A study of the biological activity of 4-(Para-Substituted phenyl)-1,2,3-selenadiazole derivatives as anti-oxidant and anti-breast cancer

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Abstract

In the present work, five ligands of substituted 1,2,3-selenadiazole have been synthesized and characterized and they have been tested as possible anti-oxidant and anti-breast cancer. The synthesized compounds were prepared by the reaction of selenium dioxide with a series of semicabazone derivatives in glacial acetic acid. The prepared compounds have been characterized using different methods. The biological activity of 1,2,3-selenadiazole compounds were examined against the growth of two types of bacterial strains (E.coli and staphylococcus aureus). Also this study determined the activity of 1,2,3-selenadiazole derivatives as antioxidants, and measured their ability towards α, α-diphenyl-β-picrylhydrazyl (DPPH) free radical scavenging. It has been found that they have good activity to reduce free radical's effects. Inhibition of 1,2,3-selenadiazole derivatives was carried out against human breast cancer cell (MCF-7) growth by MTT. The measurements showed that the derivatives had a higher inhibition rate than the complexes , the IC_{50} of compounds D_3 and D_4 was (89.5 and 44.3) µg/ ml respectively.

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1. Introduction

Selenium is a vital nutrient to health of human. It can be play as an antioxidant and it may help to prevent a lot of illness. Recently may published papers proposes that a low level of selenium might cause increasing of certain types of cancer. May researchers have been tried to study the relation between selenium intake and breast cancer in patients [1]. Organoselenium rings containing nitrogen are important category of heterocyclic compounds. They have attracted a continuous interest during the last years due to their valuable biological applications as anti-oxidant and anti-cancer agents. Selenium element has been well-known as a vital part of the vital site for numerous seleno-enzymes where selenium is existing in the seleno-cyteine also in seleno-methionine amino acid derivatives. Many types of glutathione peroxidases (such as cytosolic glutathione peroxidase that is the first recognized selenoenzyme) defend cells against peroxidative harm by reducing H_2O_2, free fatty acid hydroperoxides, and phospholipids hydroperoxides [2–6]. Organo heterocyclic selenium compounds containing nitrogen such as selenirenes, selenophenes, selenadiazoles, selenatriazoles and benzisoselanazolones show promising results in a variety of chemopreventative studies. Organo heterocyclic selenium compounds containing nitrogen are indicated biological activities as vital immune-stimulants, inhibitors of enzymes, anti-oxidants, anti-inflammatory, anti-tumor, anti-viral and anti-microbial agents [7].

The five-member ring selenium compounds which has two nitrogen atoms like 1,2,3- ; 1,2,4- ; 1,3,4 and 1,2,5-selenadiazole are investigated as antifungal and antibacterial agents [8]. Furthermore, these types of heterocyclic compounds possess significant applications in the fields of light-emitting diodes and conducting materials chemistry [9]. The interesting pharmacological activities of selenium hetero-cycles compounds are well known [10]. Furthermore, selenium element is a key constituent of numerous major metabolic pathways in human body, as well as thyroid hormones metabolism, anti-oxidant resistance system, and immune role [11]. Moreover, selenium supplementation could decrease the rate of many cancer types such as prostate, lung, colon, and liver cancers [12, 13]. As well known that many of heterocyclic molecules having nitrogen and sulfur hetero-atoms showed a varied range of biological activities [14]. Also, the diazole ring is found in frequent anti-parasitic, fungicidal, and anti-inflammatory agents [15]. Several 1,2,3-selenadiazole rings were investigated to possess anti-tumor action [16]. In view of

extraordinary pharmacological ability of selenadiazole molecules and its analog compounds and in continuation with our previous works in the biochemistry [16-19], we report here in the synthesis of 1,2,3-selenadiazoles molecules to be assessed pharmacologically as anti-tumor compounds.

1. Experimental

Solvent that used in this study were purified in according to standard procedures. A Shimadzu 8400S –Japan, FT-IR spectrophotometer has been used to record IR spectra. The UV-visible spectra of the studied compounds were recorded on (UV 1800 Shimadzo) in ethanol solvent. The melting points of studied compounds were recorded with an electro-thermal device.

2.1. Semicarbazones preparation: A General procedure

Semicarbazide hydrochloride (1.00 mmol) has been mixed with sodium acetate (1.00 mol) in absolute ethanol solvent (50 mL). Then, the mixed compounds were heated under reflux for 15 min. The mixing was filtered while warm to remove NaCl precipitation. The filtrate was then mixed with acetophenone, p-methylacetophenone, p-chloroacetophenone, p-bromoacetophenone p-methoxyacetophenone (1:1 mmol) respectively. The resulting mixtures were refluxed and 3 ml of conc. HCl were added and the mixture was heating under reflux was continued for 24 hours. The ethanol solvent was removed under vacuum and the remainder was washed with chloroform [22].

1.2. 1,2,3-selenadiazole compounds preparation: A General procedure

Semicarbazones (10 mmol) was dissolving in glacial CH_3CO_2H (45 mL) with strong stirring and moderate heating to 45-50 ºC. The resulting mixture was treated with SeO_2 powder (10 mmol) and the solution was stirring vigorously. The color of the solution converts red after ca. 5 minutes. Checking of the reaction by thin layer chromatography (TLC) indicated that the reaction was complete after 4 hours. The resulting solution was filtered then the filtrates spilled into ice water and extracted with chloroform (3×50 mL). The collective organic layers have been washed with saturated $NaHCO_3$ solution and then dried by using anhydrous $MgSO_4$ and the chloroform solvent has been removed under vacuum to give the 1,2,3-selenadiazole compounds[9].

1.3. Antibacterial Assay

The Selenadiazole compounds were dissolved in dimethyl sulfoxide (DMSO) at concentration of 50mg/ml. Antibacterial activity of Selenadiazole compounds was confirmed by the method of agar disc-diffusion in the department of biology, college of science, university of Basrah . Sterile filter paper discs (6 mm diameter) moistened with the test prepared molecules solution in DMSO of exact conc. 50mg/disc were carefully located on the agar culture plates that had been already inoculated separately with the micro-organisms. The plates were incubated at 37 degree and the diameter of the growing inhibition zones were determined after one day [20].

1.4. α, α-diphenyl-β-picrylhydrazyl free radical scavenging assay

The α, α-diphenyl-β-picrylhydrazyl free radical scavenging activity of the Selenadiazole derivatives were calculated by using the method reported previously with some modification[21]. 1 mL aliquot of each samples at 5, 10, 15, 20 and 25 mg/mL was mixed with 1 mL of 0.1 mM α, α-diphenyl-β-picrylhydrazyl in CH_3OH. The mixture was agitated strongly for one min, and left to stand in the dark for one hour at room temperature. The absorbance magnitudes was collected at 517 nm. Ascorbic and butylated hydroxytoluene acids have been used as reference control. All measurements have been bone triplicate. The free radical scavenging activity of samples, was expressed as percentage inhibition of DPPH using the following equation:

$$\%Scavenging = \frac{\text{OD of control} - \text{OD of test sample}}{\text{OD of control}} \times 100 \quad \text{....1}$$

1.5. Anti-breast cancer activity (MTT assay)

Assay is depended on 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide MTT)MTT(the transformation of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide to formazan crystals by living cells, which is determined the activity of mitochondrial. The increasing or decreasing in the viable cells amount can be identified by calculating the formazan conc. reflected in the optical density by using a plate reader at 540 and 720

nanometer. This method was generally used to calculate the *in vitro* cytotoxic properties of drugs on the cell lines or main patient cells[21].

2. Results and discussion

The first step of 1,2,3-selenadiazole preparation was included converted of a variety ketones containing α-methyl groups into their corresponding semicarbazones by the reaction with semicarbazide hydrochloride. The resulting semicarbazones molecules were reacted with selenium dioxide reagent to give 1,2,3-selenadiazole compounds through the oxidative ring closure reaction as shown in scheme 1.

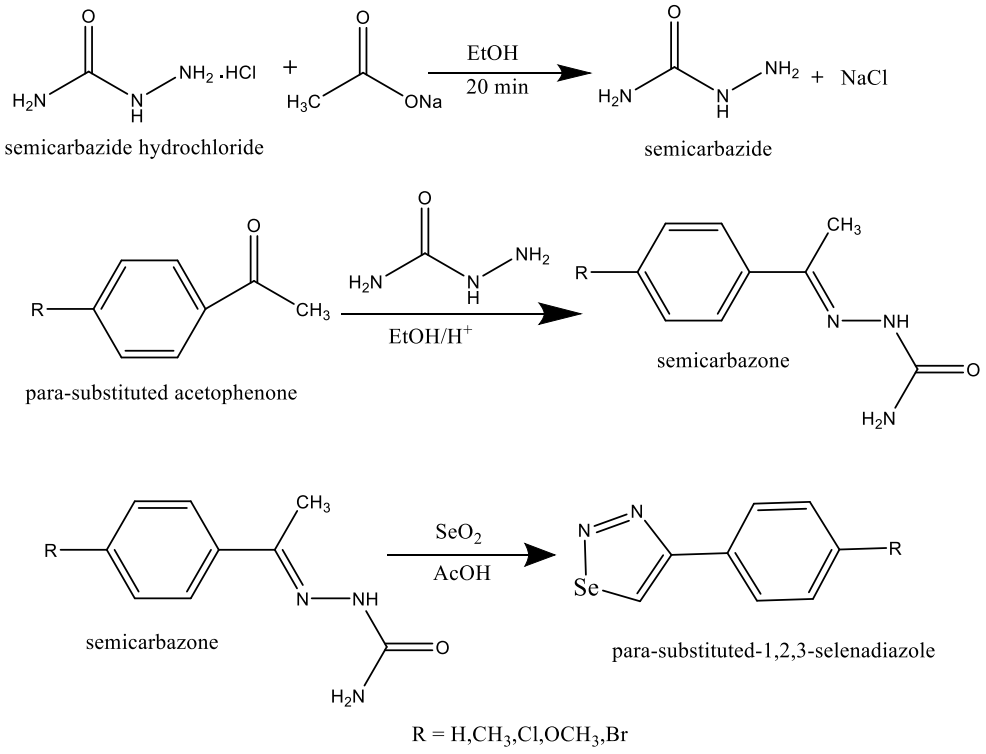


Figure 1: Scheme of general equations of 1,2,3-selenadiazole preparation

Table 1 presents the structures of the prepared semicarbazone compounds, melting point ranges and the percentage yields of the prepared semicarbazone. As shown in this table, the semicarbazone have sharp melting point and they are compatible with the literature. [22,23]

The infrared spectra of the semicarbazones compounds showed new strong band located at 1562-1582 cm^{-1} related to imine group. The carbonyl group showed strong band located at 1697-1743 cm^{-1}. Furthermore, the amide group indicated peaks located at 3433-3221 cm^{-1}. Figure 2 shown the IR spectra of acetophenone semicarbazone as example.

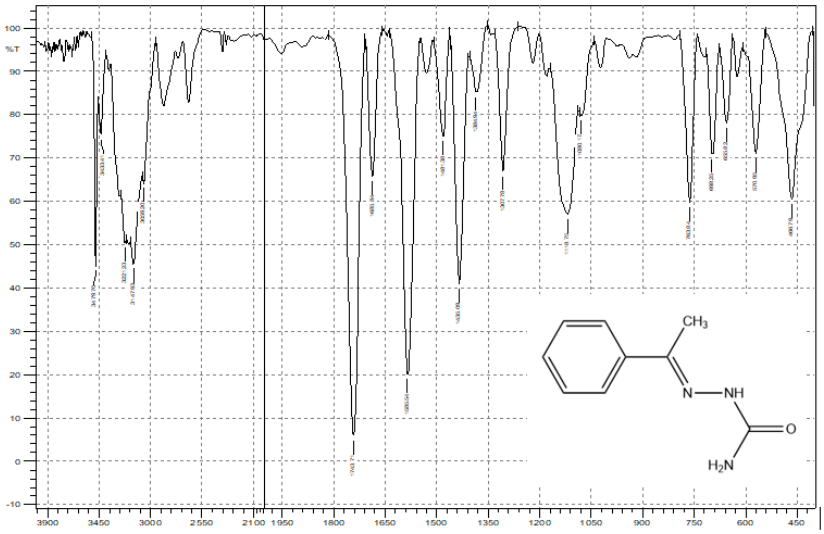


Figure 2: IR spectrum of acetophenone semicarbazone

Table 1 shown the structures of the prepared 1,2,3-selenadiazole derivatives, physical data of the products. As shown in this table, the 1,2,3-selenadiazole derivatives have sharp melting point and they are compatible with the literature [24-26]. The infrared spectra of the 1,2,3-selenadiazole derivatives indicated disappear the peaks of amids , imine and carbonyls. New peaks related to C-Se and N=N bonds have been appeared located at 509-528 cm^{-1} and 1504-1585 cm^{-1} respectively. Figure 3 shown the IR spectra of 4-phenyl-[1,2,3]-selenadiazole as example.

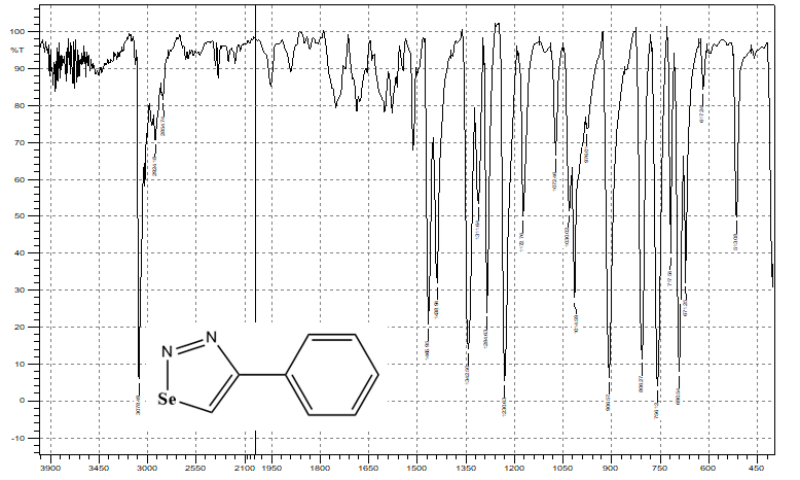
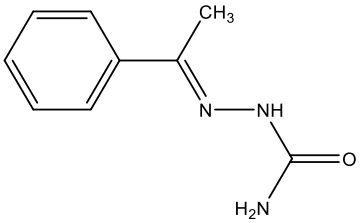
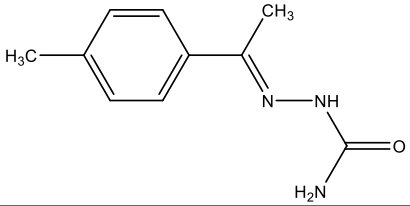
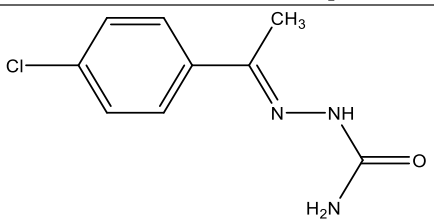


Figure 3. IR spectrum of 4-phenyl-[1,2,3]-selenadiazole

Antibacterial testing the Selenadiazole compounds were investigate to detect the antibacterial activity at conc. 50 mg/ml. The antibacterial activities were tested against Escherichia coli (Gram-negative bacteria) and Staphylococcus aureus (Gram-positive bacteria) on nutrient agar plates at 37 degree for a day by using (chloramphenicol,10 mg/ml) as reference agent.

Table 1: Structure and the physical data of the prepared semicarbazone

Name	Structure	Melting point	Yield
Acetophenone semicarbazone		203-205°C	%74
4-Methyl-acetophenone semicarbazone		207°C	%65
4-chloro- acetophenone semicarbazone		202-204°C	%67

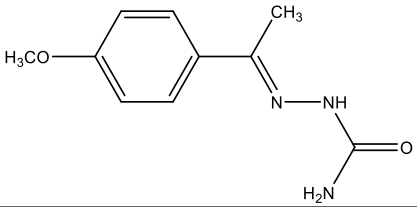
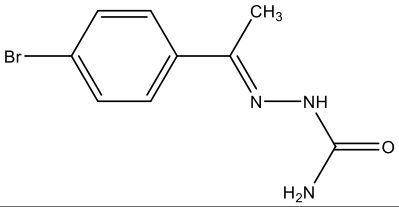
4-methoxy- acetophenone semicarbazone		195-197℃	%45
4-bromo- acetophenone semicarbazone		213-215℃	%82

Table 2: Structure and the and the physical data of the prepared 1,2,3-selenadiazole

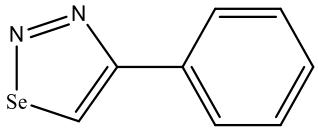
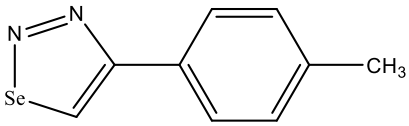
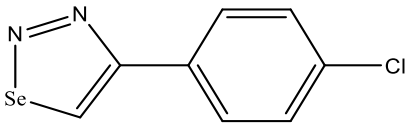
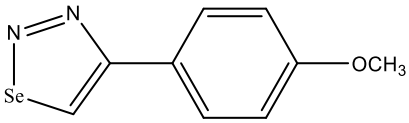
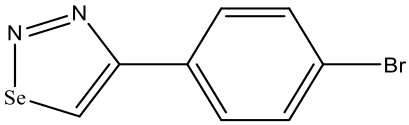
Name	Structure	Melting point	Yield
4-phenyl-[1,2,3]-selenadiazole **D1**		75-76℃	68%
4-(4-Methyl-phenyl)-[1,2,3]-selenadiazole **D2**		88-89℃	33%
4-(4-chloro-phenyl)-[1,2,3]-selenadiazole **D3**		131-132℃	65%
4-(4-methoxy-phenyl)-[1,2,3]-selenadiazole **D4**		101℃	69%
4-(4-bromo-phenyl)-[1,2,3]-selenadiazole **D5**		137-139℃	44%

Table 3. Antibacterial Activity of Selenadiazole compounds

Compound	Concentration (mg/ml)	Zone of inhibition (mm)	
		Staphylococcus aureus	Escherichia coli
C	-	0	0
S	10	40	40
D1	50	18	0
D2	50	12	0
D5	50	21	0

C; control(DMSO solvent), S; standard(Chloramphenical),D1; 4-phenyl-[1,2,3]-selenadiazole , D2; 4-(4-Methyl-phenyl)-[1,2,3]-selenadiazole , D5; 4-(4-bromo-phenyl)-[1,2,3]-selenadiazole.

The data of the Selenadiazole molecules of initial anti-bacterial testing are given in Table 3. The data indicated that, in overall, the inhibitory activities against the Gram-negative bacteria was less than that of Gram-positive bacteria. Compound D5 showed greater activity than the compound D1 and then D2 [27-29].

Table 4. α, α-diphenyl-β-picrylhydrazyl radical scavenging rate of the Selenadiazole molecules

Concentration (mg/ml)	*DPPH radical scavenging rate (%)*				
	BHT	AAC	D1	D2	D5
25	93.95 %	93.95 %	89.59%	70.13%	59.73 %
20	92.95 %	89.26 %	82.55%	48.99%	40.60 %
15	87.58 %	75.80 %	62.08%	17.78%	23.48 %
10	83.55 %	74.80 %	60.40%	22.81%	18.45 %

5	81.87 %	64.09 %	54.69%	16.10%	14.42 %

DPPH; 1,1-diphenyl-2-picrylhydrazyl, BHT; Butylated hydroxytoluene, AAC; Ascorbic acid; D1; 4-phenyl-[1,2,3]-selenadiazole, D2; 4-(4-Methyl-phenyl)-[1,2,3]-selenadiazole , D5; 4-(4-bromo-phenyl)-[1,2,3]-selenadiazole.

The Selenadiazole compounds were tested for antioxidant property by 1,1-diphenyl-2-picrylhydrazyl (DPPH) methods [21]. The nitrogen centered stable free radical α, α-diphenyl-β-picrylhydrazyl is used to describe antioxidants properties. It is reversibly decreased and the odd electron in the α, α-diphenyl-β-picrylhydrazyl free radical offers a robust absorption λ max. at 517 nm, which is have purple color. This possession makes it appropriate for spectro-photometric studies. The α, α-diphenyl-β-picrylhydrazyl stable free radical reacts with radical scavenging antioxidant and gives 1,1-diphenyl-2-picrylhydrazine. The de-colorization production is stoichiometric respecting to the captured electrons number . The antioxidant has been determined according to the change of absorbance produced of the reaction [30].

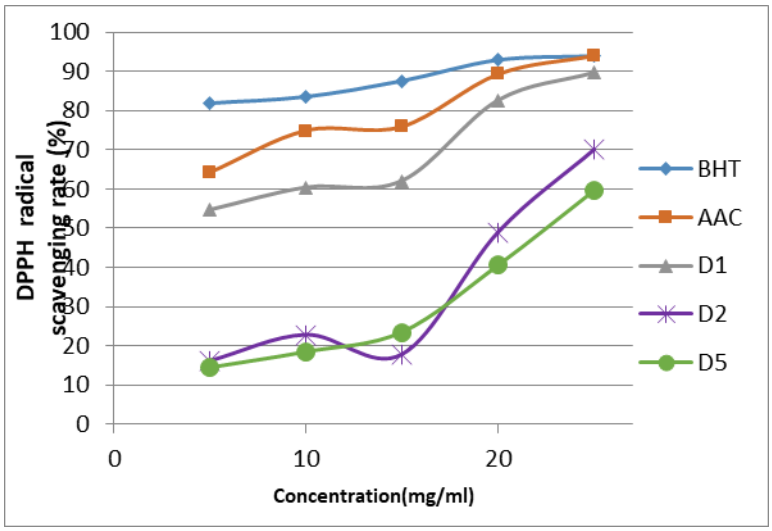


Figure 4: α, α-diphenyl-β-picrylhydrazyl free radical scavenging rate of the Selenadiazole molecules at different conc. Ascorbic and Butylated hydroxytoluene acids were used as reference control.

Carcinogenesis can be caused by free radicals both endogenous and exogenous, atherosclerosis through the interaction with cellular biological molecules , aging, and inflammation [31]. The Selenadiazole compounds exhibited high DPPH radical scavenging rate

compared with reference control of ascorbic and butylated hydroxytoluene (BHT) acids (ACC)[32]. Their does-effect relationship was shown in Table 4. and Figure 4.

Table 5 The cytotoxic effects of D3 compound in three concentrations against cell lines (MCF-7) (cell from breast cancer) was evaluated by using MTT assay

Conc.	5µg/ml	100µg/ml	125µg/ml	IC_{50}
%Inhibition of D3	42%	74%	76%	89.5µg/ml

Table 6. The cytotoxic effects of D4 compound in three concentrations against cell lines (MCF-7) (cell from breast cancer) was evaluated by using MTT assay

Conc.	5µg/ml	50µg/ml	100µg/ml	IC_{50}
%Inhibition of D4	15%	74.4%	81.7%	44.3µg/ml

The effects of cytotoxic for the synthesized molecules against cell lines (cell from breast cancer) (MCF-7) was investigated by using MTT assay. The cytotoxic actions of the investigated molecules were presented as IC_{50} µg/ml, which is the dose that decrease survival to 50% as shown in Table (5) and (6). When treated with D_3 the concentration that inhibits cancer cells to 50%(IC_{50}) of the compound is 89.5 µg/ml , while it was found that the concentration that inhibits cancer cells to 50% (IC_{50}) of compound D_4 is 44.3 µg/ml . The cells were imaged under a microscope after being stained with acridine orange-ethidium bromide for D_3 and D_4 molecules, it was found that the control group of cells maintained their original shape. While compound D_3 and D_4 show good activity to inhibit the proliferation of cancer cells. Some properties of apoptosis were observed such as , membrane separation, loss of contact with adjacent cells, and decrease in the number of cells. This indicates that the $D_3$and D_4 compounds have the potential to induced apoptosis and inhibit the cancer cell proliferation.

3. Conclusions

The antibacterial activity of 1,2,3-selenadiazole molecules was investigated against the growth of two types of bacterial strains (E.coli and staphylococcus aureus). They indicated a good activity against this type of bacterial strains. Furthermore, the studied compounds shown a good activity to reduce the free radical's effects. Inhibition of 1,2,3-selenadiazole derivatives was carried out against human breast cancer cells (MCF-7) growth by MTT , the measurements indicated that the derivatives had a higher inhibition rate than the complexes , the IC_{50} of compound D_3 and D_4 was(89.5 and 44.3) µg/ ml respectively.

References

[1] W. Wang, L. Li, S. Liu, C. Ma, S. Zhang, *Determination of Physiological Thiols by Electrochemical Detection with Piazselenole and Its Application in Rat Breast Cancer Cells 4T-1*. J. Am. Chem. Soc., 130 (2008)10846-10847

[2] V. Nascimento, E. Alberto, D. Tondo, D. Dambrowski, M. Detty, F. Nome, A. *Braga, GPx-Like Activity of Selenides and Selenoxides: Experimental Evidence for the Involvement of Hydroxy Perhydroxy Selenane as the Active Species*. J. Am. Chem.Soc. 134 (2012)138-141.

[3] D. Stoyanovsky, J. Jiang, M. Murphy, M. Epperly, X. Zhang, S. Li, J. Greenberger, V. Kagan, H. Bayir, *Design and Synthesis of a Mitochondria-Targeted Mimic of Glutathione Peroxidase, MitoEbselen-2, as a Radiation Mitigator*. ACS Med. Chem. Lett. 5 (2014) 1304-1307.

[4] J. Yan, Y. Guo, Y. Wang, F. Mao, L. Huang, X. Li. Design, *synthesis, and biological evaluation of benzoselenazole stilbene hybrids as multi-target-directed anti-cancer agents*. Eur. J. Med. Chem. 95 (2015) 220-229.

[5] A. Kremer, A. Fermi, N. Biot, J. Wouters, D. Bonifazi, *Supramolecular Wiring of Benzo-1,3-chalcogenazoles through Programmed Chalcogen Bonding Interactions.* Chem. Eur. J .22 (2016)5665-5675.

[6] G. S. M. Sundaram, D. Dhavale, J. Prior, P. Yan, J. Cirrito, N. Rath, R. Laforest, N. Cairns, J. Lee, P. Kotzbauer, V. Sharma, *Fluselenamyl: A Novel Benzoselenazole DeriVative For PET Detection of Amyloid Plaques (Aβ) in Alzheimer's Disease*. Sci. Rep-Uk. 53 (2016)554-561.

[7] F. Bailly, N. Azaroual, and J.-L. Bernier, *Design, synthesis and glutathione peroxidase-like properties of ovothiol-derived diselenides*. Bioorgan. Med. Chem. 11(2003)4623-4630.

[8] S.M.Anema, S. W. Walker, A. F. Howie, J. R. Arthur, F. Nicol, G. J. Beckett, *Thioredoxin reductase is the major selenoprotein expressed in human umbilical-vein endothelial cells and is regulated by protein kinase C*. Bioch. J. 342(1999)111-117.

[9] J.C. Davey, K. B. Becker, M. J. Schneider, St. D. L. Germain, V. A. Gaton, *Cloning of a cDNA for the type II iodothyronine deiodinase*. J. Biol. Chem. 270(1995)26786-26789.

[10] W. Croteau, S. L. Whittemore, M. J. Schneider, D. L. St. Germain, *Cloning and expression of a cDNA for a mammalian type III iodothyronine deiodinase*. Journal of Biological Chemistry, 270(1995)16569-16575.

[11] P. R . Larsen and M. J. Berry, *Nutritional and hormonal regulation of thyroid hormone deiodinases.* Ann. rev. nut. 15(1995)323-325.

[12] J. Młochowski, R. Lisiak, and S. Selvita, *Developments in the Chemistry of Selenaheterocyclic Compounds of Practical Importance in Synthesis*. Arkivoc, 6(2007)14-46.

[13] W .Hassana, C. S. Oliveira , H. Noreen , J. P. Kamdem, C. W. Nogueira, J. B.T. Rocha, *Organoselenium Compounds as Potential Neuroprotective Therapeutic Agents*. Curr. Org. Chem. 20(2016) 218-231.

[14] L. S. Galant, J. Rafique, A. L. Braga, F. C. Braga, S. Saba, R. Radi, J. Batista T. Rocha, C. Santi, M. Monsalve, M. Farina, A. F. de Bem, *The Thiol-Modifier Effects of Organoselenium Compounds and Their Cytoprotective Actions in Neuronal Cells*, Neurochem Res (2020) 120-130.

[15] A.R. Katritzky, C. A. Ramsden E. F. Scriven R. Taylor, *Comprehensive heterocyclic chemistry III*. Els. Amst., 4(2008)517-550.

[16] I. Lalezari, A. Shafiee, and S. Yazdany, *Selenium heterocycles X: Synthesis and antibacterial activity of pyridyl-1, 2, 3-thiadiazoles and pyridyl-1, 2, 3-selenadiazoles.* J. pharm. sci. 63(1974)628-629.

[17] T. Chen, Y. S. Wong, W. Zheng, J. Liu, *Caspase-and p53-dependent apoptosis in breast carcinoma cells induced by a synthetic selenadiazole derivative*. Chem.-biol. interact. 180(2009)54-60.

[18] R. Sinha and K. El-Bayoumy, *Apoptosis is a critical cellular event in cancer chemoprevention and chemotherapy by selenium compounds*. Curr. cancer drug tar. 4(2004)13-28.

[19] D. Kang, J. Lee, C. Wu, X. Guo, B. Jae Lee, J. Chun, J.Kim. *The role of selenium metabolism and selenoproteins in cartilage homeostasis and arthropathies*. Exp Mol Med 52 (2020) 1198–1208.

[20] M. P.Rayman, *Selenium and human health*. Lancet 379(2012)1256–1268

[21] K. El-Bayoumy and R. Sinha, *Mechanisms of mammary cancer chemoprevention by organoselenium compounds*. Mutat Res-Fund Mol M 551(2004):181-197.

[22] N. Joshi, B. Karale, and C. Gill, *Synthesis of some thiadiazoles, selenadiazoles and spiroheterocyclic compounds from their 2, 2-dimethyl-benzopyran precursors*. Chem. Hetero. Comp. 42(2006)681-685.

[23] B. Bhat, K. Dhar, S. Puri, A. Saxena, M. Shanmugavel, G. Qazi, *Synthesis and biological evaluation of chalcones and their derived pyrazoles as potential cytotoxic agents*. Bioorg. Med. Chem. lett. 15(2005)3177-3180.

[24] S.M.S. Atta, D.S. Farrag, A.M. Sweed, A. Abdel-Rahman, *Preparation of new polycyclic compounds derived from benzofurans and furochromones. An approach to novel 1, 2, 3-thia-, and selena-diazolofurochromones of anticipated antitumor activities*. Eur. J. Med. chem. 45(2010)4920-4927.

[25] A. Abdel-Rahman, M. Hammouda, and S. El-Desoky, *Synthesis of some new azole, azepine, pyridine, and pyrimidine derivatives using 6-hydroxy-4H-4-oxo [1]-benzopyran-3-carboxaldehyde as a versatile starting material*. Heteroatom Chemistry: Int. J. Main Group Elem., 16(2005)20-27.

[26] A. El-Shafei, A. Fadda, A. Khalil, T. Ameen, F. A. Badria, *Synthesis, antitumor evaluation, molecular modeling and quantitative structure–activity relationship (QSAR) of some novel arylazopyrazolodiazine and triazine analogs*. Bioorg. Med. Chem. 17(2009)5096-5105.

[27] S. El-Desoky, F. Badria, M. Abozeid, E. Kandeel, A. Abdel-Rahman, *Synthesis and antitumor studies of novel benzopyrano-1, 2, 3-selenadiazole and spiro [benzopyrano]-1, 3, 4-thiadiazoline derivatives*. Med. Chem. Res. 22(2013)2105-2114.

[28] K.P. Gandhi, A.S.a.R.M.L., *Antibacterial Activity of Two Medicinal Plants - Psidium guajava L. and Spinacia oleracea L*. Advan. Biot. 12(2012)1-2.

[29] B. Mahdavi, W. A. Yaacob, L.B. Din, L.Y. Heng, N. Ibrahim, *Chemical Composition, Antioxidant, and Antibacterial Activities of Essential Oils from Etlingera brevilabrum Valeton*. Rec. of Nat. Prod. 10(2016) 22-31.

[30] J. Bhomia, J. Sharma, R. Lakhne, R. Sharma, R. Gupta, R.A. Sharma, Y. Singh, *Syntheses, silylation, characterization, and antimicrobial and antifertility activities of organoboron derivatives of some bioactive monofunctional bidentate semicarbazones*. Appl. Organomet. Chem. 32(2018) 76-83.

[31] S.U. Qazi, S.U. Rahman, A.N. Awan, M. Al-Rashida, R.D. Alharthy, A. Asari, A. Hameed, J. Iqbal, *Semicarbazone derivatives as urease inhibitors: Synthesis, biological evaluation, molecular docking studies and in-silico ADME evaluation*. Bioorg. chem. 79(2018)19-26.

[32] F. Hayat, A. Salahuddin, J. Zargan, A. Azam, *Synthesis, characterization, antiamoebic activity and cytotoxicity of novel 2-(quinolin-8-yloxy) acetohydrazones and their cyclized*

products (1, 2, 3-thiadiazole and 1, 2, 3-selenadiazole derivatives). Eur. J. Med. chem. 45(2010)6127-6134.

[33] N. O'Connor, N. Sachinvala, and I. Ganjian, *Preparation of 2-Arylethynylselanylacetonitriles from 4-Aryl-1, 2, 3-selenadiazoles*. J. Hetero. Chem. 52(2015)1167-1169.

[34] A. Kumar, M.K. Muthyala, S. Choudhary, R.K. Tiwari, K. Parang, *Ionic liquid as soluble support for synthesis of 1, 2, 3-thiadiazoles and 1, 2, 3-selenadiazoles*. J. Org. Chem. 77(2012)9391-9396.

[35] A.A. Jadhav, V.P. Dhanwe, P.G. Joshi, P.K. Khanna, *Solventless synthesis of new 4, 5-disubstituted 1, 2, 3-selenadiazole derivatives and their antimicrobial studies*. Cog. Chem. 2(2016)2-12.

[36] A.Z. Al-Rubaie, S.A. Al-Jadaan, S.K. Muslim, E.A. Saeed, E.T. Ali, A.K. Al-Hasani, H.N. Al-Salman, S.A. Al-Fadal, *Synthesis, characterization and antibacterial activity of some new ferrocenyl selenazoles and 3, 5-diferrocenyl-1, 2, 4-selenadiazole*. J. Organomet. Chem. 774(2014)43-47.

[37] K.Z. Łączkowski, A. Biernasiuk, A. Baranowska-Łączkowska, S. Zielińska, K. Sałat, A. Furgała, K. Misiura, A. Malm, *Synthesis, antimicrobial and anticonvulsant screening of small library of tetrahydro-2 H-thiopyran-4-yl based thiazoles and selenazoles*. J. Enzy. Inhib. Med. Chem. 31(2016)24-39.

[38] T. Mathangiand and P. Prabhakaran, *DPPH free radical scavenging activity of the extracts of the aquatic fern Marsilea quadrifolia Linn.* Inter. J. Curr. Microb. Appl. Sci. 2(2013)534-536.

[39] M.S. Rufino, F.A. Fernandes, R.E. Alves, E.S. de Brito, Free radical-scavenging behaviour of some north-east Brazilian fruits in a DPPH system. Food Chem. 114(2009)693-695

[40] N.Z. Alias, N.L. Hassan, Z. Yusoff, S. Hasan, W.Y.W Ahmad, Synthesis, Characterization and Antioxidant Activity of 3-(2-Amino-1, 3-Selenazol-4-yl)-2H-Chromen-2-Ones Derivatives. Sains Malays. 47(2018)347-352.

دراسة النشاط البيولوجي لمشتقات البارا-1,2,3-سيلينادايازول كمضادات للاكسدة ومضادات لسرطان الثدي

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المستخلص

في الدراسة الحالية ، تم تصنيع وتشخيص خمسة مركبات 1,2,3- سيلينادايازول. تم تحضيرهذه المركبات عن طريق تفاعل ثاني أكسيد السيلينيوم مع سلسلة من مشتقات السيميكابازون في حامض الخليك الثلجي. تم تشخيص المركبات المحضرة بطرق مختلفة. تم فحص النشاط البيولوجي لمركبات 1،2،3-سيلينادايازول مقابل نمو نوعين من السلالات البكتيرية (E.coli و Staphylococcus aureus كما تضمنت هذه الدراسة تحديد نشاط مشتقات 1،2،3-سيلينادايازول كمضادات للأكسدة. ، وقياس قدرتها على إزالة الجذور الحرة α، .α-diphenyl-β-picrylhydrazyl . لقد وجد أن لها نشاطًا جيدًا لتقليل آثار الجذور الحرة. تم إجراء تثبيط لمشتقات 1،2،3-سيلينادايازول ضد نمو خلايا سرطان الثدي البشرية (MCF- 7) بواسطة MTT ، وأظهرت القياسات أن المشتقات لديها معدل تثبيط أعلى من المعقدات ، كان IC50 للمركب D3 و D4 هو 44.3 و 89.5 ميكروغرام / مل على التوالي.