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Synthesis and Characterization of New Selenonitrone Derivative and Its Effect on Breast Cancer Cell Line Viability *in Vitro*

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Abstract:

New nitrone and selenonitrone compounds were synthesized. The condensation method between N-(2-hydroxyethyl) hydroxylamine and substituted carbonyl compounds such as [benzil, 4, 4́-dichlorobenzil and 2,2́ -dinitrobenzil] afforded a variety of new nitrone compounds while the condensation between N-benzylhydroxylamine and substituted selenocarbonyl compounds such as [di(4-fluorobenzoyl) diselenide and (4-chlorobenzoyl selenonitrile] obtained selenonitrone compounds. The condensation of N-4-chlorophenylhydroxylamine with dibenzoyl diselenide obtained another type of selenonitrone compounds. The structures of the synthesized compounds were assigned based on spectroscopic data (FT-IR, ^{1}H-NMR, ^{13}C-NMR, MS and elemental analysis. The result spectra and the result of elemental analysis were verified the expected structure. The results of new selenonitron derivative (N_1) effect on the MDA-MB-231 breast cancer cells *in vitro* revealed that is an increase in the proliferation of cells with increased concentrations of selenonitron at all periods of the times.

Key words: Cell viability, MDA-MB-231 breast cancer cell line, Nitrones, Proliferation, Selenocarbonyl, Selenonitrones.

Introduction:

Nitrone has been extensively investigated, because of their utility as versatile synthetic intermediates. Nitrons are very important compounds due to their successful application, they can be used as regulators and modifiers regulators of molecular weight in radical polymerization building blocks (1). The scientists also found that nitrone can be used as building blocks in the synthesis of various natural and biologically active compounds (2).

For the preparation of nitrones, the most popular method is the condensation of aldehydes or ketones with N-monosubstituted hydroxylamines (3). However, this method is difficult to be applied to the preparation of ketonitrones having bulky groups. The synthesis of N-monosubstituted hydroxylamine is being carried out by the reaction of (benzylchloride and 2-hydroxyethylchloride) with hydroxylamine hydrochloride in presence of sodium carbonate (4). Organoselenium compounds have been aimed as targets of interest in organic synthesis.

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Dibenzoyl diselenide [$(PhCOSe)_2$] is an important example of this class showing several pharmacological properties (5-7). The synthesis of dibenzoyl diselenide is being carried out by the alkaline hydrolysis of substituted benzoylselenonitrile (the synthesis of benzoylselenonitrile is being carried out by the reaction between benzoyl chloride and potassium selenonitrile) (8-10). Benzil $(PhCO)_2$ were prepared via the condensation reaction of substituted benzaldehyde. Thus, condensation of various substituted benzil with N-(2-hydroxylethyl) amine makes it possible to synthesize a variety of nitrone compounds (11),while the condensation of various substituted dibenzoyl diselenide and benzoyl selenonitrile with N-benzylhydroxylamine and N-phenylhydroxylamine makes it possible to synthesize a variety of selenonitrone compounds (12,13). The condensation is carried out under mild conditions without affecting functional groups. Nitrones due to their photochemistry reactivity as well as their excellent radical spin-trapping capability leading to their use as antioxidants because of stable nitroxyl radicals. Organoselenium compounds also, such as containing di aryl diselenide group are exhibited significant antimicrobial (14-17), cytotoxic, antidepressant, antileukemic, antibiotic and antiurease activities

(18-20). Selenium is an essential trace element for humans and many other forms of life (21). It is an extremely vital mineral for the human body as it increases immunity (22). Also reducing inflammation and regulating blood pressure (23) . According to Institute of Medicine, Food and Nutrition Board (24) the current recommended daily allowance for selenium is 55 µg/ day for a healthy adult. The toxic levels are estimated to occur with intakes of the order of 350–700 µg/day (25). Deficiency of selenium is associated with several disease conditions such as immune impairment (26). According to Rayman (27) study, consuming plenty of naturally occurring selenium has positive antiviral effects, essential for successful male and female fertility and reproduction, and also reduces the risk of autoimmune and thyroid diseases. Selenium plays a role in cancer prevention and treatment (28).On other hands selenium-induced cell migration and proliferation in some cases (29-30).

The aim of the study is to synthesis five compounds of selenonitrone and studies the effect of less toxic compound (N_1) on viability MDA-MB-231 breast cancer cell line *in vitro*.

Materials and Methods:

All chemicals were obtained from standard commercial sources. The synthesized compounds were prepared according to literature procedures. Carbonyl selenonitrile compounds have been carried out by the reaction of the corresponding benzoyl chloride with potassium selenocyanate. The synthesis of dibenzoyl diselenide is being carried out by the alkaline hydrolysis of substituted carbonylselenonitrile. Substituted benzil compounds were synthesized by the condensation reaction of substituted benzaldehyde. Selenonitrone compounds were synthesized by the condensation of dibenzoyl diselenide and selenonitrile with [N-benzyl hydroxyl amine and N-phenyl hydroxyl amine]. Nitrone compounds were synthesized by the condensation of benzil with N-(2-hydroxyethylhydroxylamine).

Melting points were measured with an Electrothermal IA 9200 apparatus. FT-IR spectra were recorded using a Bruker spectrometer. ^{1}H and ^{13}C NMR spectra were recorded in DMSO and δ units downfield from internal reference Me_4Si. using a 300 MHz Bruker NMR spectrometer. The mass spectra were recorded on a Shimadzu QP GC-MS instrument. Elemental analysis was carried out on a Vario EL III instrument (31-36).

General Procedure for the Preparation of Carbonylselenonitrile (31, 32):

A solution of KCN (0.8gm) in absolute ethanol (50 ml) was added to a solution of selenium metal (1 gm.; 125 mole) in absolute ethanol (15 mL). The reaction mixture was refluxed for 3 h and then a solution of substituted benzoyl chloride (206 ml 0.025 mole) was added and refluxed for 2 h. The precipitate was filtered and then recrystallized from ethanol.

General Procedure for the Preparation of Dibenzoyl diselenide (33):

A solution of carbonylselenonytrile (0.28 gm; 1.02 mole) in absolute ethanol (25 ml) was added to a solution of sodium hydroxide (0.16 gm; 2.47 mole) in absolute ethanol (15 mL). The reaction mixture was stirred at 40 ^{o} C for 50 min and then the mixture was refluxed for 1 h. A solution of substituted benzoyl chloride (206 ml 0.025 mole) was added and refluxed for 2 h. The reaction mixture was cooled to R .T. and filtered. The filtrate was acidified with 10% HCl. A red solid compound was obtained, washed with a small amount of benzene and dried. The precipitate recrystallized from a mixture of methanol and dichloro methane (1:4), gave a red solid compound.

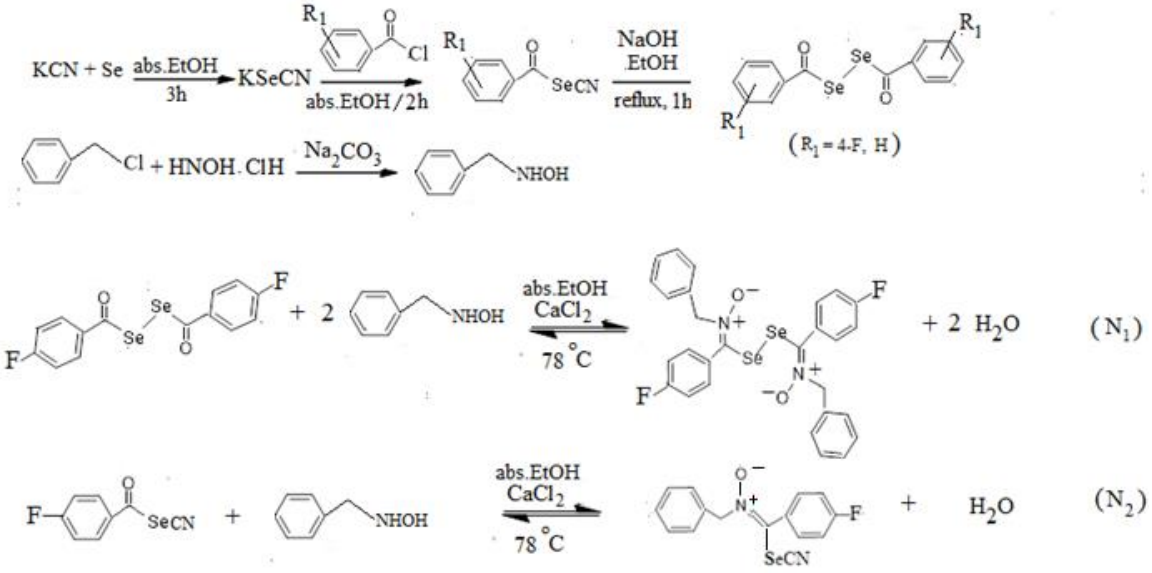
General Procedure of Preparation of Benzil (34):

A solution of KCN (2.0 gm.; 0.036 mol) in H_2O (15 ml) was added to a solution of benzaldehyde (3.7 gm.; 0.03 mole) in ethanol (30 ml). The reaction mixture was refluxed for 0.5 h. The reaction mixture was cooled. A yellow solid compound of benzoin was obtained, washed with (1: 1- water: ethanol) and dried. (14 ml) of conc. nitric acid was added to a solution of benzoin (0.4 gm.; 0.018 mol). The reaction mixture was stirred and heated at 50 ^{o} C for 11 min and then (75 ml) of H2O was added. The reaction mixture was cooled and a yellow solid compound of benzil was obtained. The mixture was filtered and the precipitate recrystallized from methanol.

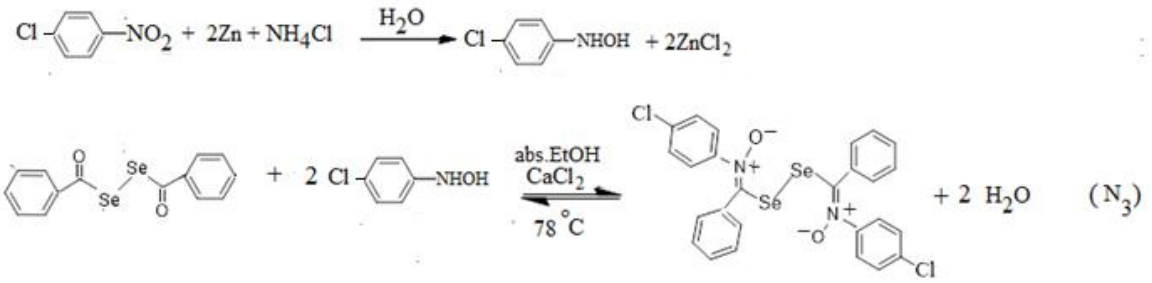
General Procedure of Synthesis Nitrone (35, 36):

A solution of diphenyl diselenide for synthesis (N_1, N_3), benzoylselenonitryl for synthesis N_2 and benzil for synthesis (N_4 and N_5)], (0.02 mole) in absolute ethanol (30 ml) was added to a solution of anhydrous $CaCl_2$ (15 gm) in absolute ethanol (30 ml) placed In a (250 ml) one-necked round-bottomed flask. The reaction mixture was stirred at 50 ^{o} C for 30 min and then a solution of N-benzylhydroxylamine [for synthesis (N_1 and N_2) as in (scheme 1)], (N-4-chlorophenyl hydroxylamine) [for synthesis (N3) as in (scheme 2)],N-(2-hydroxylethylamine) [for synthesis (N_4 and N_5) as in (scheme 3)], (0.02 mole) in absolute ethanol 30 ml was added. 3 drops of benzene sulfonic acid were added and the mixture of (N_1, N_2, N_4 and N_5) was refluxed in the dark overnight. While the mixture reaction of (N_3) was kept with stirring in dark, overnight at room temperature. The reaction mixture was cooled and the precipitate was filtered

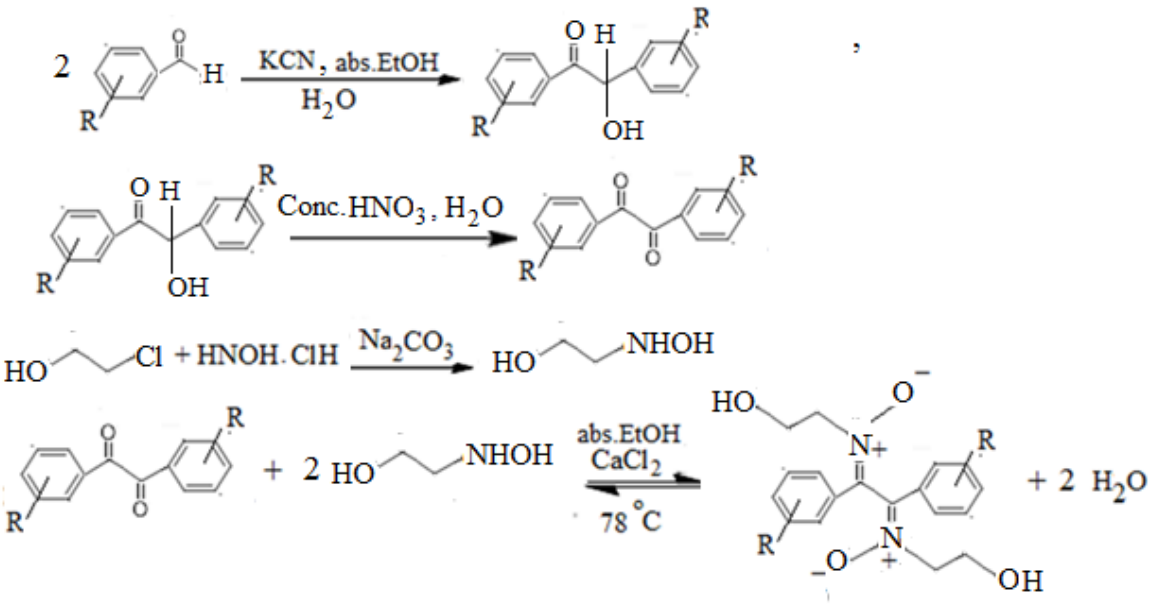
and then recrystallized from absolute ethanol. The mechanism of reaction explains in the (scheme 4). All the synthesized compounds were characterized by FTIR, ^{1}H NMR, ^{13}C NMR, mass spectroscopy and Elemental analysis (CHN) and all the results were in agreement with the theoretical calculations. Physical properties of nitrones are represented in the table (1).



(Scheme 1)

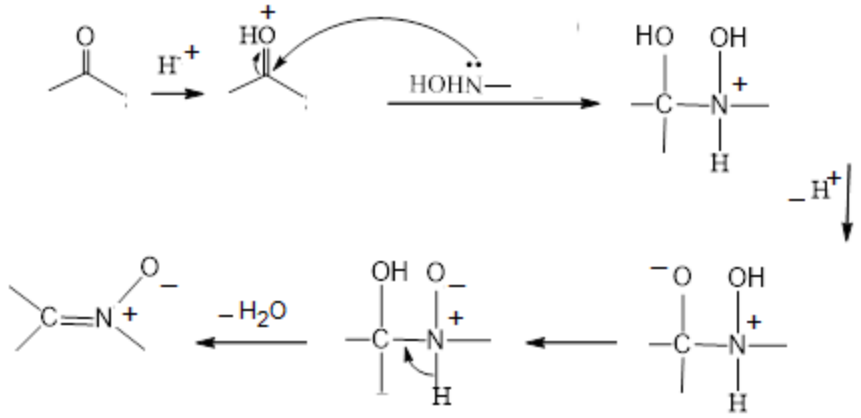


(Scheme 2)



N_4 (R= *p*– Cl), N_5 (R = *o* –NO2)

(Scheme 3)



(Scheme 4)
The mechanism of the formation of nitrone compounds

Table 1. Physical properties of nitrones

Compounds	M. p ^{o} C	Time of reaction	Yield (%)
N_1	150-152	33	63
N_2	161- 163	20	60
N_3	101-103	11	69
N_4	90-92	17	77
N_5	123-125	14	71

Cell culture:

The MDA-MB-231 breast cancer cell line (Beatrice Hunter Cancer Research Institute, Canada) is an epithelial, human breast cancer cell line that was established from a pleural effusion of a 51-year-old Caucasian female with a metastatic mammary adenocarcinoma1 and is one of the most commonly used breast cancer cell lines in medical research laboratories (37).

Cell lines were grown ,maintained and passaged in a humidified incubator at 37°C with 5% CO_2 atmosphere. Cells were cultured as a monolayer in high glucose DMEM (Dulbecco's modified Eagle's medium) supplemented with 10% fetal bovine serum (FBS) (both from Invitrogen), and antibiotics (100 IU/mL penicillin and 100 µL/mL streptomycin) according to the protocol of Beatrice Hunter Cancer Research Institute, Canada.

Cell viability assay

According to the protocol of Beatrice Hunter Cancer Research Institute, Canada, The anti-proliferative effects of selenonitrone on MDA-MB-231 cells were examined using MTT assay (38).

The Cell lines were seeded in 96-multiwell plates at a density of 4500 cells per well for 24h. before exposure to the different concentrations of compounds for 24, and 48 h respectively. Fifty uM of MTT was added to each well after the medium was decanted. Followed by 4 h. incubation. The MTT solution was discarded and the purple formazan crystals formed by the mitochondrial dehydrogenase enzymes were dissolved in 0.1N HCl in isoproponal. The absorbance was read on the Synergy Power wave plate reader at 570 nm. The percent of MTT compared to the vehicle control cells was calculated at viability.

Data were shown as a mean ± standard error and were analyzed using one-way analysis of variance (ANOVA) according to Statistical Package for Social Science (SPSS). The level of significance was set at $\alpha = 0.05$, and statistically significant changes were indicated in figures as follows: *P<0.05, **P<0.01, ***P<0.001, compared to control**.**

Results and Discussion:

Treatment of N- hydroxylamine with selenocarbonyl derivatives gave selenonitrone compounds N_1, N_2 as shown in (Scheme 1). The reaction of N- hydroxylamine with carbonyl derivatives gave nitrone compounds N_4 and N_5, as shown in (Scheme 3) in good yields (77-71)%. The yield of selenonitrones N_1, N_2 and N_3 (63, 60, 69) % This is mainly due to the easily decomposed of organoselenium compounds in light and moisture. All the IR spectra of nitrones showed the disappearance of (C=O) of carbonyl band in the region (1700-1670) cm^{-1} and the appearance peaks at the range (1619-1604) cm^{-1} due to (C=N) stretching, also peaks at the range (1290-1280) cm^{-1} due to (N-O) stretching. The (C=C) stretching showed peaks at the range (1585-1568) $cm^{-1}$and the (C-H) stretching aromatic ring showed peaks at the range (3209-3000) cm^{-1}, while showed peaks at the range (2890-2840) cm^{-1} due to (C-H) aliphatic. The (C-Se) stretching of N_1, N_2 and N_3 were showed in the range (571, 584 and 583) cm^{-1}. The (CN) stretching of nitrone (N_3) was shown in the range (2100) cm^{-1}. All the ^{1}H NMR spectra of selenonitrones and nitrones were showed multiplet signals at the range δ= (7.78-7.60) ppm for the aromatic protons rings. The spectra of nitrones were showed signals in the region δ=4.06 ppm and

δ=4.50 ppm for the two groups of CH_2 and showed signals in the region δ= (3.6-3.2) ppm (OH) stretching. Mass spectroscopy gives the molecular ion and other fragments which indicated the structure of synthesized compounds. All the nitrone compounds have been diagnosed by elemental analysis, and all the results were in agreement with the calculated values.

(N_1) *N,N′*-(diselanediyl bis ((4-fluoro phenyl) methan-1-yl-1-ylidene))bis (1-phenylmethanamine oxide)

Yellow crystals; yields: 60%; m.p. 150-152 °C; IR (ν cm-1): 161 9(ν C=N), 15 68(ν C=C), 1286 (ν N-O), 5 71(ν C-Se), 1 170(ν C-F), 3209(ν CH aromatic), 2885-287 6(ν CH aliphatic); ^{1}H NMR (DMSO, 300 MHz; δ ppm) δ: 7.84 (m, 4H, ph), 7.69 (m, 5H,Ph), 4.26 (s, 2H, CH_2, *J* = 7 Hz); ^{13}C NMR (DMSO, 300 MHz; δ ppm): 57.04, 126.10, 128.23, 129.14, 131.65, 132.66, 140.27, 142.50, 145.71, 162.33; Mass spectrum: m/z (relative intensity): 614(M+). Anal. calcd. for $C_{28}H_{22}N_2O_2F_2Se_2$: C 54.72, H 3.58, N 4.56. found: C 54.61, H 3.60, N 4.37.

(N_2)1-Phenyl-N-(1,1-(4-fluorophenyl) selenonitrile methylene) methanamine oxide

Yellow crystals; yields: 71%; m.p. 101-102 °C; IR (ν cm-1): 1612(ν C=N), 1585 (ν C=C), 1290 (ν N-O), 584 (ν C-Se), 766 (ν C-Cl), 2100 (ν CN), 3112(ν CH aromatic), 2889-2877 (ν CH aliphatic); ^{1}H NMR (DMSO, 300 MHz; δ ppm) δ: 7.66 (m,5H, ph), 7.10 (m,4H, ph), 4.06 (t, 2H, CH2, J = 7.1 Hz); ^{13}C NMR (DMSO, 300 MHz; δ ppm) δ :35.83, 114.62, 123.97, 124.68, 126.69, 128.34, 129.44, 130.41, 131.58, 133.82,162.11; Mass spectrum: m/z (relative intensity): 333(M+). Anal. calcd. for $C_{15}H_{11}N_2OFSe$: C 54.05, H 3.30, N 8.40. found: C 54.12, H 3.24, N 8.51.

(N_3) *N,N′*-(diselanediylbis (phenyl methan-1-yl-1-ylidene))bis(4-chloroaniline oxide).

Orang crystals; yields: 63%; m.p. 163-164 °C; IR (ν cm-1): 1614 (ν C=N), 1578 (ν C=C), 1280 (ν N-O), 583 (ν C-Se), 760 (ν C-Cl), 3111 (ν CH aromatic); ^{1}H NMR (DMSO, 300 MHz; δ ppm) δ: 7.54 (m, 4H,Ph), 7.90 (m, 5H,Ph), 4.12 (s, 2H, CH2, *J* = 6.8 Hz); ; ^{13}C NMR (DMSO, 300 MHz; δ ppm): 55.69, 128.09, 129.15, 130.15, 131.38, 141.50, 143.21, 144.55, 161.43; Mass spectrum: m/z (relative intensity): 646(M+). Anal. calcd. for $C_{28}H_{22}N_2O_2Cl_2Se_2$: C 52.01, H 3.40, N 4.33. found: C 52.22, H 3.29, N 4.40.

(N_4) *N,N′*-(bis (4-chlorophenyl methan-1-yl-1-ylidene)) di(2-hydroxyethanamine oxide).

Yellow crystals; yields: 77%; m.p. 127-1 29°C; IR (ν cm^{-1}): 1604(ν C=N), 1581 (ν C=C), 1285 (ν N-O), 795 (ν C-Cl), 3110(ν CH aromatic), 2890-2865 (ν CH aliphatic), 3310(ν OH),; 1H NMR (DMSO, 300 MHz; δ ppm) δ: 7.70 (m,4H, ph), 4.13 (t, 2H, CH_2, *J* = 6.9 Hz), 4.50 (t, 2H, CH_2, *J* = 7.1 Hz), 3.2 (s, OH); ^{13}C NMR (DMSO, 300 MHz; δ ppm): 123.11, 124.08, 127.44, 129.17, 130.00, 132.01, 160.28; ؟Mass spectrum: m/z (relative intensity): 396(M+). Anal. calcd. for $C_{18}H_{18}N_2O_4Cl_2$: C 54.54, H 4.54, N 7.07. found: C 54.61, H 4.40, N 7.20.

(N_5) *N,N′*-(bis (2-nitrophenyl methan-1-yl-1-ylidene)) di(2-hydroxyethanamine oxide).

Orange crystals; yields: 69%; m.p. 150-151 °C; IR (ν cm-1): 1615(ν C=N), 1580 (ν C=C), 1283 (ν N-O), (s) 1390 - (as) 1520 (ν NO_2), 3118(ν CH aromatic), 2889-2858 (ν CH aliphatic), 3308(ν OH),; ^{1}H NMR (DMSO, 300 MHz; δ ppm) δ**:** 7.60 (m,4H, ph), 4.09 (2H, CH_2), 4.33 (2H, CH_2), 3.01 (s, OH); 13C NMR (DMSO, 300 MHz; δ ppm): 121.34, 125.10, 128.22, 129.15, 131.55, 132.67, 160.23; ؟Mass spectrum: m/z (relative intensity): 418(M+). Anal. calcd. for $C_{18}H_{18}N_4O_8$: C 51.67, H 4.30, N 13.39. found: C 51.42, H 4.11, N 13.43.

A comparison was made between the five compounds prepared by a toxicity assay and found that the N_1 containing selenium was less toxic than the other four compounds therefore, this compound was tested only.

Cytotoxic effects of selenonitrone (N_1) on MDA-MB-231cancer cell line *in vitro* .

The result of the present study an effect of selenonitrone on proliferation of MDA-MB-231 cancer cell line has been shown in the table (2). It was highly significant (P≤ 0.001) between cells treated with selenonitrone and treated with control (DMSO). The study also showed highly significant difference among all concentrations of selenium compound at all periods of the treatment. Highly significant differences (P≤0.001) were found in the interaction between compounds and concentrations after 24 and 48 h.

Table 2.Analysis of variance for effect of different compound, concentrations of selenonitrone and relation between (compounds and concentrations) on the proliferation of MDA-MB-231 breast cancer cells after 24 and 48 hours.

S.O.V.	MS.	
	24h.	48h.
Compounds (Selenonitrone and DMSO)	0.021855***	0.183612***
Concentrations	0.043511***	0.096764 ***
Concentrations & Compounds	0.076179 ***	0.029043 ***

S.O.V.= source of variance , MS=mean square, ***=(P≤0.001)

In the table (3) showed at P-value less than 0.5 indicates, that there significant different effect

between cell treated with selenonitrone and DMSO vehicle control. The toxicity effect of selenonitrone varied with different concentrations. In all concentrations from 0.7µg/ml and up to 500 µg/ml after 24 h. had shown a significant effect on MDA-MB-231 breast cancer cell line as compared to the vehicle control group (DMSO) , the viability of the cell (O.D optical density) was increased in all concentrations ascending from 0.436±0.0354 to 0.696±0.0849. In (Fig.1) shown that decrease of toxicity effect of selenonitrone (N_1) on MAD-MB breast cancer cells proliferation as a compared with control group.

Table 3. Mean and SD for effect of different concentrations of selenonitrone (N_1) and DMSO on the proliferation of MDA-MB-231 breast cancer cells after 24 hours.

Compound	Selenonitrone (N_1)	DMSO	Media	P value ($p \leq 0.5$) between comp. &DMSO
Conc. (µM)	Absorbance (viability) and std.	Absorbance (viability) and std.	Absorbance (viability) and std.	0.0001992 ***
0.7	0.436±0.0354	0.442±0.0385	0.519±0.0286	
5	0.436±0.0354	0.444±0.0315		
25	0.463±0.0375	0.461±0.0167		
50	0.466±0.0212	0.480±0.0012		
250	0.583±0.0615	0.426±0.0255		
500	0.696±0.0849	0.422±0.0339		

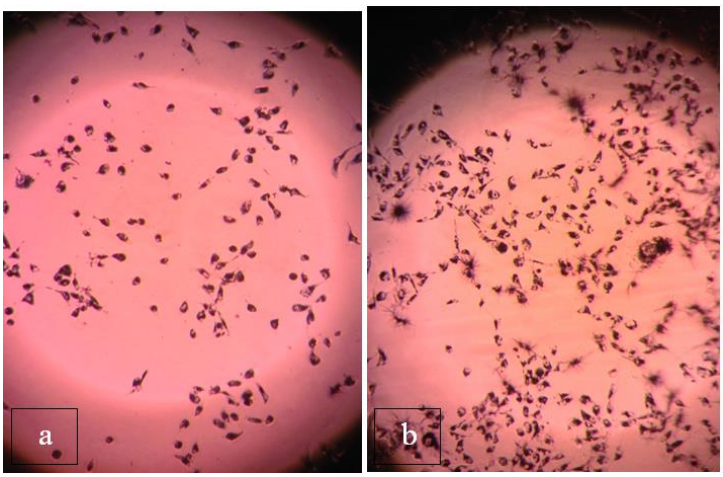


Figure 1. MAD-MB breast cancer cells proliferation incubated for 24 .(a) treated with DMSO. (b)treated with selenonitrone (N_1) at 500 µM concentration.

After 48 h. treatment, table (4) showed that there significant effect ($P \leq 0.5$) between selenium compound and DMSO vehicle control. Also showed higher increased of a stimulatory effect of selenonitrone (N1) on MAD-MB breast cancer cells proliferation at all concentrations more than incubation after 24h. The effect of selenonitrone was increased according to the increase of the concentration as compared to control group 0.502 ±0.0625, 0.520±0.0292, 0.552±0.00820, 0.571± 0.0340, 0.624±0.0341 and 0.747 ± 0.0459 respectively. Microscopic observations of selenium-treated cells revealed an active proliferation of malignant cells at 500 µM concentration compared with untreated control cells (Fig. 2).

Table 4. Mean and SD for effect of different concentrations of selenonitrone (N_1) compound and DMSO on the proliferation of MDA-MB-231 breast cancer cells after 48 hours.

Compound	Selenonitrone (N_1)	DMSO	Media	P value (≤0.5)between comp. &DMSO
Conc. (µM)	Absorbance (viability) and std.	Absorbance (viability) & std.	Absorbance (viability) and std.	0.0001833 ***
0.7	0.502 ±0.0625	0.364 ±0.0488	0.431±0.056	
5	0.520 ±0.0292	0.446 ±0.0056		
25	0.552 ±0.0082	0.449 ±0.0094		
50	0.571 ±0.0340	0.448 ±0.0247		
250	0.624 ±0.0341	0.459 ±0.0180		
500	0.747±0.0459	0.448 ±0.0581		

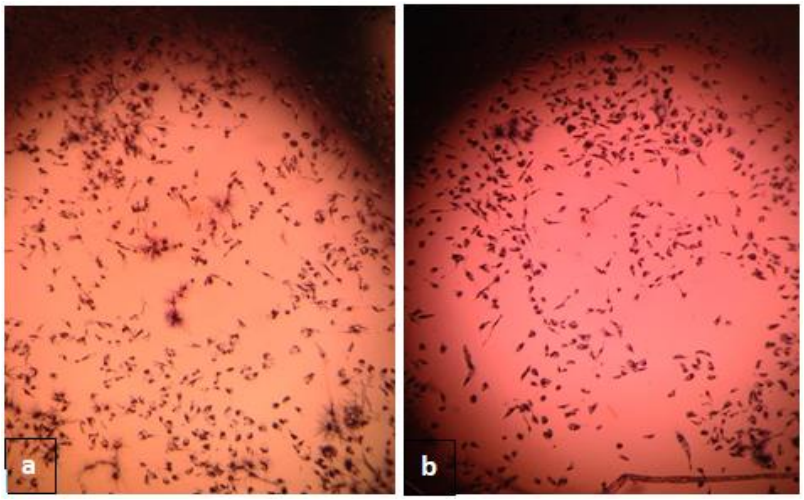


Figure 2. MAD-MB breast cancer cells proliferation incubated for 48.(a) treated with DMSO. (b)treated with selenonitrone at 500 µM concentration

Figure 3 demonstrated that selenonitrone was more effect after 48 h. than 24 h. on the growth of MAD-MB breast cancer cells in comparison to DMSO control groups. This effective increased in time and concentration- dependent manner.

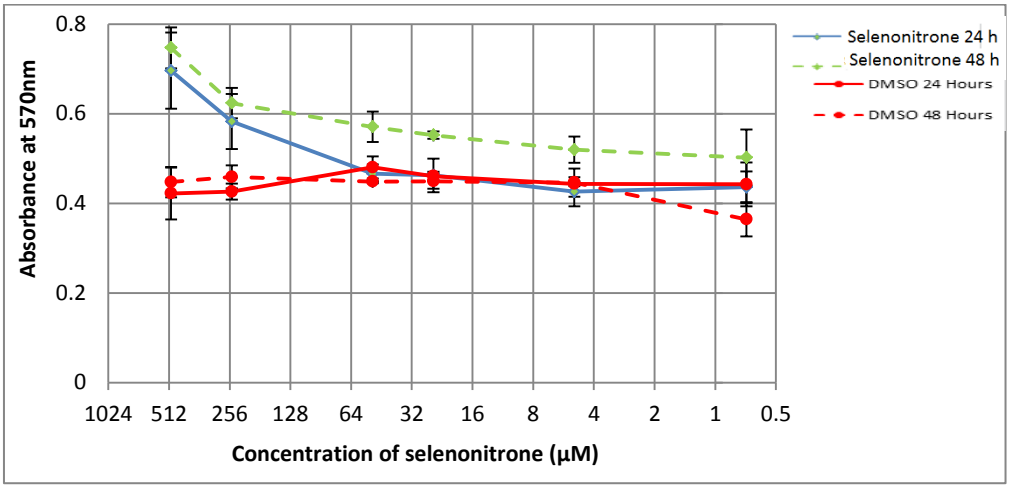


Figure 3. Absorbance of MAD-MB breast cancer cells treated with selenonitrone (N_1) and with DMSO concentrations after incubation for 24 and 48 hours

The goal of current study is to understand the roles of the selenium in cancer prevention but it is revealed unexpected results on MDA-MB-231 breast cancer cell lines, although the experiment was repeated twice and gave the same results. The results indicated that selenium applied for 24 h and 48 h. stimulated cell proliferation as a compared to untreated control cells in a concentration and time-dependent manner, that is compatible with a previous study carried by Scott *et al.*(39) found the selenium did not prevent cancer .

The data in study of Grana & Reddy (40) and Kim, *et al.* (41) support the result that obtained in the present study, they found that the selenium at low concentration leads to the promotion of cell cycle progression due to up-regulates multiple key cell cycle–related gene mRNA levels or by enhances total cellular phosphorylated proteins in HL-60 cells in serum-free culture media , particularly the G2/M transition, and/or a reduction of apoptosis primarily in G1 cells (42) ,while the Shin-Hyung *et al.* (35) showed the selenium treatment enhanced the cell growth, with 15 ng /ml of selenium the most effective in stimulating cell proliferation among various concentrations of selenium tested.

The current study agrees with a study of Petra *et al*. (43) have been reported that selenoprotein has cancer-promoting effects and agrees with Shin-Hyung (30) that demonstrated the selenium stimulates the cell growth and the proliferation of 3T3-L1 preadipocytes. Also, selenium promotes embryonic fibroblast cells, and it has a role in adipogenesis (44)

The finding results disagreement with Merrill (45); Barbosa *et al*.(46); Zeng,(26) demonstrates

that selenium induces cell cycle arrest and apoptosis, also disagree with Puspitasari *et al*.(47); Marek *et al*.(48); Valentina *et al*.(49) that have been shown selenium cause decrease cell proliferation *in vitro* and *in vivo.*

These findings also compel the medical research community to continue the search on normal cells such as beta cells, skin cells liver cell and other types of cells especially because of its importance in treating certain diseases.

Conclusions:

We have carried out the synthesis of new derivatives of nitrone and selenonitron, (two selenonitrone and three nitrones) in good yield, by the condensation method between carbonyl group and N-monosubstituted hydroxylamines.

The present study revealed that selenonitrone (N_1) was increased stimulating the cellular proliferation of MAD-MB breast cancer cell line in a concentration and time-dependent manner.

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Conflicts of Interest: None.

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تحضير وتشخيص مشتقات سيلينونايترون جديدة وتأثيرها على حيوية خط خلايا سرطان الثدي خارج الجسم الحي

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الخلاصة:

تم تحضير مركبات جديده من النترون والسيلينونترون. استخدمت طريقه التكاثف بينN-(2- هيدروكسي ايثايل)هيدروكسيل امين ومركبات الكربونيل المعوضه وهي [البنزل و 4,4- ثنائي كلوروبنزل و2,2 – ثنائي نايتروبنزل] وادت هذه الطريقه الى تحضير مجموعه جديده من مركبات النترون. بينما التكاثف بين N – بنزايل هيدروكسيل امين و مركبات السيلينوكربونيل المعوضه وهي [ثنائي(4- فلوروبنزوايل) ثنائي سيلينايد و (4- كلوروبنزوايل سيلينونايترايل)] ادت هذه الطريقه الى تحضير مركبات جديده من سيلينونترون. اما تكاثف N-(4- كلوروفينايل هيدروكسيل امين مع ثنائي بنزوايل ثنائي سيلينايد ادى الى تحضير نوع اخر من مركبات سيلينونترون. شخصت المركبات المحضرة بأستخدام تقنية تحليل العناصر الدقيق والطرائق الطيفية المختلفة كمطيافية تحت الحمراء، مطيافية فوق البنفسجية ،مطيافية الرنين النووي المغناطيسي ^{1}H،^{13}C ومطيافية الكتلة. واكد ت نتائج التحليل الطيفي وتحليل العناصر الدقيق صحة التراكيب الكيميائية المتو قعة للمركبات المحضرة في هذه الدراسة. كشفت نتائج تاثير مشتقات السيلسنونايترون الجديدة (N1) على خلايا سرطان الثدي -MDA MBخارج الجسم الحي زيادة في تكاثر الخلايا بازدياد تراكيز السلينوناتيرون وفي كل الفترات الزمنية.

الكلمات المفتاحية: حيوية الخلايا، خط خلايا سرطان الثدي MDA- MB-231، نيترونات ، التكاثر، سيلينو كربونيل، سيلينونيترونات.