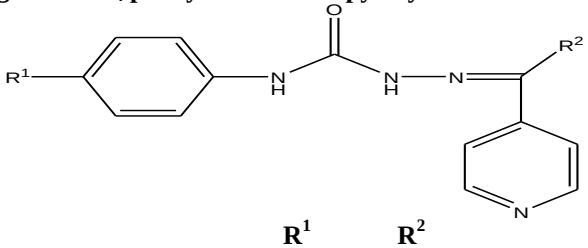
R^1	R^2	R^3
(3.24a) - H	3-Cl	$N(CH_3)_2$

Figure 23. 4- (2- phenoxy phenyl) semicarbazones



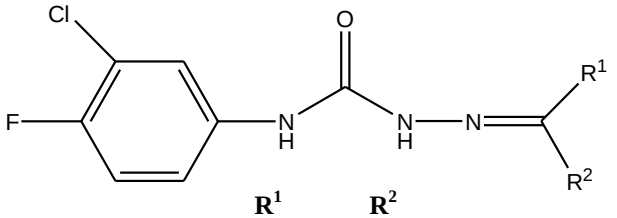
R	Ar
(3.25a) - H	2- Pyridine
(3.25b) - H	4- Pyridine

Figure 24. N_4 phenyl substituted pyridyl semicarbazones



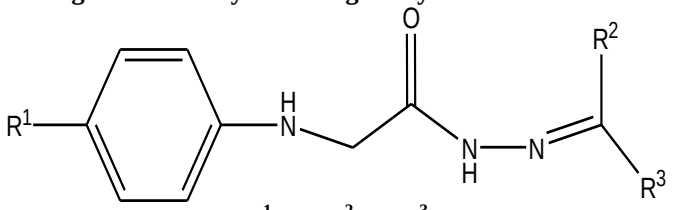
R^1	R^2
(3.26a) - Cl	CH_3

Figure 25. 3- chloro- 4- flouro phenyl substituted semicarbazones



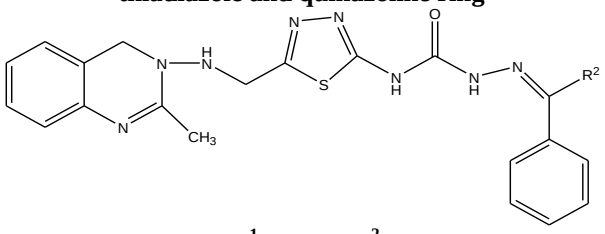
	R^1	R^2
(3.27a) -	H	4-$N(CH_3)_2$-C_6H_4

Figure 26. Methylene bridged aryl semicarbazones



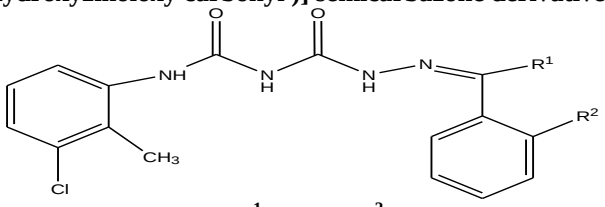
	R^1	R^2	R^3
(3.28a) – Br		H	2-Hydroxyphenyl
(3.28b) – Br		CH_3	CH_3

Figure 27. Semicarbazones containing 1, 3, 4 – thiadiazole and quinazoline ring



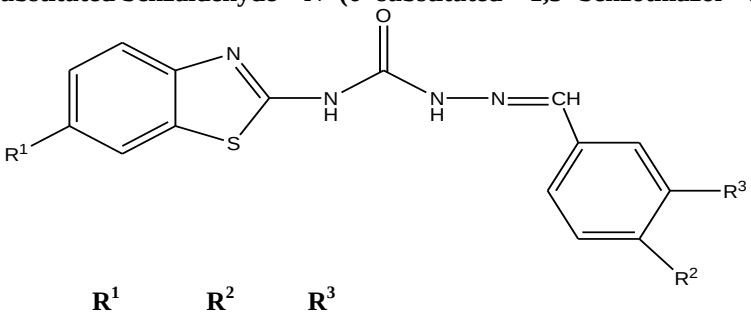
	R^1	R^2
(3.29a) –	C_6H_5	4-NO_2

Figure 28. 1-(3 chloro –2-methyl phenyl) – [(3-hydroxyzinoloxy carbonyl)] semicarbazone derivatives



	R^1	R^2
30a) -	H	2-Cl

Figure 29. - 3,4 – disubstituted benzaldehyde – N- (6- substituted – 1,3- benzothiazol – 2- yl) semicarbazone.



	R^1	R^2	R^3
(3.31a) -	F	OH	OCH_3
(3.31b) -	NO_2	H	H
(3.31c) -	NO_2	OH	OCH_3
(3.31d) -	NO2	OCH_3	OCH_3
(3.31e) -	CH_3	H	H
(3.31f) -	CH_3	OH	H

DISCUSSION AND CONCLUSION

Semicarbazones are synthetically versatile substrates, where they can be used for the synthesis of a large variety of heterocyclic compounds, and as raw material for drug synthesis. The advances in the use of semicarbazone for organic synthesis during the last twenty-five years, as well as a survey of its biological and pharmacological properties are reported in this review and in the accompanying supplementary information. The survey of the literature revealed that, semicarbazone is a versatile lead molecule for designing potential bioactive agents, and its derivatives were reported to possess broad-spectrum anticonvulsant, anxiety activities and other biological activity. Further we can conclude that many other derivatives of Semicarbazone can be synthesized which will be expected to show potent pharmacological activities.

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