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PREFACE

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CHAPTER 1

AN OVERVIEW OF HEAVY METAL POLLUTION IN WATERS

Inci ARIKAN[1]
Ceylan AYADA[2]

The health status of the person is determined according to the interaction between the genetic structure and the biological, social and physico-geochemical components. It is reported that every born baby is born with hundreds of tons of mineral, metal and fuel needs according to the socioeconomic status of the countries. That is why we know that physico-biochemical environmental elements are necessary for the continuation of our lives. However, environmental pollutants are mentioned with the accumulation of some organic and inorganic chemical substances in the physicogeochemical environment, which endangers the health of human and other organisms. While some of these environmental pollutants can be found in the normal range in non-hazardous amounts, the increased amount of them releasing into the environment may arise from human activities [1-6].

Pollutants that enter the body in various ways may cause organ and cell damage according to their organic or inorganic formation [1-5]. Therefore, environmental disease burden studies, in which quantitative assessment of environmental risk factors are carried out to determine the level of disease in the population, is important [4-8]. Thus, we can say that the environment may prepare the ground for diseases, may be the cause of the disease directly, may facilitate the spread of diseases or may affect the outcome of the diseases.

In general, approximately 9% of the total disease load can be attributed to environmental pollution. However, this rate is significantly higher in developing countries. In this case, one of the unsafe sources is seen as water exposure. Achieving safe drinking water is still a global issue for the rural population dependent on irregular water. In 2015, the World Bank identified that 46% of the world's population (3.4 billion) as rural and reported that 15% of the population did not have adequate access to water. It is estimated that the amount of water per capita will be

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CHAPTER 2

FUNCTIONAL FOODS FOR OBESITY MANAGEMENT

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Orkide DONMA[2]

INTRODUCTION

Obesity is a global health problem in both developed and developing countries. The prevalence of obesity, which is related to many metabolic disorders, such as diabetes mellitus, metabolic syndrome, cardiovascular diseases, non-alcoholic fatty liver disease and some cancers-, is increasing among all fractions of the population, including children, adolescents and adults. Aside from these diseases, it may also lead to some psychological problems, such as depression. At the same time, it is also a social problem, which adds a significant burden on health care systems. Quite many pharmacological and/or surgical solutions to treat obesity are in current use. Within this context, some drugs such as orlistat and bariatric surgery may be mentioned. However, especially in the presence of cardiovascular diseases, they may aggravate the clinical picture. [1-5]

In the meantime, alternative medicine offers some medicinal herbs to prevent and even, in some cases, to treat obesity. Each of these plants contains many bioactive compounds, which have been suggested as safe anti-obesity resources. Upon investigation of their action mechanisms, various routes have been clarified. Inhibition of enzymes concerning lipid and carbohydrate metabolisms, modulation of some certain signaling pathways are some of these mechanisms. [1, 6-10]

Recently, the interrelationship between white and brown adipose tissues has gained importance. The association between the amount of brown adipose tissue and the amount of energy expenditure is well-known. Therefore, the participation of bioactive components found in some plants into the brown adipose tissue and white adipose tissue metabolisms has drawn attention. Adipocyte browning is a promising strategy for obesity prevention. The plants, which stimulate the conversion of white adipocytes to brown adipocytes or inhibit the differentiation of

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The people with chronic diseases may prefer to proceed with phytotherapeutic applications during their treatments. They may believe that such a therapy will be less harmful for their body. However, if a plant has a pharmacological effect, it will also have side effects. For instance, flavonoids, alkaloids, terpenes, have been reported to possess hypoglycemic effects.[64] Onion ameloriates hyperglycemia and insulin resistance.[65] Garlic causes significant decreases in fasting blood glucose and glycated hemoglobin levels.[66] Garlic also demonstrates a hypotensive effect. [67] Cinnamon, due to its coumarin content, acts as a powerful anticoagulant. Coadministration of cinnamon and ginger with dabigatran significantly increases the risk of bleeding.[68,69]

In conclusion, the benefits and importance of bioactive components in medicinal plants cannot be underestimated when obesity prevention and treatment are taken into consideration. However, their multi-target activities should also be widely investigated.

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CHAPTER 3

IMMUNE-PATHOGENESIS AND DIAGNOSIS OF LATENT TUBERCULOSIS INFECTION

Deniz GAZEL[1]

Tuberculosis (TB) is one of the oldest diseases of history. *Mycobacterium tuberculosis* complex is formed by a group of bacilli (*M. tuberculosis, M. bovis, M. africanum, M. microti, M. canetti and M. caprae*). The disease progresses by the host's inflammatory response due to the development of chronic granulomatous infection. Infection usually begins with inhalation of 1-3 microns of particles containing 1-3 bacilli within the inhalation. The bacteria pass the physical barriers of the upper airway and reach the alveoli (1).

TUBERCULOSIS INFECTION

Primary infection with positive skin test (PPD+) develops at about 30% of PPD (-) patients who were exposed to TB cases. Only 10% of primary infections develop to primary tuberculosis. The existence of infection or disease depends on the balance between the resistance of the host and the virulence of the bacilli. Both natural and acquired immunity play a role in the response of the host to tuberculosis. *M. tuberculosis* bacilli reaching the alveoli can be eliminated at the beginning or can be controlled by the immune response against the bacilli, or the bacilli can multiply to form a primary tuberculosis disease following the primary infection. The bacilli, which were dormant during the primary infection, may start to multiply after years and may cause secondary tuberculosis by reactivation. The primary infection may be activated at any age after a latent period (years or decades) and may cause secondary tuberculosis in other organs, most commonly in the upper regions of the lung. The immunological responses (cellular immunity and delayed of type hypersensitivity reaction) of the host against bacillus antigens determine the type of disease. Immuno-pathogenesis of pulmonary tuberculosis is staged from initial infection to cavity formation. Weeks after the invasion of alveolar macrophages by TB bacilli, the bacilli antigens are also transported to the regional lymph nodes by the infected cells. *M.tuberculosis*-infected macrophages and dendritic cells develop a specific inflammatory response; by macrophage ac-

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CHAPTER 4

KNOWLEDGE AND ATTITUDES OF PHYSICIANS ON PHARMACOVIGILANCE

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INTRODUCTION

Despite the advancement in modern medicine, adverse drug reactions (ADRs) persist and are still relatively common [1]. Adverse drug reaction (ADR) as described by Edwards and Aronson is "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard for future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product". On the other hand, adverse drug effect is an unexpected outcome that can be attributed to some action of a drug, while an adverse event is an adverse outcome that occurs while a patient is taking a drug, which may or may not necessarily be attributable to it [2].

According to the World Health Organization (WHO), safer and healthier drug use remains a core objective of pharmacovigilance. Though newly discovered drugs undergo clinical trials in a carefully selected population of volunteers before they are made available for public consumption [3], the effectiveness and safety of these medications should be ascertained under real-life conditions. The

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Abbreviations
ADEs: Adverse drug events, ADR: Adverse drug reaction, ADRs: Adverse drug reactions, WHO: World Health Organization, TÜFAM: Turkey Pharmacovigilance Centre, OECD: Organization for Economic Cooperation and Development

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Authors' contributions
Conception and design of the study: ONE, SV, DD, AOA, MSE. Data collection: DD, GC. Statistical analysis: GC. Manuscript preparation: ONE, GC, MSE. Reviewed/edited and approved the manuscript: ONE, SV, DD, GC, AN, AOA, MSE. English grammar checking: AN. Guarantor: ONE. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
All necessary institutional permissions were obtained from Istanbul University and further approval was given by the Ethics Committee of the University (Protocol number 83045809-604.01.02). All the respondents volunteered and gave informed consent to participate in this study.

Consent for publication
Not applicable

Competing interest
The authors declare that they have no competing interests.

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CHAPTER 5

MUTATION ANALYSIS IN INFANY WITH FXI DEFIENCY

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Factor XI deficiency was first described in 1953.it is often observed in the Jewish race. Increased prekalikrein crecreine and high molecular kininogen (HK) is observed with FX activation activation occurs with negative charge.FXI operates on the intrisictive pathway.FXI is synthesized in megakaryocytes and liver. FXI is a 160-kDa glycoprotein, which separates into two 80-kDa sub- units linked by disulfide bonds. It comprises heavy chains with four repeats that have binding sites for high-molecular-weight kininogen (HK), thrombin, platelets, FIX, and FXII. There is a protease on the light chain.Serine protease is activated by the interaction of calcium, platelet and thrombin. Thrombin's role in the activation of FXI is the result of a "feed-forward loop" to promote stable clot formation and protection against fibrinolysis by throm- bin activatable fibrinolytic inhibitor (TAFI). FXI was be activated by FXII or HK, due to contact activation and the so-called intrinsic pathway. Contact activation is not thought to be as important in the physio- logic activation of FXI, and instead the activation of FXI is predominately mediated by thrombin. Relationship between FXI and fibrinolysis might explain reason, in contrast to other coagulation factor deficiencies, FXI deficiency tendency to excessive mucosal bleeding. (2) Factor XI deficiency and functional defects :Homozygotes or compound heterozygotes have an FXI level of <15 U dL and heterozygotes display levels of 25– 70 U dL or normal values [6,7]. Vertical transmission of severe Factor XI deficiency has got a poor correlation between factor XI level and bleeding tendency. It has be may be caused by different molecular variants of factor XI.but studies comparing antigenic measurements of factor XI have shown no diversity suggesting that the deficiency is due to reduced amounts of clotting factor (6,7).

There are different bleeding risks in different surgical interventions in mild factor XI deficiency. No bleeding was observed after dental extraction and tonsillectomy.

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p.W519* and c.325+1G>A) identified in this study had been previously described in other Turkish patients with FXI deficiency.

Seyma C et all reported in Turkey the patients' F11 genes were direct DNA sequencing of 11 amplicons containing the 5 untranslated region, all exons, and exon/ intron boundaries by PCR-amplified and analysed .14 patients had F11 gene mutations were observed in this analysed. Eight different mutations were reported.. Six of the mutations were recurrent mutations (p.Thr51Pro, p.Glu135X, p.Cys416Tyr, p.Gly418Val, p.Trp519X, and c.325+1G>A), two were novel mutations were ; (p.Val522Gly, and p.Cys581Arg)All the mutations were specific to the families in which they were detected, except p.Thr51Pro and p.Trp519X which were detected in two families.(34)

Heterozygous c.623C> A (p. Thr208Lys) Heterozygous c.1556G> A (p.Trp519 *) mutations in infant with factor IX defiency This mutation was not detected mutations before the turkey. FXI: C level was 1u / dL. Clinically heavy progress. In order to contribute to the determination of gene mutations in FXI deficiency in our country, the case was considered appropriate.

Disclosures

The authors state that they have no interests that might be perceived as causing a conflict or bias.

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CHAPTER 6

NUTRITION MANAGEMENT AND NURSING APPROACH IN PATIENTS UNDERGOING HEMODIALYSIS THERAPY

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NUTRITION IN HEMODIALYSIS TREATMENT

Chronic kidney patients often have to change their diets because of the ingredients contained in foods and acquire new eating habits that are very different from their ethnic and cultural preferences[1]. Therefore, it is difficult for patients to change their usual eating and drinking habits[2,3]. However, diet is a crucial part of the treatment regimen. When the patients undergoing hemodialysis therapy do not adapt fluid and nutrition restriction, complications are seen like the electrolit imbalance (such as hyperkalemia and hyperphosphatemia) and extracellular fluid volume overload (peripheric and pulmonary edema) which may lead to potential fatal conclusions [4-10]. Dietary non-compliance also has long-term chronic effects. Hyperphosphatemia causes bone disease and non-skeletal metastatic calcification. Chronic volume overload is associated with hypertension and may eventually lead to congestive heart failure. Inadequate intake of nutrients, especially protein and calorie requirements, leads to a reduction in basic proteins, such as albumin and leads to muscle loss. Therefore, it is important for patients undergoing hemodialysis therapy to apply medical nutrition treatment. However, studies show that many patients receiving HD treatment have difficulty in maintaining health promotion behaviors [11,12]. Thus, as far as possible, patients should be advised of general healthy eating principles appropriate for hemodialysis treatment. The basic nutritional requirements and the electrolytes in the risk group in hemodialysis patients are listed below.

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plain the mechanism underlying salt restriction. [15,18,19,26]. Potassium is a mineral found in many foods consumed in daily life. It is possible for patients who receive dialysis treatment not to experience hyperkalemia by taking regular dialysis treatment and keeping the potassium in balance [26]. It is as important as hemodialysis treatment for patients to learn foods containing high and low potassium and to be able to control the portions. Nurses working with these patients should check the food consumed at regular visits and work with the patient to balance the risky electrolyte according to the patient's blood values. In addition, patients should always be informed about general nutrition principles and reminders should be made [15,19,50].

Phosphorus is a mineral commonly found in the main food groups [26]. Foods with high phosphorus, alternative foods that can be preferred and appropriate cooking methods must certainly transfer to the patients and also patients must be supported. Research also shows that phosphorus control can be established and also protein intake can be maintained at a sufficient level in patients receiving diet counseling [26, 50,51].

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CHAPTER 7

PATENT DUCTUS ARTERIOSUS: A PRACTICAL CLINICAL APPROACH

Seyma KAYALI[1]

INTRODUCTION

Ductus arteriosus is a critical vascular structure during fetal life for maintaining fetal systemic blood flow that connects the descending aorta and the pulmonary artery [1]. Persistent patency of the ductus arteriosus (PDA) after birth may cause significant clinical outcomes related to the left to the right shunt and is one of the most common lesion of congenital cardiac diseases with a prevalence of 5-10% [2].

With the widespread use of echocardiography, the rate of PDA diagnosis has been increased, recently. However, it is still a great challenge for physicians to decide which PDA is harmful and needs treatment. Moreover, management strategies are changing and developing day by day and there is still not a worldwide consensus.

This review focused on the key aspects of PDA management and providing the latest recommendations about this subject at all ages

PDA in preterm infants

As the normal mechanism of ductal closure does not function effectively in preterm infants, patent ductus arteriosus is common and its incidence is inversely correlated to the gestational age of the baby. While PDA incidence is about 20% in premature babies born in the 32nd week of pregnancy, it is seen in 80-90% in extremely low birth weight babies with a gestational age below 26 weeks[3].

Because of the association with PDA and numerous morbidities in preterms, such as necrotizing enterocolitis, renal impairment, pulmonary haemorrhage, bronchopulmonary dysplasia, intraventricular haemorrhage,medications, including cyclooxygenase inhibitors and surgical ligation are frequently used in clinical practice as ductal closure treatments [4].

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'Silent PDA' is defined as incidentally diagnosed PDA by echocardiography in the absence of typical murmur [17, 21].

While hemodynamically significant PDA often requires treatment, silent PDA can be occasionally a cause of infective endocarditis, especially in older ages and there is still debate in terms of closure of silent PDA [21].

Conclusion

Ductus arteriosus is an important vascular structure during fetal life. However, if persists after the early neonatal period, significant problems can occur. Thus, to make the decision of treatment is important and in preterms, medical closure, in symptomatic patients of all ages , transcatheter or surgical closure is recommended.

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CHAPTER 8

PHYTOTHERAPEUTIC APPLICATIONS FOR INSOMNIA

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BACKGROUND

Insomnia, a severe sleep problem, is a growing health hazard. It poses a major threat to mental health, heart function and the immune system. Anxiety and depression are the two main problems affected by insomnia. Mechanisms underlying the association between insomnia, anxiety, and depression are being investigated. Poor sleep quality and depression are prevalent during pregnancy and may negatively impact maternal-fetal outcomes. Sleep problems in infants and young children are common and often underdiagnosed. Insomnia complaints in children and adolescents should be taken into account. The American College of Physicians developed a guideline on the management of insomnia in adults. Insomnia is also common in the elderly. Nonpharmacological treatment options have favorable and enduring benefits compared to pharmacological therapy. In the first line, improving sleep-hygiene parameters and considering cognitive-behavioral therapy are the nonpharmacological interventions. Then come pharmacological agents in combination with behavioral modifications. [1-8]

Chronic insomnia impairs the quality of life. It can rob the individuals of their families, jobs and even their sanity. There are prescribed medicines used for the treatment of insomnia. They are effective but, at the same time, exhibit significant adverse effects. Thus, patients are in need for an alternative treatment to cure this problem. So far, some herbs have been studied for their potential sedative and hypnotic activities. They are expected to improve sleep. Most of them exert their actions on the central nervous system with a major influence on the inhibitory gamma-aminobutyric acid (GABA), which promotes relaxation and reduce anxiety or serotonin neurological systems. [9-14]

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efficiency. Its procyanidin content increases tryptophan availability, reduces inflammation and may partially improve insomnia. Milk fermented with a strain of Lactobacillus brevis with GABA-producing capacity may improve sleep. [81-84]

Data on phytotherapeutic applications for insomnia are still not sufficient. Natural remedies are considered much safer than pharmacological agents; however, further studies are needed to evaluate their risk and the safety concerns for many supplements. Potential integrative approaches without serious side effects are being investigated. The need for a good understanding of the safety and the efficiency of medicinal plants for the treatment of insomnia stimulates further investigations to manage this commonly observed health problem.

Studies, which will be performed, should cover safe dosages, as well as doses confined to herbs suggested to be used during insomnia treatment. Standard measures designed for the quality/quantity of sleep should also considered. They are also expected to focus on active constituents in the herbs and their potential adverse effects. The matter concerning their interactions with prescribed drugs, as well as with other herbs is a great problem to be largely investigated.

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CHAPTER 9

SUICIDES WITH ELECTRONIC CIGARETTES

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BACKGROUND

Electronic cigarettes (ECs) are devices that allow various combinations of liquids (nicotine, vegetable glycerin (VG), propylene glycol (PG), and/or ethanol of various flavors) to be inhaled by heating and turning them into aerosols (1). The frequency of the use of ECs among young people is gradually increasing. The reason for its popularity is that the dose of nicotine can be individualized, various aromas are available, and the belief that it will help the user to stop smoking classic tobacco. In 2003, a Chinese pharmacist Hon invented and patented the first e-cigarette and subsequently began to be available in markets around the world (2). E-liquid with a lot of flavor and nicotine content is available in markets and on the internet. As the rules and laws regarding this are not sufficient, the nicotine dosage in e-liquid may differ. Although many European countries determine the maximum nicotine dose of 20 mg/ml, e-liquids in the range of 0-60 mg/ml can be reached in the internet environment (3). Recently, the available dose has increased to a relatively high dose of 210 mg/mL.

The widespread use of ECs and nicotine-containing liquids causes various health problems (4, 5). In addition, it increases the intentional or unintentional toxic exposure events in parallel. However, the clinical effects of e-liquid intake remain uncertain. Since different substances are present in different doses in e-liquid, it has not been possible to evaluate this until now. However, the most common features of (i) nicotine poisoning are: agitation, headache, nausea, vomiting, high blood pressure, and tachycardia; (ii) PG overdose are: hyperosmolality, hemolysis, and subsequent kidney failure and lactic acidosis; and (iii) VG overdose are: headache, nausea, vomiting, and dehydration (3).

The purpose of this article is to review suicide cases related to the consumption of ECs in the literature and highlights the health problems associated with poisoning.

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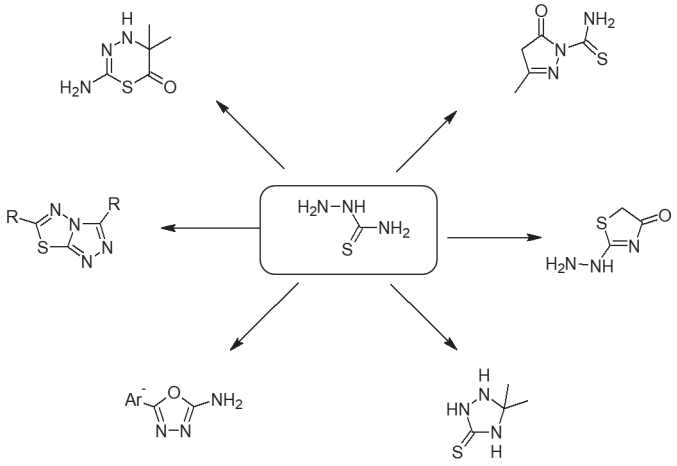
CHAPTER 10

THE REVIEW OF BIOLOGICAL ACTIVITY POTENTIAL OF THIOSEMICARBAZIDE (HYDRAZINECARBOTHIOAMIDE) DERIVATIVES

Faika Basoglu[1]
Nuray Ulusoy Guzeldemirci[2]

1. INTRODUCTION

Generally, small molecules that containnitrogen and sulfur groups are very handy for the synthesis of many novel biologically active compounds [1,2]. Thiosemicarbazide derivatives, for instance, tend to relatively easy to synthesize and can serve as the precursor, intermediate molecule, or subunit in the synthesis of heterocyclic compounds (Scheme 1) [3,4].



Scheme 1. Some heterocyclic compounds are obtained from thiosemicarbazide [3]

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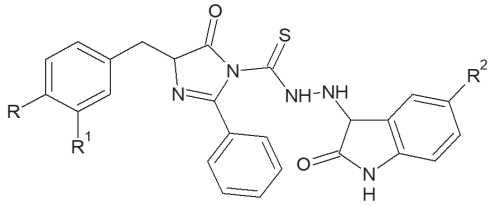
A novel series of 4-(4-Methylbenzylidene)-5-oxo-2-phenyl-imidazolidine-1-carbamodithioic acid (2-oxo-1,2-dihydro-indol-3-ylidene)hydrazide were synthesized according to the literature [83] mentioned procedures by conventional methods and evaluated for their possible anthelmintic activities [83].



62a-j

R= -H, -OCH_3, -Cl, -NO_2, -CH_3 R^1= -H, -OCH_3 R^2= -H, -Cl

4. CONCLUSION

In this review, there has been considerable interest in the development of novel thiosemicarbazide derivatives with biological activities, such as anticancer, antiviral, antibacterial and antimicrobial. This review expresses the variety and diversity in application areas of significant importance shown by thiosemicarbazides and their derivatives. Consequently, some thiosemicarbazide derivatives show good antioxidant, antifungal, and antibacterial and also these molecules and the other derivatives have got low or intermediate biological activity, such as antiviral, anticancer, analgesic, anticonvulsant.

Many researchers are still going on to improve and design new thiosemicarbazide derivatives and some studies are supported by a computational study using a molecular modeling program.

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