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SYNTHETIC APPROACHES FOR SELENOARYLAMIDE COMPOUNDS AND THEIR ANTITUMOR EVALUATION

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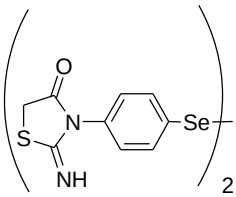
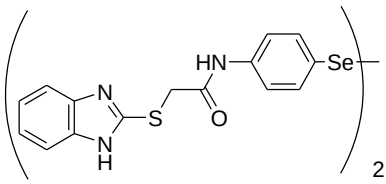
ABSTRACT

A series of selenoarylamide derivatives were synthesized through reaction of either mono or diselenoarylamine **1** and **2** with various acetyl moieties. Furthermore, the chloroacetamidoselane dimer **7** was subjected to react with different nucleophiles to furnish the corresponding derivatives **11**, **12** and **14**. The structures of these new compounds were established by spectral and elemental analyses. All of the newly synthesized compounds were evaluated as antitumor (cytotoxic) agents. Most of these compounds have shown significant antitumor activities.

Keywords: Amide derivatives, Organoselenium / Selenocyanate / Diselenides / Antitumor activity (in vitro).

GRAPHICAL ABSTRACT





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1. INTRODUCTION

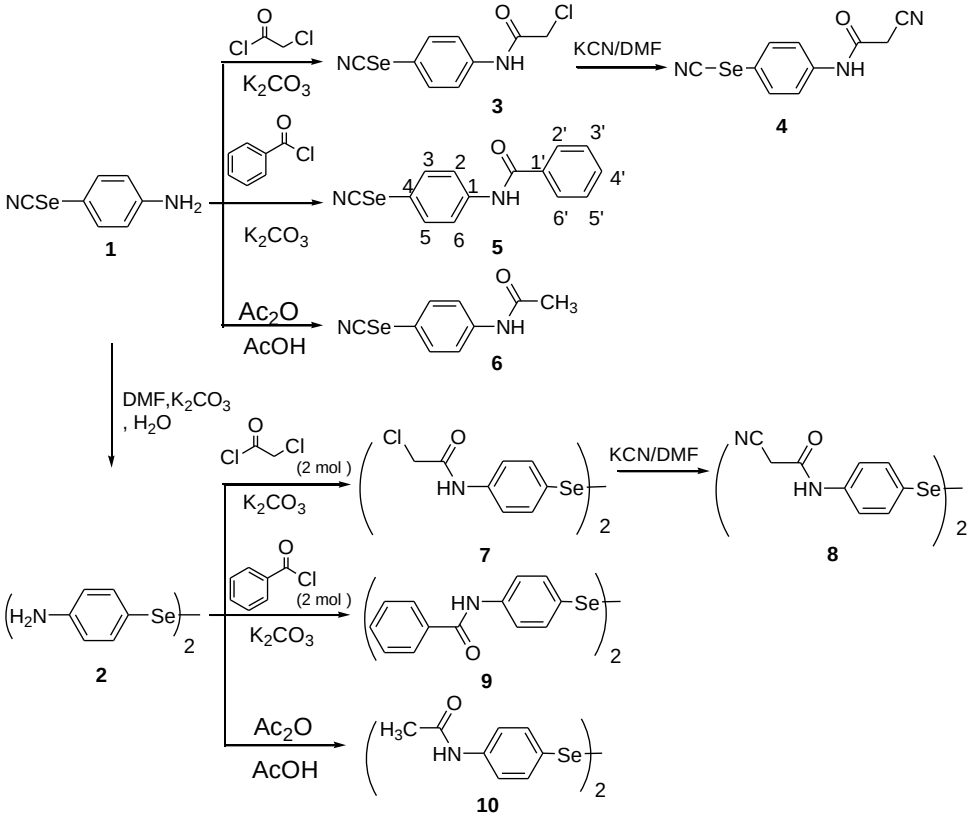
The first report on synthesis of an organoselenium compound, diethyl selenide, was in 1836 **(Löwig & Pogg, 1836)**. The interest in the use of organoselenium compounds, among them those having different selenium-containing heterocyclic systems, as potential pharmaceuticals, new materials as well as reagents and catalysts has expanded rapidly during the last three decades and lot of works concerned in this field have been published. Over the last years, selenium-containing compounds have been proven to be promising antioxidants, enzyme mimics and inhibitors, immunomodulators, cytoprotectors, antitumor, anti-inflammatory, antihypertensive and antiinfectious agents **(Mugesh, et al., 2001)**. Recently, considerable interest has been directed towards the antiviral properties of organoselenium compounds and in consequence some highly active benzisoselenazol-3(2H)-ones and diselenides have been successfully developed **(Pietka-Ottlik, et al., 2010)**.

Amide derivatives were associated with a broad spectrum of biological activities including antituberculosis **(Hegab, et al., 2007)**, anticonvulsant **(Siddiqui, et al., 2008)**, analgesic anti-inflammatory **Mehta, et al., 2010)**, insecticidal **(Graybill, et al., 1992)**, antioxidant **(Jitareanu, et al., 2013)**, and antitumor properties **(Hamama, et al., 2013 and Gouda, et al., 2012)**. Morpholine derivatives find their wide spectrum of antimicrobial activity and exhibit anthelmintic, bactericidal and insecticidal activity **(Naik & Chikhalia, 2007)**. They are also involved as an intermediate product in the synthesis of therapeutic agents. Amide derivatives also show anti-platelet activity **(Rehse, et al., 2009)**.When amides are conjugates with other aliphatic, aromatic and heterocyclic ring produces various types of biological activity. A number of aromatic and heterocyclic acid amides have been synthesized in search for new antagonists of excitatory amino acids receptors with anticonvulsant activity. Generally, benzylamides were found to be more active than other amides **(Kushwaha, et al., 2011)**.

The present work deals with synthesis of novel simple selenoarylamide with biological interest and also represents some of the salient aspect of the application of organoselenium compounds in particular.

2. RESULTS AND DISCUSSIONS
2.1. CHEMISTRY

The starting material, 4-aminophenylselenocyanate **(1)** was prepared according to literature **(Kachanov, et al., 2004)**, have a bifunctional reactive sites, the free amino and a selenocyanate groups. Under neutral or acidic conditions, compound **1** would be reacting only as a primary aromatic amine while selenocyante group is unreactive. Also, diselenide **2** was prepared with modification of the reported procedure **(Plano, et al., 2011)** as shown in (Scheme 1). reacts as aromatic amine only because the selane reactive site is hindered through its transformation to diselenide link. Accordingly, the general pathway we employed for the synthesis of amide-linked selane compounds **1-10** were summarized in (Scheme 1).

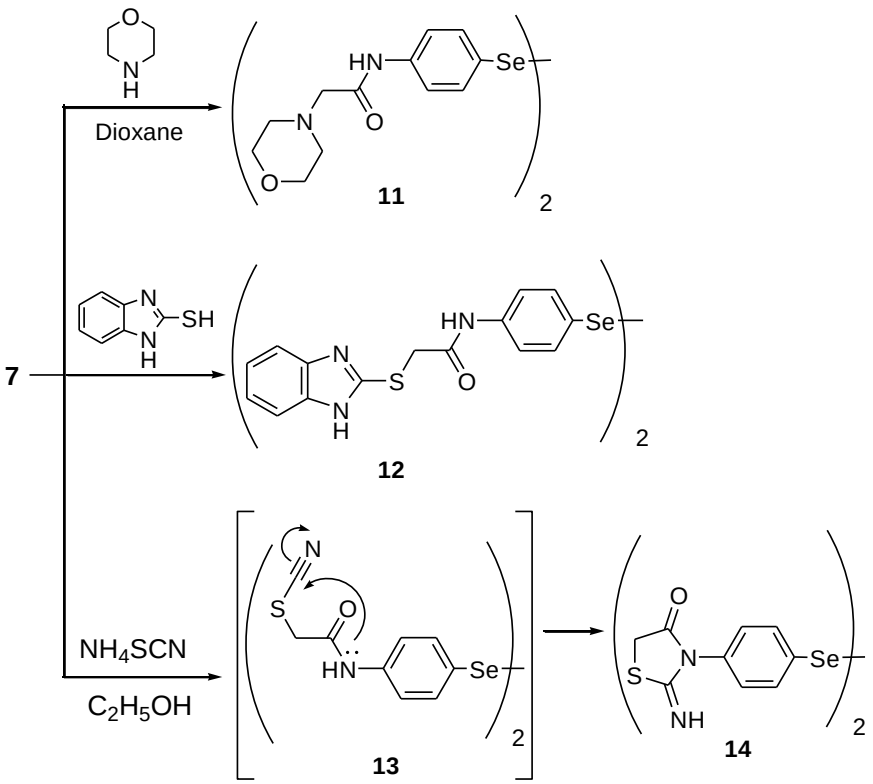


Scheme 1:

α-Chloroacetamides are highly reactive compounds **(Hennessy, E. J. and Buchwald, 2003)**, **(Lakoud, et al., 2012)**, They are extensively utilized as reactants or reaction intermediates. In this context, we synthesized 2-chloro-N-(4-selenocyanatophenyl)acetamide (**3**) and the selane dimer **7** via treatment of 4-Aminophenylselenocyanate **(1)** and diselenide **2**, successively, with chloroacetyl chloride in dry acetone containing anhydrous potassium carbonate. On the other hand, when benzoyl chloride was used instead of chloroacetyl chloride using the same experimental conditions furnished the corresponding benzamides **5** and **9**, respectively. Consequently, the reactivity of compounds **3** and **7** towards replacement of chlorine atom by cyanide group using potassium cyanide in DMF afforded, 2-cyano-N-(4-selenocyanatophenyl)acetamide (**4**) and cyano derivative of the selane dimer **8**. Acetylation of **1** and **2**, sequentially, with acetic anhydride / acetic acid mixture (1:1molar ratio) furnished the corresponding mono and bis actamides **6** and **10**, respectively.

Moreover, the synthetic strategies adopted for the synthesis of the amide containing heterocyclic rings are depicted in Scheme 2. Thus, compound **7** was transformed with secondary amine such as morpholine in dioxane furnished bis-morpholino-N-phenylacetamide derivative **11**. In a similar manner, treatment of **7** with thiole derivative as benzimidazole-2-thione in boiling dioxane afforded a sole product, 3-(1H-benzo[d]imidazol-2-ylthio)-N-(4-(2-(4-(2-(1H-benzo[d]imidazol-2-ylthio) acetamido) phenyl) diselanyl) phenyl) acetamide (**12**) (Scheme 2).

Eventually, the synthetic potentiality of compound **7** was implemented. Thus, treatment of compound **7** with ammonium thiocyanate in ethanol gave the non-isolable intermediate **13**, which was converted in situ to thiazoline derivatives **14**. The structures of the latter products was established on the basis of elemental analysis and spectral data.



Scheme 2:

2.2. BIOLOGICAL ACTIVITY ANTITUMOR INVESTIGATIONS

Effect of drugs on the viability of Ehrlich ascites cells (EAC) in vitro **(Dashora, et al., 2011)**:

Ehrlich ascites cells (EAC) viability assay was used to examine the cytotoxic effect of the newly synthesized compounds as they have a very well-known established model **(Karrer, et al., 1965)**. The desired concentrations of tumor cells (2×106 cells per 0.2 ml) were obtained by dilution with saline (0.9% NaCl). The percentage of viable cells was estimated by the trypan blue **(Sheeja, et al., 1997)** exclusion test. Viability of the cells used in control experiments exceeded 95%. Below this percentage, the cells were discarded and the entire procedure was

repeated. Results for the EC_{100}, EC_{50} and EC_{25} values of the active compounds are summarized in Table 1.

Table (1) : In vitro potential antitumor activity of seleno analogues using EAC assay.

Compound No.	% Deadth		
	100 µg/ml	**50 µg/ml**	**25µg/ml**
5-FU	99.0%	54.7%	29.8%
3	80.4%	40.0%	19.3%
4	87.6%	42.1%	23.6%
5	71.9%	35.6%	17.4%
6	81.7%	39.8%	18.5%
7	65.2%	31.6%	16.1%
8	64.9%	30.0%	15.5%
9	67.6%	34.0%	16.7%
10	67.5%	33.9%	17.0%
11	66.0%	33.3%	16.4%
12	72.2%	36.8%	17.1%
14	62.7%	31.1%	14.8%

The dead % refers to the % of the dead tumor cells. 5-Fluorouracil(5-FU) is well known cytotoxic agent

As shown in table 1 all of the tested compounds showed high to moderate antitumor activity For selenocyanate products **3**-**6** the order of reactivity is **4 > 6 > 3 > 5**. This findings indicate that electron deactivating substituents such as R-CO- (R= CH_2-CN, $ClCH_2$) increase the cytotoxic activity if compared with the analogue **5** where R= C_6H_5. However, for diselenide compounds **7**-**10** the order of reactivity is **9 > 10 > 7 > 8**. Anomalous to our anticipation this results reflect that the diselenides **8**, **10**, **7** and **9** showed less cytotoxic effect than their corresponding mono selenium analogues **4**, **6**, **3** and **5** which illustrate that the presence of two selenium atoms retard their cytotoxic activity. Moreover, the order of reactivity of diselenides **11**, **12**, and **14** which corporate heterocyclic residue is **12 > 11 > 14**. Accordingly, the one with benzoimidazolylthio residue **12** perform higher cytotoxic effect than that contains morpholinyl residue **11**. Finally, the diselenide compound **14**

bearing imidothiazolidinone moiety indicates least cytotoxic response compared to the rest of all diselenide derivatives.

CONCLUSION

Efficient and convenient synthesis of selenoarylamide compounds from easily accessible starting materials such as 4-aminophenyl-selenocyanate is accomplished. Structural elucidations of the newly synthesized compounds are achieved on the basis of elemental analysis and spectral data. Furthermore, all of the new prepared selenoarylamides are subjected to antitumor screening where mono selenium analogues manifested high cytotoxic potencies compared to those of the respective diselenide analogues. However, the rest of the tested compounds exhibit considerable cytotoxic effect.

3. EXPERIMENTAL

All melting points are in degree centigrade (uncorrected) and were determined on Gallenkamp electric melting point apparatus. Elemental analyses were carried out at Micro analytical Center, Faculty of Science, Cairo University. IR spectra were recorded (KBr), (ύ cm^{-1}) on a Mattson 5000 FTIR Spectrophotometer at Micro analytical Center Faculty of Science, Mansoura University. The ^1H NMR Spectra were measured on a Varian Spectrophotometer at 300 MHz, using TMS as an internal reference and DMSO-d_6 or $CDCl_3$ as solvent at Chemistry Department, Faculty of Science, Cairo University. The chemical shifts (δ) are reported in parts per million and where referenced to the residual solvent peak. The ^1H NMR* Spectra were measured on a Varian Spectrophotometer at 500 MHz, using TMS as an internal reference and $CDCl_3$ as solvent at National Research Center, Cairo; MS equipment and/or a Varian MAT 311A Spectrometer, at Microanalytical Center, Faculty of Science, Cairo University. Reaction mixtures were monitored by thin layer chromatography (TLC) using EM science silica gel coated plates with visualization by irradiation with ultraviolet lamp. Biological Testings were carried out at Drug Department, Faculty of Pharmacy, Mansoura University, Mansoura, Egypt. Ehrlich cells (Ehrlich ascites carcinoma, EAC) were derived from ascetic fluid from diseased mice (the cells were purchased from the National Cancer institute, Cairo, Egypt).

Synthesis of selenochloroacetamides 3, 7 and selenobenzamides 5, 9.
General Procedure

To a solution of the corresponding selane derivatives **1** or **2** (1.0 mmol) in dry acetone (15 ml) containing K_2CO_3 (1g), chloroacetyl chloride (1.0 mmol or 2.0 mmol) was added dropwise with stirring at 0-5^0 C. Stirring was continued for 4 h and the reaction mixture was poured into ice cooled water. The resulting precipitate was collected, dried and recrystallized from ethanol to afford the corresponding chloro acetamide derivatives **3** and **7**, consecutively. On the other hand, when benzoyl chloride was used in lieu of chloroacetyl chloride following the aforementioned procedure, furnished the benzamides **5** and **9**, respectively.

2-chloro-N-(4-selenocyanatophenyl)acetamide (3)
Pale yellow crystals; yield 72%; m.p. 190^{o}C (ethanol); R_f = 0.25 [pet. ether (60-80)/ethyl acetate (4:1.5)]; IR (KBr): ν/cm^{-1} = 3265 (NH), 2943 (CH, str.), 2145 (CN), 1680 (C=O amide), 1616(C=C); 1H-NMR* (DMSO-d6) δ (ppm): 4.32 (s, 2H, CH_2), 7.65-7.43 (m, 4H, aromatic-H), 10.72 (br, 1H, NH); MS (EI, 70 ev) *m/z* (%)= 273 (M^+, 44.6), 224(7.7), 119(14.2), 118(100.0, base peak), 105(6.0), 91(4.7), 90(18.6), 78(61.4), 76(23.5), 64(15.1), 63(85.0) , 53(1.0), 49(19.6); Anal. Calcd. for $C_9H_7ClN_2OSe$ (273.58): C, 39.51; H, 2.58 %. Found: C, 39.67; H, 2.76%.

N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-chloroacetamide) (7)
Yellow crystals; yield 79%; m.p. 170^{o}C (EtOH); R_f = 0.15 [pet. ether (60-80)/ethyl acetate (4:1.5)]; IR (KBr): ν/cm^{-1} = 3345 (NH), 2953 (CH,str.), 1664 (C=O amide), 818(Se-Se); 1H-NMR* (DMSO-d6) δ (ppm): 4.22 (s, 4H, $2CH_2$), 7.52-7.48 (m, 8H, aromatic-H), 10.42 (br, 2H, 2NH); MS (EI, 70 ev) *m/z* (%)= 495 (M^+, 19.3), 250(30.8), 248 (57.3), 172(92.7), 170 (6.0), 169 (100.0, base peak), 91(2.2), 90 (44.5), 79 (52.1), 76 (96.7), 64 (24.9), 53 (3.5); Anal. Calcd. for $C_{16}H_{14}Cl_2N_2O_2Se_2$ (495.12): C, 38.81 H, 2.85 %. Found: C, 38.62 H, 2.91 %.

N-(4-selenocyanatophenyl)benzamide (5)
Silver crystals; yield 70%; m.p. 170^{o}C (ethanol); R_f = 0.275 [pet. ether (60-80)/ethyl acetate (4:0.5)]; IR (KBr): ν/cm^{-1} = 3343 (NH), 2154 (CNSe), 1665 (C=O amide); 1H-NMR (DMSO-d6) δ (ppm): 7.54 (m, 3H, aromatic-H_3'+H_4'+H_5'), 7.72 (d, 2H, *J*= *Hz*, aromatic-H_3+H_5), 7.95

(d, 2H, *J= Hz*, aromatic-H_2'+H_6'), 7.98 (d, 2H, *J= Hz*, aromatic-H_2+H_6), 10.44 (br, 1H, NH); MS (EI, 70 ev) *m/z* (%)= 301 (M^+, 5.1), 195(2.8), 105 (100.0, base peak), 91 (8.1), 77(82.7), 76 (7.4), 91(20.3), 64 (5.6), 53 (1.7), 51 (31.8); Anal. Calcd. for $C_{14}H_{10}N_2OSe$ (301.2): C, 55.83 H, 3.35 %. Found: C, 55.72 H, 3.60%.

N,N'-(4,4'-diselanediylbis(4,1-phenylene))dibenzamide (9)
Yellow crystals; yield 88%; m.p. 260^{o}C (ethanol); R_f = 0.42 [pet. ether (60-80)/ethyl acetate (4:2)]; IR (KBr): ν/cm^{-1} = 3330 (NH), 2148 (CNSe), 1668 (C=O amide) , 814 (Se-Se); MS (EI, 70 ev) *m/z* (%)= 552 (M^++2, 9.0), 276(4.9), 181(5.6), 119(4.9), 103(4.2), 79(9.0), 64(20.1), 53(36.1), 51 (100.0, base peak) ; Anal. Calcd. for $C_{26}H_{20}N_2O_2Se_2$ (550.37): C, 56.74; H, 3.66 %. Found: C, 56.51; H, 3.50%.

General Procedure for Preparation of 4 and 8

A mixture of **3** or **7** (2 mmol) and potassium cyanide (3 mmol, 6 mmol) in DMF (15 mL) was heated at 60^{o}C for 3 h. The reaction mixture was left to cool then poured into ice cold water. The formed precipitate was filtered off, dried and recrystallized from (EtOH / DMF) to give **4, 8**, respectively.

2-cyano-N-(4-selenocyanatophenyl)acetamide (4)
Reddish brown crystals; yield 60%; m.p. 170^{o}C (EtOH / DMF); R_f = 0.15 [ethyl acetate]; IR (KBr): ν/cm^{-1} = 3288 (NH), 2153 (CNSe), 2215 (CN), 1729 (C=O amide); 1H-NMR (DMSO-d6) δ (ppm): 4.12 (s, 2H, CH_2), 7.60-7.44 (m, 4H, aromatic-H), 10.02 (br, 1H, NH); MS (EI, 70 ev) *m/z* (%)= 265 (M^+ +1, 0.1), 238(0.1), 181(0.2), 83(1.2), 79(22.8), 77(100.0, base peak), 52(45.1), 50(22.6); Anal. Calcd. for $C_{10}H_7N_3OSe$ (264.14): C, 45.47 H, 2.67 %. Found: C, 45.22; H, 2.55%.

N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-cyanoacetamide) (8)
Brown crystals; yield 69%; m.p. 230^{o}C (EtOH / DMF); R_f = 0.1 [ethyl acetate]; IR (KBr): ν/cm^{-1} = 3295 (NH), 2923 (CH, str.) 2214(CN), 1727 (C=O amide); 1H-NMR (DMSO-d6) δ (ppm): 3.79 (s, 4H, 2CH_2), 7.70-7.21 (m, 8H, aromatic-H), 10.15 (br, 2H, 2NH); MS (EI, 70 ev) *m/z* (%)= 476 (M^+, 0.1), 238(0.6), 92(100.0, base peak), 91(15.0), 79(13.9), 76(6.0), 68(4.1), 64(3.5), 53(4.3); Anal. Calcd. for $C_{18}H_{14}N_4O_2Se_2$ (476.25): C, 45.39; H, 2.96 %. Found: C, 45.12; H, 2.72%.

General Procedure for Preparation of 6 and 10

A mixture of 4-selenocyanatoaniline (**1**) (1.00 mmol), acetic anhydride (0.1 ml) and glacial acetic acid (0.1 ml) was heated in an oil bath at 60 – 65^{o}C for 1 h. The reaction mixture was allowed to cool at room temperature and then recrystallized from ethanol to give **6.** However, replacing the selenocyanate derivative **1** by the diselenide derivative **2** and using (2.00 mmol) equivalents of acetic anhydride and glacial acetic acid in the above procedure afforded **10.**

N-(4-selenocyanatophenyl) acetamide (6)

Pale Yellow crystals; yield 78%; m.p. 210^{o}C (EtOH); R_f = 0.325 [pet. ether (60-80)/ethyl acetate (4:2.5)]; IR (KBr): ν/cm^{-1} = 3246 (NH), 2146 (CNSe), 1673 (C=O amide), 1606(C=C); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.06 (s, 3H, CH_3), 7.71-7.48 (m, 4H, aromatic-H), 10.13 (br, 1H, NH); MS (EI, 70 ev) *m/z* (%) = 239 (M^+, 80.4), 237(43.8), 133 (4.7), 119(22.0), 118 (100.0, base peak), 105 (3.3), 91(20.3), 76 (2.6), 64 (13.5), 53 (1.5); Anal. Calcd. for $C_9H_8N_2OSe$ (239.13): C, 45.20; H, 3.37 %. Found: C, 45.45; H, 3.42%.

N,N'-(4,4'-diselanediylbis(4,1-phenylene))diacetamide (10)

Yellow crystals; yield 75%; m.p. 160^{o}C (EtOH); R_f = 0.05 [pet. ether (60-80)/ethyl acetate (4:2.5)]; IR (KBr): ν/cm^{-1} = 3255 (NH), 1669 (C=O amide), 816 (Se-Se); ^{1}H-NMR (DMSO-d_6) δ (ppm): 2.13 (s, 6H, $2CH_3$), 7.59-7.52 (m, 8H, aromatic-H), 10.21 (br, 2H, 2NH); MS (EI, 70 ev) *m/z* (%) = 426 (M^+, 55.4), 214(32.6), 212 (18.0), 184 (100.0, base peak), 134(2.0), 91 (82.0), 79(86.8), 64 (44.6), 53 (7.3); Anal. Calcd. for $C_{16}H_{16}N_2O_2Se_2$ (426.23): C, 45.09; H, 3.78 %. Found: C, 45.18; H, 3.90%.

Synthesis of N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-morpholinoacetamide) (11)

A mixture of N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-chloro acetamide) (**7**) (0.5 g, 1mmol) with morpholine (0.174 g, 2 mmol) and few drops of triethylamine in dioxane (10 ml) was refluxed for 10 h and the reaction mixture poured into ice cooled water. The resulting precipitate was collected, dried and recrystallized from ethanol.

Yellow crystals; yield 53%; m.p. 130^{o}C (EtOH); R_f = 0.175 [ethyl acetate)]; IR (KBr): ν/cm^{-1} = 3330 (NH), 2970 (CH,str.), 1674 (C=O

amide), 814(Se-Se); 1H-NMR* (DMSO-d6) δ (ppm): 2.60 (m, 16H, $8CH_2$), 3.59 (s, 4H, $2CH_2$),7.51 (d, 4H, *J= 8.5 Hz*, aromatic-H), 7.58 (d, 4H, *J= 8.5 Hz*, aromatic-H), 9.84 (br, 2H, 2NH); MS (EI, 70 ev) *m/z* (%) = 596 (M^+, 0.1), 299(0.4), 298 (0.2), 250(0.4), 198(4.0) 172(32.6), 170(14.2), 143(5.0), 100 (100.0, base peak), 86(2.4),72 (14.4), 70 (32.9), 55 (36.1); Anal. Calcd. for $C_{24}H_{30}N_4O_4Se_2$ (596.44): C, 48.33; H, 5.07 %. Found: C, 48.11 H, 5.14%.

3-(1H-benzo[d]imidazol-2-ylthio)-N-(4-(2-(4-(2-(1H-benzo[d]imidazol-2-ylthio) acetamido) phenyl) diselanyl) phenyl) acetamide (12)

A mixture of N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-chloroacetamide) (**7**) (0.49 g , 1.00 mmol) and 1-H-benzo[d] imidazole-2-thiole (0.2 g, 2.00 mmol) was refluxed for 15 h in dioxane (30 ml) containing 5 drops of triethylamine. The solid product that separated on cooling was filtered off and recrystallized from ethanol.

Yellow crystals; yield 52%; m.p. 130°C (EtOH); R_f = 0.25 [pet. ether (60-80)/ethyl acetate (4:3)]; IR (KBr): ν/cm^{-1} = 3440 (br,2 NH), 3332 (br,2 NH), 2924 (CH,str.), 1670 (C=O amide), 815(Se-Se); 1H-NMR (DMSO-d6) δ (ppm): 4.27 (s, 4H, $2CH_2$), 7.11 (d, 4H, *J= 3 Hz*, aromatic-H), 7.14 (d, 4H, *J= 3 Hz*, aromatic-H) 7.61-7.43(m, 8H, aromatic-H), 10.63 (br, 4H, 4NH); MS (EI, 70 ev) *m/z* (%)= 722 (M^+, 0.1), 215 (100.0, base peak), 190(23.0), 175 (78.1), 150(28.5), 117 (11.2), 92 (66.1), 91 (21.6), 79 (13.22), 76 (18.4); Anal. Calcd. for $C_{30}H_{24}N_6O_2S_2Se_2$ (722.60): C, 49.86 H, 3.35 %. Found: C, 49.61; H, 3.26%.

3,3'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-iminothiazolidin-4-one)(14)

A solution of N,N'-(4,4'-diselanediylbis(4,1-phenylene))bis(2-chloro-acetamide) (**7**) (0.05 mol) and NH_4SCN (0.2 mol) in ethanol (50 ml, 95%) was refluxed for 10 h and allowed to stand overnight. The formed precipitation was filtered off, washed with H_2O, dried and recrystalized from EtOH/ DMF.

Yellow crystals; yield 65%; m.p. 230°C (EtOH / DMF); R_f = 0.375 [pet. ether (60-80)/ethyl acetate (4:3.5)]; IR (KBr): ν/cm^{-1} = 3258 (NH), 2965 (CH,str.), 1678 (C=O amide), 1629(C=N), 820(Se-Se); 1H-NMR* (DMSO-d6) δ (ppm): 3.98 (s, 4H, $2CH_2$), 7.72-7.55 (m, 8H, aromatic-H), 11.26 (br, 1H, NH), 11.80 (br, 1H, NH); MS (EI, 70 ev) *m/z* (%)= 541

(M^++1, 7.9), 540(M^+, 3.4), 336(100.0, base peak), 156(4.5), 155(9.0), 101(11.2), 84(4.5), 65(4.5), 51(9.0); Anal. Calcd. for $C_{18}H_{14}N_4O_2S_2Se_2$ (540.38): C, 40.01; H, 2.61 %. Found: C, 40.13; H, 2.70%.

REFERENCES

Dashora, N.; Sodde, V.; Bhagat, J.; Prabhu, K. S.; Lobo R., antioxidant Activities of Dendrophthoe falcata (L.f.) Etting, Pharm. Crops, **2011**, 2, 1- 7.

Gouda, M. A., Berghot, M. A.; Baz, E. A.; Hamama, W. S., Synthesis, Antitumor and Antioxidant Evaluation of some new thiazole and thiophene derivatives incorporated coumarin moiety, Med. Chem.Res., **2012**, 21, 1062-1070.

Graybill, T. L.; Ross, M. J.; .Gauvin, B. R.; Gregory, J. S., Harris, A. L.; Ator, M. A.; M.Rinker J.; Dolle, R. E., Synthesis and evaluation of azapeptide-derived inhibitors of serine and cysteine proteases, Bioorg. Med.Chem.Lett. **1992**, 2, 1375-1380.

Hamama , W. S.; Gouda, M. A.; Abd El-Wahab, M.H.; Zoorob. H.H., Synthesis, Antioxidant and Antitumor Evaluation of Certain New N-Substituted-2-amino-1,3,4-thiadiazoles, J. Med. Chem. Res., **2013**, 22, 3556-3565.

Hegab, M. I.; Abdel-Fattah, A.-S.M.; Yousef, N.M., Synthesis, X-ray Structure and Pharmacological activity of some-٦,٦disubstituted chromeno [4,3-b] and chromeno-[3,4-c]-quinolines, Archiv. der Pharmazie, Chemistry in Life Sciences, **2007**, 340, 396-399.

Hennessy, E. J.; Buchwald, S. L., Synthesis of Substituted Oxindoles from α-Chloroacetanilides via Palladium-Catalyzed C−H Function-alization, J. Am. Chem. Soc., **2003**, 125, 12084-1285.

Jitareanu, A.; Tataringa, G.; Zbancioc, A-M.; Tuchilus, C.; Balan, M.; Stanescu, U., Cinnamic acid Derivatives and 4-Aminoantipyrine Amides synthesis and evaluation of biological properties, Res. J. Chem. Sci., **2013**, 3, 9-13.

Kachanov, V. A.; Slabko, Y. O.; Baranova, V. O.; Shilova, V. E. and Kaminskii, A.V., Triselenium dicyanide from malononitrile and selenium dioxide. One-pot synthesis of selenocyanates, Tetrahedron lett., **2004**, 45, 4461-4463.

Karrer, K.; Rubini, J. R., On the Fate of Labelled Ehrlich Ascites Cells in Mice, an Autoradiographic Study Using H3 Thymidine Medicina et Pharmacologia Experimentalis, **1965**, 13, 124-130.

Kushwaha, N.; Saini, R. K.; Kushwaha, S. K. S., Synthesis of some Amide derivatives and their Biological activity , Int. J. Chem.Tech. Res., **2011**, 3, 203-209.

Lakoud, S. G.; Berredjem, M.; Aouf, N. E., efficient method for the synthesis of aminophosphonates via the Michaeles-Arbuzov reaction, Phosphorus, Sulfur, Silicon and the Related Elements, **2012**,187, 762-768.

Löwig, C.; Pogg, J. Ann., **1836**, 37, 552.

Mehta, N.; Aggarwal, S.; Thareja, S.; Malla, P.; Misra, M.; Bhardwaj, T. R.; Kumar, M., synthesis, pharmacological and toxicological evaluation of amide derivatives of ibuprofen, Int. J. Chem.Tech. Res., **2010**, 2, 233-238.

Mugesh, G.; du Mont, W.W.; Sies, H., Chemistry of biologically important synthetic organoselenium compounds. Chem. Rev., **2001**, 101, 2125-2179.

Naik, T. A.; Chikhalia, K. H., studies on synthesis of pyrimidine derivatives and their pharmacological evalution, E-J.Chem., **2007**, 4, 60-66.

Pietka-Ottlik, M.; Potaczek, P.; Piasecki, E., Mlochowski, J. Crucial role of selenium in the virucidal activity of benzisoselenazol -3(2H)-one and related diselenides, Molecules, **2010**, 15, 8214-8228.

Plano, D.; Baquedano, Y.; Moreno-Mateos, D.; Font, M., Jiménez-Ruiz, A.; Palop J. A.; Sanmartín C., Selenocyanates and diselenides: A new

class of potent antileishmanial agents, Eur. J. Med. Chem., **2011**, 46, 3315-3323.

Rehse, K.; Kotthaus, J.; Khadembashi, L., New 1H-pyrazole-4-carboxamides with antiplatelet activity, Arch. Pharmazie, Chem. in Life Sci., **2009**, 340, 27-30.

Sheeja, K. R.; Kuttan, G.; Kuttan R., Cytotoxic and antitumour activity of Berberin , Amala Res. Bull., **1997**, 17, 73-76.

Siddiqui, N.; Alam, M. S.; Ahsan, W., Synthesis, anticonvulsant and toxicity evaluation of 2-(1H-indol-3-yl)acetyl-N-(substituted phenyl) hydrazine carbothioamides and their related heterocyclic derivatives, Acta Pharma., **2008**, 58, 445-454.

الملخص العربي

تم في هذا البحث تخليق مركبات جديدة من الأميدات الاروماتية المحتوية علي ذرة سيلينيوم واحدة وأيضا المحتوية علي ذرتين من السلينيوم، وتم ذلك عن طريق تفاعل أمين أروماتى أحادي أو ثنائي سيلينيوم مع هاليدات الأسيل، ومن جانب أخر تم تفاعل ثنائي السيلينيوم ٧ مع النيوكليوفيلات المختلفة ليعطي الأميدات المشتملة علي بعض الانوية غير المتجانسة الحلقة . تم اثبات التراكيب البنائية للمركبات الجديدة من خلال التحاليل العنصرية الدقيقة ومن نتائج الطيف.

كما تم دراسة فاعلية المركبات الجديدة ضد بعض الخلايا السرطانية، وكانت بعضها ايجابية الفاعلية.