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Synthesis of *N*-(Aryl)-2-(phenylselanyl)acetamides and Their Antimicrobial Activities

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ABSTRACT

Novel *N*-(aryl)-2-(phenylselanyl)acetamides (**5a -5l, 6, 7**) were synthesized by the reaction of 2-(phenylselanyl)acetyl chloride with substitute arylamine derivatives in dry benzene**.** The structures of these compounds were characterized by the spectroscopic methods such as FT-IR, ^{1}H-NMR, ^{13}C NMR and HRMS. Furthermore, all the synthesized compounds were tested *in vitro* for their antimicrobial and antifungal activity. The obtained results were compared with conventional reference antibiotics Ciprofloxacin and Griseofulvin's results. Their antioxidant potentials were evaluated using in vitro antioxidant models known as DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging activities. Some of the tested compounds exhibited significant antibacterial, antifungal and antioxidant activities. Particularly, compound **5h** showed more pronounced activity than reference antibiotics against *Staphylococcus aureus*. Compounds **5f** and **5i** showed excellent levels of antifungal activity against *Penicillium roquefortii* and *Aspergillus niger*. All the compounds showed moderate antioxidant activities.

Key Words: *Selenium, antibacterial activity, antifungal activity, antioxidant activity, DPPH*

1. INTRODUCTION

Selenium is an important trace element for human and animal health. Adult human beings have to take up 15 µg/kg of selenium daily [1-6]. Selenium deficiency is associated with several disease conditions such as immune impairment, cancer, and heart diseases [7, 8]. Although the use of elemental selenium as medicine is strongly limited, its numerous organic and inorganic derivatives are used in industry, agriculture, and medicine. Recent years, stable organoselenium compounds which have biological activity such as antioxidant, antibacterial, antiviral, antifungal, antiparasitic, antihistamine and anticancer effects were synthesized and investigated [9-15].

Antioxidant research is an important topic in the medical field as well as in the food industry. The oxidation induced by Reactive Oxygen Species (ROS) can result in cell membrane disintegration, membrane protein damage and DNA mutation which can initiate (or propagate) the development of many diseases such as cancer, liver

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injury and cardiovascular disease [16]. The body possesses such defense mechanisms as enzymes and antioxidant nutrients which arrest the damaging properties of ROS. However, continuous exposure to chemicals and contaminants may lead to an increase in the amount of free radicals in the body beyond its capacity to control them, and cause irreversible oxidative damage [17-19]. Therefore, antioxidants with free radical scavenging activities may have use in the prevention and therapeutics of diseases caused by free radicals and oxidants [20].

Selenium compounds have been studied for their antioxidant properties and their ability to prevent disease. The protective effects of selenium compounds against disease are commonly attributed to radical scavenging and enzymatic decomposition of oxygen metabolites [21]. Reports have shown that selenium-containing organic molecules are generally more potent antioxidants than 'classical' antioxidants, and this fact serves as an impetus for increasing interest in the rational design of synthetic organoselenium compounds [22-24]. In fact, the interest in the biochemistry, pharmacology and toxicology of organoselenium compounds has increased since the 1980s, when literature data demonstrated that ebselen was a promising antioxidant and mimetic of the antioxidant selenoenzyme glutathione peroxidase [25]. Several studies have shown the protective effects of organoselenium compounds against a number of models of oxidative stress [22,26–29]. Organoselenium compounds also have neuro-protective [30], anti-inflammatory [31], antidepressant-like [32-34], antinociceptive [35] and anticonvulsant properties [36, 37].

Antioxidant activity is one of the most important functions of selenium. This activity is considered to be dependent on the chemical forms of selenium. Selenium is a catalytic cofactor for the important endogenous antioxidative system of the human body. There are 25 human selenoproteins which act as antioxidant defense and the cancer-preventive system [38-42]. Organoselenium compounds are very important due to these properties.

In this work, we studied the synthesis and antibacterial properties of novel *N*-(aryl)-2-(phenylselanyl)acetamide derivatives. *N*-(aryl)-2-(phenylselanyl)acetamide derivatives (**5a-5l, 6** and **7**) were evaluated for their antimicrobial and antifungal activities against *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, *Klebsiella pneumonia*, *Penicillium roqueforti* and *Aspergillus niger*.

2. EXPERIMENTAL PART

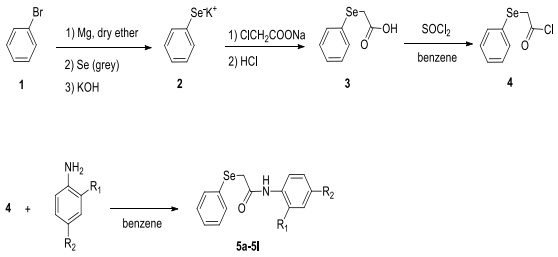
2.1. General

The chemicals used in the synthesis of the novel *N*-(aryl)-2-(phenylselanyl)acetamide derivative were purchased from Aldrich Chemical Company. All chemicals and solvents used for the synthesis were spectroscopic reagent grade. All mps were determined in sealed capillaries and are uncorrected. MS was performed by means of a Waters ACQUITY UPLC analyser with combine Micromass LCT Premier TM XE TOF-MS and electrospray ionization (ESI); results agreed satisfactorily with calculated values. IR spectra were recorded on a Mattson-1000 series and reported in reciprocal centimeters (cm^{-1}). ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ solvent and recorded with a Bruker Spectrospin Avance DPX-300 Ultrashield instrument. Chemical shifts are given in parts per million (δ) downfield from tetramethylsilane as internal standard. The numbering system used in the experimental corresponds to the current CA index names. Reagent grade solvents were used for all extraction and chromatography. The solvents and reagents were purified and dried beyond commercial reagent grade. Thin layer chromatography (TLC) analysis was performed on E. Merck 0.25 mm precoated silica gel 60 F-254 and visualized with UV illumination. The crude products were purified by column chromatography on silica gel (Merck 60 0.040–0.060 nm). The absorption spectra were measured using a Shimadzu UV-1800 UV-Vis spectrometer. 2-(Phenylselanyl)acetic acid was prepared by the method in the literature [43].

2.2. Synthesis

General Procedure for the Synthesis of N-(aryl)-2-(phenylselanyl)acetamide derivatives **(5a-5l, 6** and **7).**

A mixture of compound **3** (10 mmol) and an equivalent amount of thionyl chloride in dry benzene (20 mL) was refluxed in an oil bath for 2 h. Then substitute aniline (10 mmol) was added and refluxed for an additional 3 h (TLC control). The reaction mixture was cooled to room temperature and extracted with %10 $NaHCO_3$ solution. The organic phase dried over anhydrous Na_2SO_4. After evaporating the solution under reduced pressure, a solid appeared and recrystallized from ethanol.



Compound	R_1	R_2
5a	-H	-Br
5b	-H	-Cl
5c	-H	-F
5d	-H	$-CH_3$
5e	-H	$-OCH_3$
5f	-H	$-NO_2$
5g	-Br	-H
5h	-Cl	-H
5i	-F	-H
5j	$-CH_3$	-H

5k	$-OCH_3$	-H
5l	$-NO_2$	-H

Scheme 1. Synthesis of *N*-(aryl)-2-(phenylselanyl)acetamide derivatives

***N*-(4-Bromophenyl)-2-(phenylselanyl)acetamide (5a).** Yield: 59%; m.p., 123-124℃; IR (ν_{max}, cm^{-1}): 3232 (N-H), 3110, 3060 (=C-H), 2967 (C-H), 1656 (C=O, amide I), 1613 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.66 (s, 2H, CH_2), 7.25-7.66 (m, 9H, Ar-H), 8.15 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$, ; δ, ppm): 31.8 (CH_2), 117.2, 121.4, 128.3, 128.5, 129.7, 132.0, 132.8, 136.6 (Aryl), 167.09 (C=O). HRMS (EI): $C_{14}H_{13}BrNOSe^+$, calc. 369.9346; $[M+H]^+$: 369.9344.

***N*-(4-Chlorophenyl)-2-(phenylselanyl)acetamide (5b).** Yield: 63%; mp 108-109 ℃; IR (ν_{max}, cm^{-1}): 3244 (N-H), 3081, 3045 (=C-H), 2971 (C-H), 1642 (C=O, amide I), 1597 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.70 (s, 2H, CH_2), 7.25-7.60 (m, 9H, Ar-H), 8.07 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.3 (CH_2), 121.0, 123.1, 128.2, 128.5, 129.6, 129.7, 132.8, 136.1 (Aryl), 166.9 (C=O). HRMS (EI): $C_{14}H_{13}ClNOSe^+$, calc. 325.9851; $[M+H]^+$: 325.9850.

***N*-(4-Florophenyl)-2-(phenylselanyl)acetamide (5c):** Yield: 62%; mp 107-108 ℃; IR (ν_{max}, cm^{-1}): 3251 (N-H), 3066, 3043 (=C-H), 2969 (C-H), 1654 (C=O, amide I), 1607 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.68 (s, 2H, CH_2), 6.75-7.58 (m, 9H, Ar-H), 8.07 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.2 (CH_2), 115.8-115.5 (J_{C-F} = 22.5 Hz), 121.6-121.7 (J_{C-F} = 8.2 Hz), 128.1, 128.6, 129.7, 132.7, 133.5, 157.9-161.2 (J_{C-F} = 242.2 Hz) (Aryl), 166.9 (C=O). HRMS (EI): $C_{14}H_{13}FNOSe^+$, calc. 310.0146; $[M+H]^+$: 310.0121.

***N*-(p-Tolyl)-2-(phenylselanyl)acetamide (5d).** Yield: 53%; mp 90-91 ℃; IR (ν_{max}, cm^{-1}): 3264 (N-H), 3078, 3061 (=C-H), 2953 (C-H), 1649 (C=O, amide I), 1606 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 2.35 (s, 3H, CH_3), 3.71 (s, 2H, CH_2), 7.06-7.63 (m, 9H, Ar-H), 8.02 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 20.1 (CH_3), 31.4 (CH_2), 119.9, 128.1, 128.7, 129.5, 129.6, 132.6, 134.3, 134.9 (Aryl), 166.6 (C=O). HRMS (EI): $C_{15}H_{16}NOSe^+$, calc. 306.0397; $[M+H]^+$: 306.0381.

***N*-(4-Methoxyphenyl)-2-(phenylselanyl)acetamide (5e).** Yield: 56%; mp 106-107 ℃; IR (ν_{max}, cm^{-1}): 3258 (N-H), 3069, 3047 (=C-H), 2977 (C-H), 1681 (C=O, amide I), 1594 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.71 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3), 6.85-7.60 (m, 9H, Ar-H), 8.02 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.2 (CH_2), 55.5 (OCH_3), 114.2, 121.8, 128.7, 128.9, 129.6, 130.6, 132.6, 156.7 (Aryl), 166.6 (C=O). HRMS (EI): $C_{15}H_{16}NO_2Se^+$, calc. 322.0346 $[M+H]^+$: 322.0369.

***N*-(4-Nitrophenyl)-2-(phenylselanyl)acetamide (5f).** Yield: 61%; mp 92-94 ℃; IR (ν_{max}, cm^{-1}): 3242 (N-H), 3071, 3026 (=C-H), 2972 (C-H), 1666 (C=O, amide I), 1611 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.71 (s, 2H, CH_2), 7.31-8.23 (m, 9H, Ar-H), 8.29 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.8 (CH_2), 119.4, 125.1, 128.1, 128.5, 129.8, 133.1, 143.4, 143.7 (Aryl), 167.7 (C=O). HRMS (EI): $C_{14}H_{13}N_2O_3Se^+$, calc. 337.0091; $[M+H]^+$: 337.0056.

***N*-(2-Bromophenyl)-2-(phenylselanyl)acetamide (5g).** Yield: 58%; mp 75-77 ℃; IR (ν_{max}, cm^{-1}): 3260 (N-H), 3059, 3025 (=C-H), 2983 (C-H), 1641 (C=O, amide I), 1578 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.75 (s, 2H, CH_2), 6.53-8.41 (m, 9H, Ar-H), 8.91 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.8 (CH_2), 113.6, 121.5, 121.5, 125.4, 128.1, 128.2, 128.5, 129.6, 132.3, 132.6, 132.7, 135.6, (Aryl), 166.9 (C=O). HRMS (EI): $C_{14}H_{13}BrNOSe^+$, calc. 369.9346; $[M+H]^+$: 369.9275.

***N*-(2-Chlorophenyl)-2-(phenylselanyl)acetamide (5h).** Yield: 56%; mp 93-94 ℃; IR (ν_{max}, cm^{-1}): 3232 (N-H), 3109, 3042 (=C-H), 2966 (C-H), 1646 (C=O, amide I), 1582 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.77 (s, 2H, CH_2), 6.16-8.39 (m, 9H, Ar-H), 8.90 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.83 (CH_2), 115.9, 118.9, 121.2, 123.1, 124.9, 127.7, 128.5, 129.1, 129.4, 129.6, 132.8, 134.5 (Aryl), 166.9 (C=O). HRMS (EI): $C_{14}H_{13}ClNOSe^+$, calc. 325.9851; $[M+H]^+$: 325.9813.

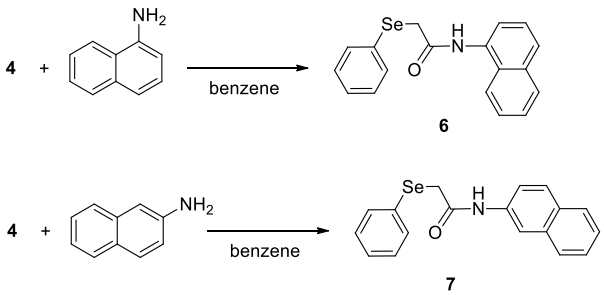
***N*-(2-Florophenyl)-2-(phenylselanyl)acetamide (5i).** Yield: 52%; mp 84-85 ℃; IR (ν_{max}, cm^{-1}): 3240 (N-H), 3067, 3029 (=C-H), 2966 (C-H), 1654 (C=O, amide I), 1616 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.60 (s, 2H, CH_2), 6.92-8.19 (m, 9H, Ar-H), 8.36 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.6 (CH_2), 114.7-114.9 (J_{C-F} = 19.5 Hz), 121.6, 124.5-12.6 (J_{C-F} = 7.5 Hz), 124.7, 126.1, 127.8, 128.2, 128.5, 129.6, 132.9, 133.1, 151.0-154.2 (J_{C-F} = 242.2 Hz) (Aryl), 167.1 (C=O). HRMS (EI): $C_{14}H_{13}FNOSe^+$, calc. 310.0146; $[M+H]^+$: 310.0133.

***N*-(o-Tolyl)-2-(phenylselanyl)acetamide (5j).** Yield: 44%; mp 88-90 ℃; IR(ν_{max}, cm^{-1}): 3282 (N-H), 3071, 3025 (=C-H), 2962 (C-H), 1646 (C=O, amide I), 1608 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 2.15 (s, 3H, CH_3), 3.80 (s, 2H, CH_2), 7.04-7.88 (m, 9H, Ar-H), 8.29 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 17.5 (CH_3), 31.4 (CH_2), 122.2, 122.3, 125.2, 127.1, 127.8, 128.6, 128.6, 128.8, 129.6, 130.4, 131.7, 135.5 (Aryl), 166.4 (C=O). HRMS (EI): $C_{15}H_{16}NOSe^+$, calc. 306.0397; $[M+H]^+$: 306.0338.

***N*-(2-Methoxyphenyl)-2-(phenylselanyl)acetamide (5k).** Yield: 49%; mp 97-98 ℃; IR (ν_{max}, cm^{-1}): 3332 (N-H), 3051, 3002 (=C-H), 2960 (C-H), 1666 (C=O, amide I), 1608 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.71 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3), 6.72-7.48 (m, 9H, Ar-H), 8.76 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.9 (CH_2), 55.7 (OCH_3), 110.0, 110.4, 115.1, 118.5, 119.6, 121.0, 124.0, 127.9, 128.9, 129.5, 132.9, 148.8 (Aryl), 166.7 (C=O). HRMS (EI): $C_{15}H_{16}NO_2Se^+$, calc. 322.0346; $[M+H]^+$: 322.0301.

***N*-(2-Nitrophenyl)-2-(phenylselanyl)acetamide (5l).** Yield: 53%; mp 121-122 ℃; IR (ν_{max}, cm^{-1}): 3261 (N-H), 3067, 3042 (=C-H), 2991 (C-H), 1667 (C=O, amide I), 1603 (N-H, amide II). ^{1}H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.82 (s, 2H, CH_2), 7.25-8.75 (m, 9H, Ar-H), 10.91 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 32.1 (CH_2), 119.8, 122.0, 123.5, 125.7, 128.2, 128.3, 129.5,

133.2, 133.2, 134.4, 135.8, 136.5 (Aryl), 168.8 (C=O). HRMS (EI): $C_{14}H_{13}N_2O_3Se^+$, calc. 337.0091; $[M+H]^+$: 337.0018.



Scheme 2. Synthesis of *N-(Naphthalen-1-yl)-2-(phenylselanyl)acetamide* **(6)** and *N-(Naphthalen-2-yl)-2-(phenylselanyl)acetamide* **(7)**

***N*-(Naphthalen-1-yl)-2-(phenylselanyl)acetamide (6).** Yield: 66%; mp 127-128 °C; IR (ν_{max}, cm^{-1}): 3227 (N-H), 3039, 3018 (=C-H), 2969 (C-H), 1651 (C=O, amide I), 1637 (N-H, amide II). ^1H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.93 (s, 2H, CH_2), 7.31-7.96 (m, 12H, Ar-H), 8.84 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.3 (CH_2), 120.1, 120.6, 125.2, 125.3, 125.9, 126.4, 126.6, 127.5, 128.3, 129.6, 132.0, 134.2 (Aryl), 166.2 (C=O). HRMS (EI): $C_{18}H_{16}NOSe^+$, calc. 342.0397; $[M+H]^+$: 342.0408.

***N*-(Naphthalen-2-yl)-2-(phenylselanyl)acetamide (7).** Yield: 58%; mp 120-121 °C; IR (ν_{max}, cm^{-1}): 3244 (N-H), 3076, 3050 (=C-H), 2966 (C-H), 1646 (C=O, amide I), 1613 (N-H, amide II). ^1H NMR (300 MHz, $CDCl_3$; δ, ppm): 3.75 (s, 2H, CH_2), 7.28-8.12 (m, 12H, Ar-H), 8.84 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$; δ, ppm): 31.5 (CH_2), 116.5, 119.6, 125.2, 126.6, 127.6, 127.7, 128.6, 128.8, 129.7, 130.8, 132.7, 133.7, 134.9 (Aryl), 166.9 (C=O). HRMS (EI): $C_{18}H_{16}NOSe^+$, calc. 342.0397; $[M+H]^+$: 342.0430.

2.3. Biological Screening

2.3.1. Antibacterial activity

The bacterial subcultures for *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, *Escherichia coli* ATCC 25922, *Klebsiella pneumonia*, *Penicillium roqueforti* and *Aspergillus niger* were obtained from Gazi University, Faculty of Science, Biology Department. Bacterial strains were cultured overnight at 37 °C in nutrient broth and the yeast were cultured overnight at 30 °C in Sabouraud dextrose broth for antibacterial and antifungal activity tests. These stock cultures were stored in the dark at 4 °C during the survey. Antibacterial activities of the compounds were determined by using the disc diffusion method. The antimicrobial screening was performed using Mueller – Hinton Agar (MHA) for bacteria and Sabouraud dextrose agar (SDA) for yeast. The culture suspensions were prepared and adjusted by comparing with 0.5 Mc Farland turbidity standard tubes. MHA and SDA (20 mL) were poured into each sterile Petri dish after injecting cultures (100 µL) of microorganisms and distributing medium in Petri dish homogeneously. Test compounds were filtered with a pore size of 0.45 µm. Each compound (100 µg) was dissolved in 1 mL of DMSO. Empty sterilized 6 mm discs (Whatman No: 1) were impregnated with 20 µL of each compound. Discs were placed on agar plates, and the plates were incubated at 37 °C for 24 h. Inhibition zones formed on the medium were evaluated in mm (Table 1). Studies were performed in duplicate and the inhibition zones were compared to those of reference discs. The solvent control (DMSO) did not show any antimicrobial activity.

2.3.2. DPPH radical scavenging activity

Antioxidant activity of the test compounds was determined by diphenylpicrylhydrazyl (DPPH) radical scavenging method in literature with some modifications [44]. Different concentration of the test compound (10-1000 µg/mL) in methanol were mixed with 1 mM of methanolic DPPH solution to a final volume of 2.0 mL, incubated for 30 min at room temperature in the dark and absorbance was measured at 517 nm. Blank was carried out in the same manner without the test compounds, and ascorbic acid was taken as the standard. The experiment was performed in triplicate and the percentage radical scavenging was determined as follows[(Absorbance of blank - Absorbance of test)/ Absorbance of blank] x 100

The radical-scavenging activity of the samples was expressed in terms of IC_{50} which concentration in µM required for a 50% decrease in absorbance of DPPH radical.

3. RESULTS AND DISCUSSION

We followed the general synthetic method shown in Scheme 1 and 2 to prepare fourteen *N*-(aryl)-2-(phenylselanyl)acetamide derivatives (**5a-l, 6,7**). These compounds were obtained in good yields (44 – 66%). The purity of compounds was confirmed by TLC. The structures of the synthesized *N*-(aryl)-2-(phenylselanyl)acetamide derivatives **5a-l, 6, 7** were confirmed by FT-IR, ^1H NMR, ^{13}C NMR and HRMS. All spectral data were in agreement with the assigned structures.

Phenyl bromide (**1**) was converted to 2-(phenylselanyl)acetic acid (**3**) by earlier reported Grignard method [21]. Reaction of compound **3** with thionyl chloride in dry benzene yielded 2-(phenylselanyl)acetyl chloride (**4**). A novel organoselenium compounds (**5a-5l**) were synthesized by treating **4** with substitute aniline derivatives in dry benzene.

In the FTIR spectra of compound **5a-5l** were observed characteristic bands of secondary amide in the regions 3200 cm^{-1} (N-H) and there were no absorption bands for (O-H) belonging to compound **4**. In addition to, stretching vibrations of C=O bands and bending vibrations of the N-H appeared in the region 1650 cm^{-1} and around 1610 cm^{-1}, respectively. For compound **4**, the FTIR spectrum exhibited a characteristic band at 1704 cm^{-1} due to a C=O group. Decrease in the carbonyl stretching frequency evidenced the conversion of carboxylic acid to amide.

In the ^{1}H NMR spectrum, the -COOH signal disappeared when compound **4** was converted to compounds **5a-5l**; instead a new signals originating from amide -NH were observed. The high-resolution mass spectra of the **5a-5l** showed molecular ion peaks that were consistent with their molecular formula.

As seen in Table 1, the synthesized *N*-(aryl)-2-(phenylselanyl)acetamide derivatives showed antibacterial activity against Gram-positive bacterial strains: *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, Gram-negative bacterial strains: *Escherichia coli* ATCC 25922, *Klebsiella pneumonia* and fungal strains: *Penicillium roqueforti; Aspergillus niger*. The reference antibiotic Ciprofloxacin and Gresiofulvin were used as positive control for comparison.

The results showed that compounds **5b**, **5d**, **5f**, **5h**, **5k** and **6** exhibited good antibacterial activity and **5b**, **5f**, **5g**, **5i**, **6** and **7** exhibited good antifungal activity at a concentration of 100 μg/mL as that of standard antibiotics Ciprofloxacin and Gresiofulvin. In case of Gram-positive bacteria, compounds **5h, 5b** and **6** were found to be most effective against *Staphylococcus aureus* with zone of inhibition ranging between 17 mm and 19 mm and the compounds **5d, 5b, 5k** and **6** were most effective against *Bacillus subtilis* with zone of inhibition ranging between 18 mm and 20 mm. . Furthermore, compound **5h** showed more pronounced activity than reference antibiotics against *Staphylococcus aureus*. Compounds **5f** and **5i** showed excellent levels of antifungal activity against *Penicillium roquefortii* and *Aspergillus niger*.

TABLE 1. Antimicrobial activity of *N*-(aryl)-2-(phenylselanyl)acetamide derivatives (**5a-l, 6,7**).

Zone of inhibition in mm						
	Gram-positive bacterial strains		Gram-negative bacterial strains		Fungal strains	
Compound	B. subtilis	S. aureus	E. coli	K.pneumoniae	P. roquefortii	A.Niger
5a	12	13	8	14	5	-
5b	19	18	13	16	9	14
5c	8	12	-	8	-	3
5d	20	14	21	15	-	5
5e	6	5	12	19	6	-
5f	9	11	17	21	11	16
5g	14	6	9	16	9	12
5h	16	19	13	17	-	7
5i	13	11	-	-	13	19
5j	8	13	16	14	3	5
5k	19	15	14	16	-	1
5l	9	6	9	12	-	-
6	18	17	23	18	7	12
7	13	9	11	10	6	14
DMSO	-	-	-	-	-	-
Ciprofloxacin	21	17	27	23	-	-
Gresiofulvin	-	-	-	-	4	15

Gram-positive bacterial strains: *B. subtilis: Bacillus subtilis, S. aureus: Staphylococcus aureus*, Gram-negative bacterial strains: *E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae, Fungal strains: P. Roquefortii: Penicillium roquefortii; A. Niger: Aspergillus niger*. The concentration of test compounds was 100 μg/mL. Solvent used DMSO.

A rapid, simple and inexpensive method to measure antioxidant capacity of substances involves the use of the free radical, 2,2-diphenyl-1-picrylhydrazyl (DPPH).This assay is based on a decolorization technique by UV-vis spectroscopy at 517 nm in which the radical is generated directly in a stable form before reaction with putative antioxidants. All the synthesized compounds were screened for their antioxidant activity by DPPH radical scavenging assay. Ascorbic acid was taken as the positive control. The 50% inhibitory concentrations expressed as IC50 is shown in the Table 2. All the tested compounds showed DPPH radical quenching activity in a concentration dependent manner, compound 5e showed maximum activity (IC50 = 37.77 μg/mL). The test compounds, such as 5a, 5d, 5f, 5i, 5l and 6 showed the IC50 at 78.95, 81.93, 96.54, 53.37, 77.69 and 99.01 μg/mL, respectively. However, the remaining test compounds showed the IC50 values above 100 μg/mL

TABLE 2. DPPH radical scavenging activity of *N*-(aryl)-2-(phenylselanyl)acetamide derivatives (**5a-5l, 6,7**).

Compound	IC_{50} (μM)	Compound	IC_{50} (μM)
5a	78.95	**5h**	208.62
5b	124.61	**5i**	53.37
5c	219.78	**5j**	149.73
5d	81.93	**5k**	118.16
5e	37.77	**5l**	77.69
5f	96.54	**6**	99.01
5g	201.31	**7**	113.63
Vitamin C	24.61		

Vitamin C was used for positive control. IC_{50} value was termined to be the effective concentration at which DPPH radical was scavenged by 50%. The IC_{50} value was obtained by interpolation from linear regression analysis.

4. CONCLUSIONS

New series of N-(aryl)-2-(phenylselanyl)acetamides (**5a - 5l**, **6**, **7**) derivatives were synthesized and their antimicrobial activities were evaluated and these activities were compared with the activities of standard drugs. Some of the tested compounds exhibited significant antibacterial and antifungal activities. Furthermore, antioxidant activity of all the synthesized compounds were investigated. All the tested compounds showed DPPH radical quenching activity. Therefore, the synthesized compounds are considered to be important both in the production of new drugs and in the synthesis of more complex organoselenium compounds.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

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