Journal of Environmental Studies [JES] 2019. 19: 14-21

Original Paper

Antiproliferative Activity of two compounds isolated from *Artemisia sieberi*

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Rec. 4 Mar, 2019 Accept. 1 Apr, 2019

Abstract

This study described the isolation and structure elucidation of secondary metabolites from,*Artimisiasieberi (*Asteraceae), known for its therapeutic and medicinal properties, it was used in both traditional and modern medicine.*Artimisiasieberi*was collected at the flowering stage. Dried aerial parts were powdered and subjected to different chromatographic methods of extraction followed by different methods of purification through normal phase and reversed phase chromatography, eg. column chromatography (CC) and high performance liquid chromatography (HPLC), respectively.Phytochemical investigation of *A. sieberi*afforded a 3α,8β-dihydroxygermacr-4(15),9-dien-6α,7β,11αH,12,6-olide (**1**) and a flavonoid 3'-hydroxy-genkwanin **(2)**.The structures of the compounds were elucidated by means of spectroscopic analyses, including (EI-MS and 1D /2D NMR) techniques.Cytotoxic effects of these two known compounds were examined against, three different human cancer cell lines, **MCF-7** (breast), **HCT116** (colon) and **HepG-2** (liver).Viability was assessed by the standard colorimetric assay using the tetrazolium, 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) and can be regarded as an potent source of lead compounds in drugs development to combat cancer.

Keywords:*Artimisiasieberi,* 3α,8β-dihydroxygermacr-4(15),9-dien-6α,7β,11αH,12,6-olide, 3'-hydroxy-genkwanin, HepG-2, HCT-116, MCF-7, MTT.

Introduction:

Artemisia is one of the largest and most widely distributed genera belonging to the family *Asteraceae*. This genus composed of about 500 diverse species distributed mainly in the temperate zones of Europe, Asia and North America. These species are perennial, biennial and annual herbs or small shrubs (Bora & Sharma, 2011; Wright, 2005). *Artemisia* species have a high economic value in several fields, as food plants and in the treatment of many diseases such as hepatitis, cancer, inflammation and infections by fungi, bacteria, and viruses. Furthermore, several species of *Artemisia* are used in folk medicine as anthelminthic, antispasmodic insecticidal, antiatherogenic, hepatoprotective, antihyperglycemic, antihypertensive and in traditional Chinese medicine for the treatment of gynecopathy, amenorrhea, bruise and rheumatic disease (Cho et al., 2015; Obolskiy, Pischel, Feistel, Glotov, & Heinrich, 2011; Saadali, Boriky, Blaghen, Vanhaelen, & Talbi, 2001; Stebbings, Beattie, McNamara, & Hunt, 2015). Previous phytochemical reports of the genus *Artemisia* reveal that the *Artemisia* species are rich of terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols and acetylenic compounds .(Alwahibi et al., 2016)Among these bioactive compounds; artemisinin is a highly oxygenated sesquiterpene, containing 1,2,4-trioxane ring

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which is responsible for its antimalarial activity (Brown, 2010).Artemisinin exerts not only antimalarial activity but also profound cytotoxicity against tumor cells (Efferth, 2007).

*Artemisia sieberi*or 'the desert worm wood' is locally knownas 'Shih' in Arabic countries and 'Dermaneh' inIran. *A. sieberi*a prominent perennial dwarf greywoolly shrub that grows in open fields, road sidesand waste ground of the Irano-Turanian steppesof Spain, North Africa and the Middle East, Sinai,Jordan, Syria, Iraq, Iran and Afghanistan (Migahid, 1978). *A. sieberi*is a shrubby, perennial land rough plant, with the height of 30-50cm spider web villies, and stems full of flowers straight rising from base. Leaves are oval and petiolate. Having petioles and full of rectangular banicule flowers, narrow and nearly hyacinth from (Bremer, 1993).

Experimental:

General Experimental Procedures:

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a JEOL ECA-600 spectrometer (600 MHz for ^{1}H and 150 MHz for ^{13}C, respectively). All chemical shifts (δ) are given in ppm units with a reference to TMS as an internal standard and coupling constants (*J*) are reported in Hz. EI‑MS was performed on a Finnegan LCQ ion trap mass spectrometer and HR-EI-MS experiments were performed on Fourier transform ion cyclotron mass spectrometer. EI-MS experiments were performed using a Thermo ISQ Single Quadrupole system). High performance liquid chromatography (HPLC) was performed on an Agilent pump equipped with an Agilent-G1314 variable wavelength UV detector at 254 nm and a semi-preparative reverse-phase column (Econosphere™, RP-C_{18}, 5 µm, 250 × 4.6 mm, Alltech, Deerfield, IL, USA). Silica gel 60 (230–400 mesh) was used for column chromatography. Pre-coated silica gel plates (Kieselgel 60 F_{254}, 0.25 mm) were used for TLC analyses. Spots were visualized by heating after spraying with 10% H_2SO_4.

Plant material:

The aerial parts of *Artemisiasieberi* were collected from the north area of Saudi Arabia(near Zahaw) in April 2014, identified by a team of expert taxonomists at the Herbariumunit, and deposited at the Herbarium of the College of Pharmacy, King Saud University,Riyadh, Saudi Arabia (voucher number 16375).

Extraction and isolation:

Aerial parts (1 kg) of the plants were powdered and extracted twice with aqueous methanol(80%) at room temperature. Combined extracts were evaporated in vacuo at 45 ºC to yielda dark brown residue ca. 85 g. Initial separation was performed by means of liquid–liquidextraction of the crude extract with *n*-hexane, CH_2Cl_2, EtOAc, and BuOH, respectively. TheCH_2Cl_2 fraction was subjected to silica gel column (6 × 120 cm) eluting with *n*-hexane (3L)followed by a gradient of *n*-hexane-CH_2Cl_2 up to 100% CH_2Cl_2 and CH_2Cl_2–MeOH up to15% MeOH (2L each of the solvent mixture) to afford eight major fractions. The *n*-hexane–CH_2Cl_2 (1:3) fraction was chromatographed on silica gel column (3 × 90 cm) elutedwith *n*-hexane–EtOAc (6:1, 4:1, 2:1) to afford **1** (25 mg) as fine white crystals. The CH_2Cl_2(100%) fraction was chromatographed on a Sephadex LH-20 column (3 × 90 cm) elutedwith *n*-hexane–EtOAc (6:1, 4:1, 2:1). Collected sub-fractions were re-chromatographedby RP HPLC using MeOH/H_2O (70–30%) to afford **2** (17 mg).

Antiproliferativeof isolated compounds

Chemicals Used:

Dimethyl sulfoxide (DMSO), MTT and trypan blue dye was purchased from Sigma (St. Louis, Mo., USA). Fetal Bovine serum, DMEM, RPMI-1640, HEPES buffer solution, L-glutamine, gentamycin and 0.25% Trypsin-EDTA were purchased from Lonza.

Cell lines:

MCF-7 cells (human breast cancer cell line), HepG-2 cells (human Hepatocellular carcinoma) and HCT-116 (colon carcinoma) were obtained from the American Type Culture Collection (ATCC, Rockville, MD). The cells were grown on RPMI-1640 medium supplemented with 10% inactivated fetal calf serum and 50µg/ml gentamycin. The cells were maintained at 37 ºC in a humidified

atmosphere with 5% CO_2 and were subcultured two to three times a week.

Cell viability assay:

For antitumor assays, the tumor cell lines were suspended in medium at concentration $5x10^4$ cell/well in Corning® 96-well tissue culture plates, then incubated for 24 h. The tested compounds were then added into 96-well plates (three replicates) to achieve twelve concentrations for each compound. Six vehicle controls with media or 0.5 % DMSO were run for each 96 well plate as a control. After incubating for 24 h, the numbers of viable cells were determined by the MTT test. Briefly, the media was removed from the 96 well plates and replaced with 100 µl of fresh culture RPMI 1640 medium without phenol red then 10 µl of the 12 mM MTT stock solution (5 mg of MTT in 1 mL of PBS) to each well including the untreated controls. The 96 well plates were then incubated at 37°C and 5% CO_2 for 4 hours. An 85 µl aliquot of the media was removed from the wells, and 50 µl of DMSO was added to each well and mixed thoroughly with the pipette and incubated at 37 °C for 10 min. Then, the optical density was measured at 590 nm with the microplate reader (SunRise, TECAN, Inc, USA) to determine the number of viable cells and the percentage of viability was calculated as [1-(ODt/ODc)]x100% where ODt is the mean optical density of wells treated with the tested sample and ODc is the mean optical density of untreated cells.The relation between surviving cells and drug concentration isplotted to get the survival curve of each tumor cell line after treatment with thespecified compound.The 50% inhibitory concentration (IC_{50}), the concentration required to cause toxic effects in 50% of intact cells, was estimated from graphic plots of the dose response curve for each conc. using Graphpad Prism software (San Diego, CA. USA) (Gomha, Riyadh, Mahmmoud, & Elaasser, 2015; Mosmann, 1983)**.**

Statistical Analysis:

All results are expressed as mean ± standard deviation (SD). Statistical differences between correlated samples were evaluated using Graphpad Prism software (San Diego, CA. USA).

Results and Discussion:

Structure Elucidation of compound 1 and 2

The molecular formula of compound **1**was established as $C_{15}H_{22}O_4$usingEI-MS data giving molecular ion peak at *m/z* 266; DBE = 5, suggesting the presence of five degrees of unsaturation.

The EI-MS mass spectral fragments at *m/z* 247.96 $[M\text{-}H_2O]^+$, 176.90 $[M - H_2O – CH(CH_3)COO]^+$, 106.97 $[M - H_2O – CH(CH_3)COO – CH(OH)CH_2CH{=}CHCH_3]^+$, indicating the presence of a carbonyl group, hydroxyl groups and lower fragments,suggesting the characteristic sesquiterpene nature of the isolated compound.

^{1}H-NMR, ^{13}C-NMR and 2D NMR in ($CDCl_3$) spectroscopic data (Table **1**) suggested the presence of a 5-membered lactone ring bounding to a germacradiene system.

The ^{13}C-NMR andDEPT spectra revealed the presence of 15 carbons: threequaternary, six methine, four methylene and two methylcarbons.

The ^{1}Hand ^{13}C-NMR spectra of compound **1**, revealed the presence of a proton signal at (δ_H 2.50, 1H, m, H-11) and carbon signal at (δ_C 42.1, C-11) which is typical for a saturated lactone ring, indicating the absence of an *exo*-methylene group at C-11.

There is no evidence of sp^2-hybridized methylene carbon peak and also the resonance of an upfield doublet (δ_H 1.29, 3H, d, J = 7.6 Hz) and (δ_C15.8), suggesting the presence of a methyl (Me-13) attached to C-11.

The ^{1}H-NMR spectrum indicated the presence of an *exo*-methylene group at (δ_H 5.01, 1H, d, J = 2.1 Hz, H-15a) and (δ_H 5.28, d, J = 2.1 Hz, H-15b).Also, indicated the presence of a double bond between C-9 and C-10, supporting by the presence of a doublet at (δ_H 5.12, d, J = 9.6 Hz) typical for an olefinic hydrogen, which was assigned to H-9.

The position of the double bond can also be confirmed by HMBC correlations from H-9 to C-1 at (δ_C 36.5) and C-14 at (δ_C /17.4), from Me-14 to C-1 at (δ_C 36.5), C-9 at (δ_C 128.1) and to C-10 at ($\underline{\delta_C}$ 138.0).

^{1}H-NMR spectrum showed the presence of an olefinic methyl group at (δ_H 1.49, 3H, s, Me-14); a secondary methyl group at (δ_H 1.30, 3H, d, J = 6.9 Hz, Me-13).

Two hydroxymethine groups at (δ_H 3.71, 1H, m, H-3) and (δ_H 4.18, 1H, t, J = 9.6 Hz, H-8), the deshielded chemical shift of H-3, H-8 indicated the presence of two hydroxyl groups at position C-3 and C-8.

The signal at (δ_H 2.04-2.06) for methylene protons H-1 appeared upfield compared to the previous compounds, which indicated the absence of the hydroxyl group at C-1 in compound **1**.

Two upfield methylene groups at (δ_H 1.89-1.91, 2H, m, H-2) and (δ_H 2.1, 1H, dd, J = 16.5, 4.4 Hz, H-5a; δ_H 2.85, 1H, dd, J = 16.5, 2.1 Hz, H-5b).

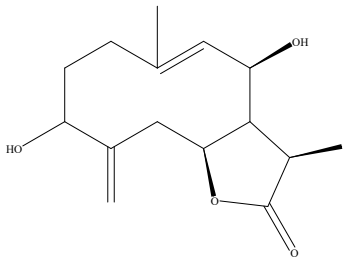
Also, showed two methineprotons at (δ_H 1.91, 1H, m, H-7) and (δ_H 2.50, 1H, m, H-11) as well as the signal at (δ_H 3.78, 1H, m), H-6.The H-6 downfield value indicated the presence of a geminal functionality oxygen atoms in the molecule belonged to a lactone ring.

The ^{13}C-NMR and DEPT spectra of compound **1** showed the resonance of15 carbons, which were ascribed to: two methyl carbons at (δ_C15.8 and 17.4 for C-13 and C-14), three methylene carbons at (δ_C 36.5, 35.9 and 42.1 for C-1, C-2 and C-5); one sp^2 methylene carbon at (δ_C113.4), corresponding to an *exo*methylenecarbon C-15; two methinecarbons at (δ_C 59.0 and 42.1 for C-7 and C-11) and one sp^{2}methinecarbon at (δ_C 128.1), C-9, three oxygenated methine carbons (δ_C 76.4, 83.8, and 71.8 for C-3, C-6 and C-8); three quaternary carbons (δ_C 151.8, 138.0 and 179.9 for C-4, C-10 and C-12), two of them are olefinic quaternary and the third belongs to carbonyl carbon of ester. These signals were determined to be quaternary carbons and did not exhibit ^{1}H/^{13}Cone-bond correlations at HMQC experiment and these signals disappear in DEPT 135 experiment.

Most important COSY spectrum of compound **1** showed cross-peaks between the signal at (δ_H 1.30, 3H, d, J = 7.6 Hz, Me-13) with the signal at (δ_H2.50, 1H, m), corresponding to the H-11 methine proton, the signal of olefinic proton (δ_H 5.12, d, J = 9.6 Hz, H-9) with the proton of (δ_H 4.18, IH, t, J = 9.6 Hz, H-8), the proton of (δ_H 4.18, IH, t, J = 9.6 Hz, H-8) with protons of H-7 and H-9.Additionally, there was cross-peaks between the signal at (δ_H2.1, 1H, dd, J = 16.5, 4.4 Hz, H-5a) with the signals at (δ_H 2.85, 1H, dd, J = 16.5, 2.1 Hz, H-5b) and (δ_H 3.78, 1H, m, H-6), the signal of (δ_H 2.85, 1H, dd, J = 16.5, 2.1 Hz, H-5b) with the proton of H-5a and H-6, the signal of *exo*-methylene proton (δ_H 5.01, 1H, d, J = 2.1 Hz, H-15a) with the proton of H-15b at (δ_H 5.28, d, J = 2.1 Hz), reciprocally (Table**1**).

On the basis of the HMBC correlations, the location of an *exo*-methylene group was assigned at position C-4/C-15 which was confirmed from the correlation of H_2-15 at (δ_H 5.01, 5.29), toC-3 at (δ_C 76.4), C-5 at (δ_C 42.1) and C-4 at (δ_C 151.8).

The location of the methyl groups were established with the aid of long-range hydrogen-carbon correlations from the HMBC experiment which indicated the long-range correlations of Me-14 at (δ_H1.49, 3H, s) with C-1 at (δ_C 36.5), an olefinic carbon C-9 at (δ_C 128.1), a quaternary carbon C-10 at (δ_C 138.0), confirming that the methyl group was attached to the quaternary carbon at C-10. HMBC have no correlations between Me-14 and C-5 which means no connectivity between C-5 and C-10.



Another important correlation from a secondary methyl group Me-13 at (δ_H 1.30 3H, d, J = 7.6 Hz)with C-11 at (δ_C 42.1), C-7 at (δ_C59.0) and a carbonyl carbon C-12 at(δ_C179.9), confirming that Me-13 was connected to C-11.

The position of the lactone ring was deduced from the presence of long range correlations of H-11 at (δ_H2.50, m) with(δ_C59.0, C-7), (δ_C71.8,C-8) (δ_C179.9, C-12) and methyl carbon (δ_C 15.8, C-13); H-7 at

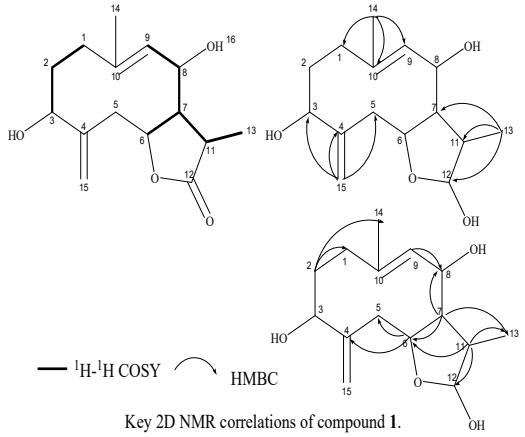
(δ_H1.91) with(δ_C 83.8, C-6), (δ_C71.8, C-8) (δ_C128.1, C-9) andH-6at (δ_H 3.78) with (δ_C151.8, C-4), (δ_C71.8, C-8), confirming that the lactone ring at C-6/C-7.

The above information led to the characterization of compound**1**as3α,8β-dihydroxygermacr-4(15),9-dien-6α,7β,11αH,12,6-olide.

The NMR data were in good agreement with previously published data (Gordon, Van Derveer, & Zalkow, 1981; Mohamed et al., 2017).

Position of 1	$\delta_H$mult.(*J* in Hz)	δ_C(Type)	**COSY** ^{1}**H↔**^{1}**H**	**HMBC** ^{1}**H↔**^{13}**C**
H_2-1	2.04-2.06 m	36.5 (CH_2)	H-2	C-2, C-3, C-10, C-14, C-9
H_2-2	1.89-1.91 m	35.9 (CH_2)	H-1, H-3	C-1, C-3, C-4,C-10, C-14
H-3	3.71 m	76.4 (CH)	H-2	C-4, C-5, C-15
H-4	…….	151.8 (C)	……	……
H-5_a	2.13 dd (16.5, 4.4)	42.1 (CH_2)	H-5_b, H-6	C-4, C-6, C-15
H-5_b	2.85 dd (16.5, 2.1)		H-5_a, H-6	C-4, C-6, C-15
H-6	3.78 m	83.8 (CH)	H-7, H-5_a, H-5_b	C-4, C-8
H-7	1.91 m	59.0 (CH)	H-11, H-8	C-5, C-8, C-9
H-8	4.18 t (9.6)	71.8 (CH)	H-7, H-9	C-11, C-7, C-10
H-9	5.12 d (9.6)	128.1 (CH)	H-8	C-14, C-1
H-10	……	138.0 (C)	……	……
H-11	2.50 m	42.1 (CH)	H-13, H-7	C-13, C-12, C-7, C-8
H-12	……..	179.9 (C)	……	……
H-13	1.30 d (7.6)	15.8 (CH_3)	H-11	C-11, C-7, C-12
H-14	1.49 s	17.4 (CH_3)	……	C-10, C-9, C-1
H-15_a	5.01 d (2.1)	113.0 (CH_2)	H-5_b	C-3, C-4, C-5
H-15_b	5.28 d (2.1)		H-5_b	C-3, C-4, C-5

Table 1:^{1}H (600 MHz), ^{13}C-NMR (150 MHz) DEPT, H^1-H^1 COSY and HMBC spectral data of compound **1**recorded in $CDCl_3$



Key 2D NMR correlations of compound **1**.

The molecular formula of compound **2** was established as $C_{16}H_{12}O_6$usingEI-MS data giving molecular ion peak at *m/z* 299.96 DBE = 11, suggesting the presence of eleven degrees of unsaturation.

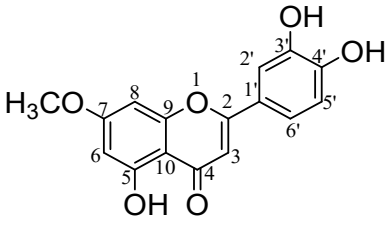
The EI-MS mass spectral fragments at *m/z* 285.42 $[M\text{-}CH_3]^+$, 282.89 $[M\text{-}H_2O]^+$, 190.99 $[M\text{- ph-}(OH)_2]^+$ and 158.15 ($[M\text{- ph-}(OH)_2, \text{-}OCH_3]^+$), confirming the presence of an oxygenated methyl, phenyl groups and hydroxyl groups.

The complete structure of compound **2** was elucidated by the use of ^{1}H-NMR and^{13}C-NMR which provided an evidence for a flavonoid skeleton (Table 2).

The ^{1}H-NMR (DMSO) and ^{13}C-NMR (DMSO) spectra of compound **2**showed the presence of signals at δ_H 12.99 (1H, s, OH-5), six sp^{2}methine groups at δ_H 7.55 (1H, d, *J* = 8.0 Hz, H-6'); δ_C 120.7 (C-6'), 7.52 (1H, s, H-2');δ_C110.4 (C-2'), 6.94 (1H, d, *J* = 12.0 Hz, H-5'); δ_C 116.2 (C-5'), δ_H 6.84 (1H, s, H-3);δ_C 103.5 (C-3), δ_H 6.5 (1H, s, H-8);δ_C 94.5 (C-8), δ_H 6.19 (1H, s, H-6),δ_C99.2 (C-6), one oxygenated methyl group δ_H 3.86 (3H, s,

OCH_3); δ_C 56.0 (4-OCH_3), nine tertiary sp^2 carbon atom atδ: 182.2 (C-4), 164.6 (C-7), 164.2 (C-2), 161.8 (C-5), 157.8 (C-9), 151.1 (C-4'), 148.4 (C-3'), 122 (C-1'), 104.1 (C-10). All these data were in good agreement with those of 3'-hydroxy-genkwanin.

The molecular weight suggested the occurrence of a further oxygen function which must be a hydroxyl, carbonyl and ether groups. The presence of seven oxygenated carbon atoms was confirmed by the presence of the seven signals atδ: 181.8 (C-4), 165.1 (C-7), 164.2 (C-2), 161.8 (C-5), 157.8 (C-9), 151.1 (C-4'), 148.2 (C-3').



(2)

Therefore, compound **2**is characterized as3'-hydroxy-genkwanin(Park et al., 2014; Zeng & Quesheng).

Position	$\delta_H$mult.(*J* in Hz)	δ_C(Type)
H-1	……	……
H-2	……	164.2 (C)
H-3	6.83, s	103.5 (CH)
H-4	……	182.2 (C)
H-5	……..	161.8 (C)
H-6	6.19, s	99.2 (CH)
H-7	……...	164.6 (C)
H-8	6.5	94.5 (CH)
H-9	…….	157.8 (C)
H-10	……...	104.1 (C)
H-1'	……..	122 (C)
H-2'	7.52 s	110.4 (CH)
H-3'	……..	148.4 (C)
H-4'	……	151.1 (C)
H-5'	6.94 d (12)	116.2 (CH)
H-6'	7.55 d (8)	120.7 (CH)
-OCH_3	3.86 s	56 (CH_3)

Table2:^{1}H (600 MHz), ^{13}C-NMR (125 MHz) and DEPT spectral data of compound **2**recorded in DMSO.

Antiproliferative activity:

To evaluate the antiproliferative activity of compound 1, their anti-proliferative potential against MCF-7 cells (human breast cancer cell line), HepG-2 cells (human Hepatocellular carcinoma) and HCT-116 (colon carcinoma) were assessed using a cell viability assay with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). The cells were treated at concentrations 500 µg/mL, 250 µg/mL, 125 µg/mL, 62.5 µg/mL, 31.25 µg/mL, 15.6 µg/mL, 7.8 µg/mL and 3.9 µg/mL for 24 h. The anticancer drug, cisplatin was used as a positive control. Compound 1showed IC_{50} (146 ± 3.5, 173 ± 4.6, 115 ± 3.4) *µg/ml*. respectively(Fig. 1-3) andcompound 2showed IC_{50}(13.6 ± 0.3, 22.5 ± 0.3, 15.4 ± 0.5) *µg/ml*. respectively(Fig. 4-6).

Conclusion:

Investigation of *Artimisiasieberi*affordeda 3*α*,8*β*-dihydroxygermacr-4(15),9-dien-6*α*,7*β*,11αH,12,6-olide and 3'-Hydroxy--genkwanin;have potential to be anti-cancer drugs.

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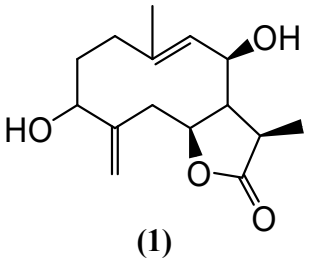
النشاط المقاوم للخلايا السرطانية لمركبين معزولين من نبات الأرتيميزيا سيبيري

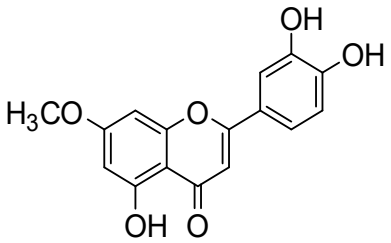
كانت النباتات الطبية و لازالت محط اهتمام العلماء بغية اكتشاف مواد طبيعية فعالة تستعمل في الطب و الصيدلة حيث أكثر من نصف سكان الكرة الأرضية يستعملون هذه الأدوية. وأكثر مواد التجميل رواجا مصنوعة من الموارد الطبيعية. يعتبر الأرتيميزيا من أشهر أجناس العائلة المركبة ، والذي يضم العديد من الأنواع من بينها أرتيميزيا سيبيري ، وهو شجيرة كثيفة معمرة تنبت في الحقول المفتوحة وجوانب الطرق والسهول في إسبانيا، وشمال أفريقيا، والشرق الأوسط، والأردن، وسوريا، والعراق، وإيران، وأفغانستان ، ويصل ارتفاعها ما بين 30-50 سم، وتستخدم أنواع الأرتيميزيا على نطاق واسع في الطب الشعبي.اشتملت الدراسة الفيتوكيميائية لنبات أرتيميزيا سيبريعلى استخلاص وفصل ووصف ما يحتويه من مواد فعالة حتى يمكن الاستفادة منها في التطبيقات البيولوجية والحيوية المختلفة. وقد تم فصل وتعريف مركبين في صورة نقية من نبات الأرتيميزيا سيبيري.

(1) 3α,8β-dihydroxygermacr-4(15),9-dien-6α,7β,11αH,12,6-olide.

(2) flavonoid 3'-hydroxy-genkwanin.



(1)



(2)

دراسة الفاعلية البيولوجية للمركبات المفصولة.

أولا : مقاومة بعض الخلايا السرطانية

تم تقييم المركبات المعزولة (1-2) بالنسبة لتأثيرها السام على ثلاثة أنواع من الخلايا السرطانية وهي MCF-7 (سرطان الثدي) وHCT116 (سرطان القولون) و HepG-2 (سرطان الكبد) وقد أثبتت الدراسة أن لهذه المركبات نشاطا مقاوماللخلايا السرطانية وذلك من خلال معرفة الحد الأدنى للتركيز (IC_{50}) القادر علي تثبيط نمو الخلايا السرطانية وقد وجد أن الحد الأدنى للمركبات المعزولة كالآتي:

بالنسبة للمركب (1) 146 ، 173 ، 115 ميكرو جرام لكل ملي

بالنسبة للمركب (2) 13.6 ، 22.5 ، 15.4 ميكرو جرام لكل ملي

وبالتالي نتوقع من اختبار السمية الخلوية أن المركبات المعزولة بتركيزات عالية من المحتمل أن تكون بمثابة أدوية مضادة للسرطان.