WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 9, 881-893. Review Article ISSN 2277– 7105

# A COMPREHENSIVE REVIEW ON THE CHEMISTRY AND BIOLOGICAL PROPERTIES OF SEMICARBAZIDE DERIVATIVES

**Swati Pathak[1]*, Amrita Singh[2] and Abhinav Prasoon Mishra[3]**

[1]Research Scholar, Advance Institute of Biotech & Paramedical Sciences, Kanpur (UP) IN.

[2]Associate Professor, Advance Institute of Biotech & Paramedical Sciences, Kanpur (UP) IN.

[3]Professor, Advance Institute of Biotech & Paramedical Sciences, Kanpur (UP) IN.

Article Received on
12 April 2023,

Revised on 02 May 2023,
Accepted on 22 May 2023

DOI: 10.20959/wjpr20239-28249

***Corresponding Author**
**Swati Pathak**
Research Scholar, Advance Institute of Biotech & Paramedical Sciences, Kanpur (UP) IN.

## ABSTRACT

Due to their vast range of biological actions and role as building blocks in many different classes of significant pharmacological compounds, semicarbazide derivatives have attracted a lot of attention. It is a white solid that dissolves in water; derived from urea. The review was emphasized on the structure, chemistry, and different biological properties of semicarbazide derivatives using in-vitro or animal models. Researchers have been focusing on semicarbazone derivative synthesis and biological evaluation because of their potential as great therapeutic agents for treating a wide variety of disorders affecting both humans and animals. The biological properties of semicarbazones and thiosemicarbazones are often linked to their coordination of metal ions. Studies have shown that the semicarbazone moiety and its many derivatives have powerful pharmacological effects. It concludes that semicarbazide analogues are highly promising in the development of new medications for the treatment of numerous epidemic and infectious diseases like cancer, epilepsy, infection (protozoa, viral etc.), hepatic-failure, pain & inflammation and many more. It would be convenient to purchase for each humankind.

**KEYWORDS:** Semicarbazide, Structure, Pharmacological activity, Anticancer, anti-inflammatory.

## INTRODUCTION

Due to their vast range of biological actions and role as building blocks in many different classes of significant pharmacological compounds, semicarbazide derivatives have attracted a

lot of attention.[1,2] Inorganic and pharmaceutical chemistry rely heavily on semicarbazones and their derivatives.[3] Important chemicals like semicarbazones and thiosemicarbazones are produced through the condensation of semicarbazides and the reaction of different ketones or aldehydes.[4] When an oxygen atom in a semicarbazone is swapped out for a sulfur atom, a thiosemicarbazone is formed. These thiosemicarbazones form chelating ligands and complexes with metallic cations upon interaction.[5] It is a white solid that dissolves in water; derived from urea.

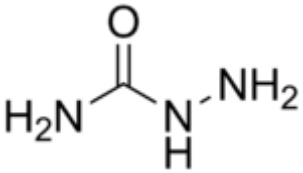

**Fig. 1: Structure of semicarbazide (*IUPAC- aminourea).***

Molecular formula- $OC(NH_2)(N_2H_3)$

Molar mass- 75.08 g/mol

Melting point- 96ºC

Researchers have been focusing on semicarbazone derivative synthesis and biological evaluation because of their potential as great therapeutic agents for treating a wide variety of disorders affecting both humans and animals.[6,7] Also showing anticonvulsant effects were certain 1-5 hydrazones and semicarbazones. he maximal electroshock seizure (MES) screen showed that aryl semicarbazones provided greater protection.[8] The presence of a more electronegative group at the para position of the aryl ring is the reaction that affords increased safety. One of the most useful types of study for understanding the relationship between molecule structure and electronic states is vibrational spectroscopy.[9]

**Co-ordination with metal ions**

The biological properties of semicarbazones and thiosemicarbazones are often linked to their coordination of metal ions;.[10] Chelating ligands like semicarbazone and thiocarbazone typically form complexes with metallic cations.[11]

❖ **Nickle**

Nickel can serve as an active site for certain enzymes in biological systems, including hydrogenases and dehydrogenases. Nickel centers are present in the active sites of numerous ureases, methyl coenzymes-M-methyl reductase, and hydrogenase, all of which contribute to the mutagenicity of nickel compounds.[12] Biological activity against the bacterium test[13] has been demonstrated for both stable six-coordinated Ni (II) complexes with thiosemicarbazone

and semicarbazone ligand and labile four-coordinated Ni (II) complexes with tridentate thiosemicarbazone and semicarbazone ligand. Staphylococcus aureus and Escherichia coli are also significantly inhibited by nickel (II) complexes containing octadiensemicarbazones.

*Antineoplastic and cytotoxic activities of nickel (II) complexes of thiosemicarbazone and semicarbazone* -

In mouse and human tissue developed tumor cells, thiosemicarbazone nickel (II) complexes were revealed to be potent cytotoxic agents. Each medication had a somewhat different profile across the various a nor histological subtype. When exposed to the nickel complex, the Ehrlich ascites carcinoma showed the most in vivo activity. The DNA polymerase, PRPP-aminotransferase, IMP-dehydrogenase, dihydrofolate reductase, thymidine kinase, and thymidylate synthetase activities, as well as the purine and DNA synthesis in L1210, were all suppressed by this compound. DNA strand scission in L1210 was observed after only 24 hours of incubation, and DNA viscosity decreased. The DNA topoisomerase II inhibitor L1210 was absent from the nickel complexes.

- **Zinc**

It is present in high concentrations in human erythrocytes, making it an essential trace element.[14] With a mean adult body weight of 2.3 g, they are the second most abundant trace element in the human body. As a symmetrical (d10) transition metal, zinc (II) has strong interactions with O, N, and S donor ligands. Zinc is a necessary component for all known biological processes (especially those involving proteins and enzymes). It may play a crucial role in preserving the shape and integrity of proteins in the body or take part in chemical catalysis.[15] More than 300 enzymes (across six different classes) have been characterized so far.

*Transferases – Isomerases*

*Oxidoreductases – Lyases*

*Hydrolyses – Ligases*

Complexes of thiosemicarbazide and thiosemicarbazone with Zn (II) in tetrahedral and octahedral coordination geometry have been reported.[16] Zinc complexes require a third coordinating center, which is provided by the carbonyl group in addition to ligands like ethyl acetoacetate semi carbazone and thiosemicarbazone.

### ❖ Cadmium

This is why finding cadmium-containing ores is a rare occurrence.[17] Chelation of cadmium with nitrogen donor ligands, such as semicarbazone and thiosemicarbazone molecules, results in the formation of complexes.[18] Soft donor atoms (S>>N>>O) generate the most stable Cd (II) complexes. Increases in the number of coordination groups given by semicarbazone and thiosemicarbazone derivative ligands are correlated with enhanced complex stability.[19]

### ❖ Copper

Most organisms include copper, a first-row transition metal crucial to life.[20] Copper catalyzes redox processes in living systems, most notably the oxidation of water to oxygen.[21] Since the copper (II) complexes include unpaired electrons, they are invariably paramagnetic. Chemical and biological research on Schiff base compounds containing thiosemicarbazone and related transition metal complexes has increased in recent years due to their biological activity.[22] Semicarbazones and thiosemicarbazones, which lack coordination, are less active biologically than Cu (II) and iron (II) metal complexes.

### ❖ Cobalt

The chelating N, O donor ligand is the most often employed ligand for stabilizing the cobalt (III) ion in aqueous solution. Antibacterial and antiviral drugs have been developed using cobalt (III) complexes synthesized using ligand donor sets. The series of Cobalt (III) complexes integrates N, O donor ligands and is one of the most promising classes of Co (III) complexes.[23] Enantioselective reduction, dioxygen carriers, and oxygen activators[24] are also employed. Together with semicarbazone, it also helps create bioactive chemicals.[25]

### ❖ Manganese

It is needed for healthy living in all living organisms. There is potential for metalloproteinase action. It can exist in any of the five oxidation states in metalloproteinase, including mixed valence levels.[26] The astra nuclear manganese complex[27] is found in photosystem II. As homogeneous catalysts, manganese coordination compounds are becoming more and more effective. Peroxidase, superoxide dismutase, and dioxygenase are just a few of the enzyme systems that have been identified to contain mononuclear manganese active sites.[28] The bioinorganic chemistry field benefits greatly from manganese metal complexes.[29,30]

**Biological activities**

The pace at which a molecule enters a cell is controlled, in part, by its lipophilicity, which is affected by coordination.[31,32] In addition, the metal complex might have more activity than the free ligand. Either binding to a metal in vivo is crucial for the mechanism of action, or the metal complex acts as a vehicle for activating the ligand as the cytotoxic agent. Drug resistance may be drastically lowered if efforts were coordinated.[33]

**Anti-protozoa**

- *Neelam and Kakalu, (2012)* A variety of 5-nitrofuryl semicarbazone (nitrofurazone) derivatives have been developed for the treatment of Chagas disease, a major problem in Central and South America. Triatoma infestans and triatoma retroviral are bloodsucking insects that transmit the protozoan parasite Trypanosoma cruzi, the causative agent of Chagas disease. A replacement with different electrical and steric characteristics has been introduced to the N-4 position of the nitrofurazone molecule.[34] Mice inoculated with the parasites and in vitro tests against T. cruzi epimastigote.

**Anticancer**

- *Ali et al. (2012)* Vanillin semicarbazone was tested for its anticancer effects in a study using Swiss albino mice bearing the Ehrlich ascites carcinoma (EAC) cell line. The effectiveness of VSC was evaluated by measuring the inhibition of cell growth, the reduction of tumor weight, the extension of survival time, and the changes in depleted hematological parameters after intraperitoneal administration of the compound at three doses (5, 7.5, and 10 mg/kg i.p.). All of these measures were also analyzed using a typical medication dose of 0.3 mg/kg (i.p.) bleomycin. The most effective dose was 10 mg/kg (i.p.), which was shown to be quite similar to the effectiveness of 0.3 mg/kg (i.p.) bleomycin. VSC was shown to have low toxicity toward the host organism.[35]

- *Islam et al. (2012)* To find chemicals with anticancer properties, benzophenone semicarbazone (BSC) was produced and described. The effects of several compounds on Ehrlich Ascites Carcinoma (EAC) cells in Swiss albino mice were evaluated by measuring tumor weight, observing how long the mice lived while carrying tumors, counting the number of dead tumor cells, and so on. Hematological characteristics were also assessed, including the number of red blood cells, the number of white blood cells, and the hemoglobin content of the blood. The data demonstrated that BSC is effective in inhibiting the growth of EAC cells. These findings were evaluated in comparison to those

obtained with the gold standard medication bleomycin. It's possible that the BSC chemical is an effective anticancer treatment.[36]

- *Jia et al. (2020)* The sesquiterpene lactone parthenolide is highly effective against cancer. Several semicarbazone and thiosemicarbazone derivatives of parthenolide were produced and tested for their anticancer efficacy to see if they may enhance the compound's already impressive biological activity. Many of the derivatives evaluated in vitro exhibited more cytotoxicity than parthenolide when used against 5 human tumor cell lines. The anticancer efficacy of five substances was further investigated in mice. Positive anticancer activity against mouse colon tumors and minimal immunological toxicity were observed for compound 4d in an in vivo study. Compound 4d's effects on cell apoptosis and cell cycle distribution were also investigated. Multiple interactions between 4d and NF-B were found through molecular docking studies. Our results highlight semicarbazones as a novel class of chemicals with intriguing anticancer action.[37]

**Analgesic, anti-inflammatory & anti-arthritic**

- *Mohsin et al. (2012)* Two schiff bases, acetophenone semicarbazone (ASC) and benzophenone semicarbazone (BSC), were synthesized and described in order to investigate their anti-inflammatory and analgesic properties in swiss albino mice. Throughout the course of the investigation, two doses of the test substances, 25 and 50 mg/kg (p.o.) for each, were selected. The 'carragenan induced mice paw edema inhibition' approach was used to assess the compounds' ability to reduce inflammation. Both the 'acetic acid induced writhing' and the 'tail immersion' tests were used to ascertain the analgesic efficacy. All information was compared to those for reference medications given at a dose of 10 mg/kg (p.o.). Anti-inflammatory and analgesic effects have been observed with both ASC and BSC. At 50 mg/kg (p.o.), the test compounds' anti-inflammatory and analgesic actions were quite like those of conventional medicines at 10 mg/kg (p.o.). Both ASC and BSC have been shown to be effective painkillers and anti-inflammatories.[38]

- *Luisa et al. (2005)* Vascular adhesion protein-1 (VAP-1), also known as human semicarbazide-sensitive amine oxidase (SSAO), is a copper-containing amine oxidase (AOC3, EC 1.4.3.6) with enzymatic and adhesive properties. Primary amines are oxidatively deaminated by SSAO, yielding the appropriate aldehyde and freeing hydrogen peroxide and ammonia in the process. Inflamed arteries contain an increase in

membrane-bound SSAO, which acts as an adhesion molecule between leukocytes and activated endothelial cells. The adhesion cascade appears to entail both direct adhesive and enzymatic actions. The enzymatic and adhesion functions of SSAO/VAP-1 are inhibited by the orally bioavailable SSAO inhibitor LJP 1207 [N- (2-phenyl-allyl)-hydrazine hydrochloride]. Mortality, weight loss, and colonic cytokine levels are all drastically decreased by LJP 1207 in a mouse model of ulcerative colitis. Treatment with the SSAO/VAP-1 inhibitor significantly reduced inflammation, damage, and ulceration scores in this model of colitis, as measured by quantitative histopathology. LJP 1207 increased survival time after lipopolysaccharide (LPS)-induced endotoxemia and decreased serum levels of tumor necrosis factor- and interleukin 6. In the rat carrageenan footpad model, both therapeutic and preventative treatment of LJP 1207 significantly suppressed swelling and inflammation. Taken together, the findings raise the possibility that small molecule inhibitors of SSAO/VAP-1 could be useful in the treatment of both acute and chronic inflammatory disorders.[39]

- *Vaishali et al. (2019)* A person's immune system reacts with inflammation in the face of an infection, irritation, or injury. The bloodstream acts as a conduit for immune cells to travel to the affected area. Increased blood flow (heat, ergo inflammation) causes the nearby blood vessels to open up and turn a bright red. Enzymes process arachidonic acid in the cell membrane to create prostaglandins via a number of processes (fig.1). Inflammatory cells produce huge amounts of prostaglandin E2 (PGE2), which contributes to pain, inflammation, and fever. Arachidonic acid is transformed into prostaglandin (PGH2) by the enzymes cyclooxygenase (COX)-1 and -2. Non-steroidal anti-inflammatory medicines can help with rheumatoid arthritis symptoms, but they don't stop the condition from getting worse over time. Most medical professionals agree that preventing further articular damage from rheumatoid arthritis requires early treatment with cytotoxic or disease modifying anti-rheumatic medications (DMARDs). The purpose of this study is to investigate the anti-inflammatory properties of semicarbazones in a rat model of Serotonin-induced edema and to assess the efficacy of the most effective compounds in a model of Freund's adjuvant-induced arthritis.[40]

**Antibacterial**

- *Elham et al. (2016)* Analytical and spectroscopic techniques, including elemental analysis, infrared spectroscopy, and nuclear magnetic resonance spectroscopy, were used

to confirm the structures of a series of hydroxyl semicarbazone derivatives of substituted diaryl ketones and acetophenones that were produced. Excellently pure hydroxysemicarbazones were obtained via a condensation reaction between N-hydroxy semicarbazide and substituted diaryl ketones or acetophenones. S. aureus, E. coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Micrococcus luteus were some of the bacterial strains tested after the produced hydrazones were tested for their inhibitory activity. Compounds 2, 6, and 7 showed the most bioactivity among the derivatives examined. Compounds 2 and 6 were shown to be selective against gram-negative bacteria, and the analysis of their activity data suggested that this was due in large part to their hydrophilicity.[41]

**Antiviral**

- *Valeria et al. (2020)* By derivatizing 5-acetyl benzimidazoles, which we previously described, we were able to investigate two series of (thio)semicarbazone- and hydrazone-based benzimidazoles and assess the effect of the change on the antiviral activity. Compounds 6, 8, 16, and 17 were effective dual inhibitors of influenza A virus and human coronavirus. These compounds contained 5-(thio)semicarbazone and 5-hydrazone functionalities in addition to the 2-benzyl ring on the benzimidazole core structure. Only drugs with a 2-[(benzotriazol-1/2)-yl)methyl]benzimidazole scaffold, such as 5-thiosemicarbazone (25) and 5-hydrazone (22), have been shown to be effective against respiratory syncytial virus (RSV). These compounds were found to be the most powerful antiviral medicines, with activity levels comparable to the FDA-approved medication ribavirin. The SAR of these compounds in relation to their binding manner to the target RSV F protein was described by the molecular docking study, which also revealed the crucial interactions for future evaluation.[42]

**Anticonvulsant**

- *Ahsan et al. (2013)* Semicarbazones are thought to exert their anticonvulsant effects by blocking the sodium ion (Na(+)) channel, which is thought to be owing to the existence of an aryl binding site with an aryl/alkyl hydrophobic group, a hydrogen bonding domain, and an electron donor group. Among a long list of semicarbazones described by Dimmock et al., 4-(4-fluorophenoxy) benzaldehyde semicarbazone (C0102862, V102862) stands out as the series' lead molecule. When compared to carbamazepine (PI

101), phenytoin (21.6), and valproate (2.17), C0102862 had a higher protective index (PI > 315) in MES (oral) screening.[43]

**Hepatoprotective**

- *Islam et al. (2013)* Acetone semicarbazone (ASC) was tested in vivo for its hepatoprotective effects in both healthy and Ehrlich ascites carcinoma (EAC)–infected male Swiss albino mice. To counteract the toxicity caused by EAC cells, the effects of a drug dose of 2.0 mg/kg body weight for 14 days were analyzed for their effects on biochemical and behavioral markers. Histopathology research on the safeguarding properties of ASC was also evaluated. The modest toxicity caused by ASC injection resulted in insignificant weight loss and behavioral (salivation, diarrhea, muscle numbness) abnormalities in normally developing mice during the treatment period. Slight adjustments were seen in the normal mice's biochemical parameters after receiving ASC; they included glutamate pyruvate transaminase, glutamate oxaloactate transaminase, alkaline phosphatase, serum glucose, cholesterol, urea, triglyceride, and billirubin. Even while treatment was ongoing, these parameters returned to normal with time. When administered to mice harboring EAC cells, the ASC completely reversed the harmful effects of the EAC cells. Histological examination of several organs from wild-type mice given ASC did not reveal any major abnormalities. Due to its potent protective effect in mice harboring EAC cells, ASC can be safely formulated into a potential anticancer medication.[44]

## CONCLUSION

Studies have shown that the semicarbazone moiety and its many derivatives have powerful pharmacological effects. It concludes that semicarbazide analogues are highly promising in the development of new medications for the treatment of numerous epidemic and infectious diseases like cancer, epilepsy, infection (protozoa, viral etc.), hepatic-failure, pain & inflammation and many more. It would be convenient to purchase for each humankind.

**Funding**

Nil.

**Conflict of interest**

None.

**REFERENCES**


1. J.D. Warren, D.L. Woodward, R.T. Hargreaves, 4-Substituted semicarbazones ofmono- and dichlorobenzaldehydes as antihypertensive agents, J. Med. Chem, 1977; 20: 1520–1521.
2. O.T. Wong, I.H. Hall, J.M. Chapman, The hypolipidemic activity ofl N 3 aethylphthalimido butan 3 semicarbazone in rodents, Pharm. Res, 1989; 6: 230–234.
3. M.C. Alliegro, M.A. Alliegro, E.J. Cragoe, B.M. Glaser, Amiloride inhibition of angiogenesis, J. Exp. Zool, 1993; 267: 245–252.
4. Wilfredo H, and Juan P: Complexes of Semicarbazone and Thiosemicarbazone. Journal of Chemical science, 2006; 14: 10-20.
5. Shalin K, Dhar ND, and Sharma NP: Application of metal complexes of Schiff, base. Journal of Scientific and Industrial research, 2009; 68: 181- 187.
6. S.E. Assis, A.M. Bruno, D.A. Molina, G.M. Conti, C.H. Gaozza, Synthesis, DNA interaction and antineoplastic activity of semicarbazone derivatives, Farmaco, 1996; 51: 419–423.
7. L.T.S. Rocha, K.A. Costa, A.C.P. Oliveira, E.B. Nascimento, C.M. Bertollo, F. Araújo, L.R.Teixeira, S.P. Andrade, H. Beraldo, M.M. Coelho, Antinociceptive, antiedematogenic and antiangiogenic effects of benzaldehyde semicarbazone, Life Sci, 2006; 79: 499–505.
8. J.R. Dimmock, R.N. Puthucode, J.M.S. Hetheriangton, J.W. Quail, U. Pugazahenthi, J.P.Stables, (Aryloxyl) aryl semicabazones and related compounds: a novel class of anticonvulsant agents possessing high activity in the maximal electroshock screen, J.Med. Chem, 1996; 39: 3984 3997.
9. K. Unverferth, J. Engel, N. Hofgen, A. Rostock, R. Gunther, H.J. Lankau, Synthesis, anticonvulsant activity and structure activity relationships of sodium channel blocking3 aminopyrroles, J. Med. Chem, 1998; 41: 63 73.
10. Farrell N: Synthesis, characterization and antimicrobial activities of some metal (II) amino acid complexes. Coordination Chemistry Review, 2012; 2(3): 809-840.
11. West D, Padhye S, and Sonawane P: In Structure and Bonding, Springer-Verlag. New York 1991: 76; 1-49.
12. Kirchgessner M, and Schnegg A: Activity of proteases, leucine arylamidase and alpha-amylase in pancreatic tissue during nickel deficiency. Nutrition and Metabolism, 1979; 23: 62-64.
13. Kasuga N, Sekino K, Kuomo C, Shimada M, and. Nomiya K: Synthesis, structural characterization and antimicrobial activities of 4- and 6- coordinate nickel (II) complexes

with three thiosemicarbazones and Semicarbazone ligands. Journal of Inorganic Biochemistry, 2001; 84: 55.

14. Sharma R, Rawat S, and Nagar M: Synthesis, Characterization and Antibacterial Activity of Some Transition Metal cis 3,7-dimet-hyl-2,6 octadiensemicarbazone Complexes. Transition Metal Chemistry, 2006; 31: 201-215.
15. Lindskog S: Structure and Mechanism of Carbonic Anhydrase. Pharmacology and Therapeutics, 1997; 74: 1-20.
16. Zundahl S: Chemical Principles. Houghton Mifflin Company Boston New York third edition 2013. 15. Dowling C, and Perkin G: Synthesis, characterization and in vitro evaluation of anticancer activity of a new water-soluble thiosemicarbazone ligand and its complexes Polyhedron, 2006; 15: 2463-2475.
17. Osredkar J, and Sustar N: Copper and Zinc, biological role and significance of copper/zinc imbalance. Journal of clinical toxicology, 2011; 3: 2-18.
18. Wedepohl K: The composition of the continental crust Geochemical et Cosmochimica Act, 2015; 59(7): 1217–1232.
19. Nordberg G, and Nogawa K: Cadmium in Chapter 23 in Handbook of the Toxicology of Metals, 2007; 3: 445–486.
20. Sharma R, Agarwal S.K, Rawat S, and Nagar M: Synthesis, characterization and antibacterial activity of some transition metal cis-3,7-dimethyl2,6-octadiensemicarbazone complexes. Transition Metal Chemistry, 2006; 31: 201-206.
21. Jerome D, and Yeung J: Diagnosis and Management of psoriasis. Canadian family Physician, 2017; 63(4): 278-285.
22. Zhang X, Fan Y, and Xiao Y: Molecular study on copper- mediated tumor proteasome inhibition and cell death. International Journal of oncology, 2010; 37: 81-87.
23. Renade S. and Panday V: Transition metals in human cancer II. The science of the total environment, 1984; 40: 245-257.
24. Reddy K., and Babu P: Synthesis, spectral studies and nuclease activity of mixed ligand copper (II) complexes of hetero aromatic semicarbazones/thiosemicarbazones and pyridine. Journal of In0rganic Biochemistry, 1999; 77: 169.
25. Klaassen CD, Amdur MO and Doull J: Toxicology the Basic Science of Poisoning, sixth ed. McGraw-Hill, Medical Publishing Division, New York, third edition, 1986.
26. Jiang Y, and Zheng W: Cardiovascular toxicities Upon Manganese Exposure. Cardiovascular toxicology, 2005; 5(4): 345-354.

27. Table E. and Table V.: Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, Iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc, 2011.
28. Greger J.L: Dietary standards for manganese: overlap between nutritional and toxicological studies. The Journal of nutrition, 2012; 128(2): 368S371S.
29. Lonnerdal B, Keen C.L, and Hurley L.S: Manganese binding proteins in human and cow's milk. The American Journal of Clinical Nutrition, 1985; 41(3): 550-559.
30. Couper J: On the effects of black oxide manganese when inhaled into the lungs. British annals of medicine, Pharmacy, vital statistics and general science, 2006; 1: 41-42.
31. Garoufis A, Hadjikakou S.K, and Hasjiliadis N: Palladium coordination compound as anti-viral, anti-fungal, anti-microbial and anti-tumor agent. Coordination Chemistry Review, 2009; 253: 1384-1397.
32. El-Shazly R.M, and Al-Hazmi G.A: Synthesis and spectroscopic characterization of cobalt (II) Thiosemicarbazone complexes. Journal of Coordination Chemistry, 2006; 59, 8: 845–859.
33. Farrell N: Synthesis, characterization and antimicrobial activities of some metal (II) amino acid complexes. Coordination Chemistry Review, 2012; 2(3): 809-840.
34. Jafri L, Ansari F, Jamil M, Kalsoom S, Qureishi S and Mirza B: Microwave-assisted synthesis and Bioevaluation of some semicarbazones. Chemical Biology and Drug Design, 2012; 79: 950-959.
35. Neelam B, and Kakalu H: Synthesis and in vitro antiprotozoal activity of semicarbazone derivatives. Bioinorganic And medicinal chemistry, 2012; 16: 4.
36. Ali Shaikh M Mohsin, M Abul Kalam Azad, Mele Jesmin, Shamim Ahsan, M Mijanur Rahman, Jahan Ara Khanam, M Nazrul Islam, and Sha M Shahan Shahriar. *In vivo* anticancer activity of vanillin semicarbazone, 2012; 2(6): 438–442.
37. Islam Khairul, Shaikh M Mohsin Ali, Mele Jesmin, and Jahan Ara Khanam. *In vivo* Anticancer Activities of Benzophenone Semicarbazone against Ehrlich Ascites Carcinoma Cells in Swiss Albino Mice, 2012; 9(4): 242–247.
38. Jia Xinxin, Qi Liu, Shiyi Wang[a], Binglin Zeng, Guohua Du, Chen Zhang, Yan Li. Synthesis, cytotoxicity, and *in vivo* antitumor activity study of parthenolide semicarbazones and thiosemicarbazones. Bioorganic & Medicinal Chemistry, 2020; 28, 13, 1: 115557.
39. Ali Shaikh M Mohsin, Mele Jesmin, M Abul Kalam Azad, M Khairul Islam, Ronok Zahan. Anti-inflammatory and analgesic activities of acetophenonesemicarbazone and

benzophenone semicarbazone. sian Pacific Journal of Tropical Biomedicine, 2012; S1036-S1039.

40. Luisa M. Salter-Cid, Eric Wang, Anne M. O'Rourke, Andrew Miller, Hongfeng Gao, Li Huang, Arnie Garcia and Matthew D. Linnik. Journal of Pharmacology and Experimental Therapeutics November, 2005; 315(2): 553-562.
41. Vaishali K. Chavan, C. T. Chopade, S. G. Wadatkar, A. G. Nerkar, Swati Deshmukh. Evaluation of Some Semicarbazones for Anti-Inflammatory and Anti-arthritic Activity in Rats. Current Trends in Pharmacy and Pharmaceutical Chemistry, 2019; 1(3): 37-47.
42. Elham Hariri, Arash Mahboubi, Mohammad Fathi, Parisa Rahmani, Kamaleddin Haj Mohammad Ebrahim Tehrani, Mohammad Babaeian, Vida Mashayekhi, and Farzad Kobarfard. Synthesis and Antibacterial Activity of Novel Hydroxy Semicarbazone Derivatives, 2016; 15(l): 29–35.
43. Valeria Francesconi, Elena Cichero, Silvia Schenone, Lieve Naesens, Michele Tonelli. Synthesis and Biological Evaluation of Novel (thio)semicarbazone-Based Benzimidazoles as Antiviral Agents against Human Respiratory Viruses. Molecules, 2020; 25, 25(7): 1487.
44. Mohamed Jawed Ahsan. Semicarbazone analogs as anticonvulsant agents: a review. Cent Nerv Syst Agents Med Chem, 2013; 13(2): 148-58.
45. Islam Farhadul, Shaikh Mohummad Mohsin Ali, and Jahan Ara Khanam. Hepatoprotective effect of acetone semicarbazone on Ehrlich ascites carcinoma induced carcinogenesis in experimental mice. Asian Pac J Trop Biomed, 2013; 3(2): 105–110.