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Biochemical and biophysical properties of a novel homoisoflavonoid extracted from *Scilla persica* HAUSSKN

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ABSTRACT

In this study isolation and structural elucidation of a homoisoflavonoid, 3-(3′,4′-dihydroxybenzyl)-8-hydroxy-5,7-dimethoxychroman-4-one (Scillapersicone **1**), is reported from *Scilla persica* HAUSSKN. The structure was solved by a single crystal X-ray analysis. The unit cell parameters are $a = 11.7676\ (2)$ Å, $b = 20.1174\ (4)$ Å, $c = 7.8645\ (9)$ Å, $\beta = 93.544\ (2)°$, $V = 1858.23\ (7)$ Å^3, monoclinic space group $P2_1/c$ and four symmetry equivalent molecules in an unit cell. The structure was consistent with the UV, IR, 1D and 2D NMR, HRFAB-MS data. The optimized molecular geometry agrees closely that obtained from the single crystal X-ray crystallography. Furthermore, cytotoxicity of this compound was evaluated by MTT assay on AGS and WEHI-164 cancerous cell lines.

1. Introduction

Scilla persica HAUSSKN is a perennial herb belonging to the *Liliaceae* family [1]. It is known as a foodstuff and important plant in traditional medicine for promoting blood circulation, reducing inflammation, as an analgesic [2], and antibacterial agent [3]. Previous studies on *Scilla* species revealed triterpenoid [4], stilbenoids [5] and cardiac glycosides [6] as well as homoisoflavanones [7–11], which showed antibacterial and anti-angiogenic activities, and inhibited *in vitro* the growth and sporogenesis of several microorganisms [7,8,11,12]. Homoisoflavonoids purely represent a modification of the flavonoid-type skeleton. Feeding experiments showed that the biosynthesis of 3-benzylchroman-4-ones consists in modification of the C_6—C_3—C_6 chalcone/flavonoid pathway by insertion of an extra carbon atom [13]. These compounds were mainly discovered from plants belonging to the *Liliaceae* family and a few other plant species [14], and they were recorded to be responsible for biomedical activities of these plants, such as antioxidant activity [15–17], cytotoxic activity [18–20], inhibition of platelet aggregation [21], cough relief [22], hyperglycemia [23], anti-fungal [12], anti-inflammatory, anti-allergic, antihistaminic and angioprotective activities. They have been also detected as potent phosphodiesterase inhibitors [11,24,25]. In this paper, we report the isolation, structural elucidation, and physical chemistry of a novel homoisoflavonoid, Scillapersicone **1**, which was obtained from fresh bulbs of *S. persica* (Figs. 1 and 2). Moreover, the cytotoxicity of this compound on AGS and WEHI-164 cancerous cell lines is reported.

Abbreviations: AGS, Adenocarcinoma Gastric Stomach; CC, Column Chromatography; CCDC, Cambridge Crystallographic Data Center; DFT, Density Functional Theory; DMEM, Dulbecco's Modified Eagle's Medium; FBS, Fetal Bovine Serum; FMO, Frontier Molecular Orbital; HR-EIMS, High Resolution Electron Impact Mass Spectroscopy; HMBC, Heteronuclear Multiple Bond Correlation; HOMO, Highest Occupied Molecular Orbital; HSQC, Heteronuclear Single Quantum Coherence; LUMO, Lowest Unoccupied Molecular Orbital; VLC, Vacuum Liquid Chromatography; MEP, Molecular Electrostatic Potential; MEP, Molecular Electrostatic Potential; MPA, Mullikan charge analysis; MTT, 3-[4,5-dimethylthiazol-2-yl]2,5-iphenyltetrazolium Bromide; NBO, Natural Bond Orbital; WEHI-164, Skin From Mouse Fibrosarcoma.

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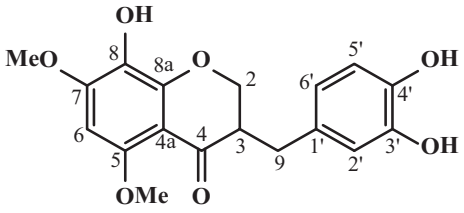

Fig. 1. Chemical structure of Scillapersicone (**1**).

2. Materials and methods

2.1. Plant material

Fresh bulbs of *Scilla persica* HAUSSKN were collected in the village of Valliv from Sardasht, West Azerbaijan Province, Iran, in March 2012 at an altitude of 1700–1800 m. The plant was identified by Afsaneh Kolbadi (Agriculture and Natural Resources Research Center, Sari, Iran), and a voucher specimen (No. 6334) was deposited in the Herbarium of the same institute.

2.2. Instruments and materials

UV spectra were obtained in MeOH using a Shimadzu UV-PC 2501 spectrometer. IR spectra were recorded on a Perkin-Elmer FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were measured by a Bruker (400 MHz for ^{1}H and 100 MHz for ^{13}C in CD_3COCD_3) spectrometer with TMS as an internal standard. Melting points were determined by an electrothermal melting point apparatus. HRFAB-MS spectra were acquired using a Shimadzu AXIMA-CFR Plus mass spectrometer. Silica gel (70–230, 230–400 mesh, silica gel for TLC and Sephadex LH-20, Merck) were used for VLC and CC. TLC was performed on Merck F_{254} silica gel plates (10 × 10 cm). Spots were detected by spraying anisaldehyde-H_2SO_4 reagent followed by heating. X-ray diffraction experiments were performed on a Gemini four circle kappa diffractometer of Agilent Technologies using mirrors-collimated Cu Kα radiation ($\lambda = 1.5418$ Å).

2.3. Extraction and isolation of Scillapersicone

The bulbs (500 g) of *S. persica* were crushed and extracted with $CHCl_3$ (3 × 4 L, r.t. for 24 h). The solvent was removed under reduced pressure at 50 °C to afford 6 g of a light brown gum. A portion (3 g) was fractionated on a VLC eluted with n-Hexane–EtOAc–MeOH [100:0:0, 95:5:0, 90:10:0, 80:20:0, 70:30:0, 60:40:0, 40:60:0, 10:90:0, 0:90:10, 0:80:20, 0:70:30 and 0:50:50 (v/v) at 0.5, 1.2, 0.4, 0.65, 0.65, 1.0, 1.4, 1.4, 1.2, 0.7, 0.6 and 0.8 L, respectively] to obtain fractions Fr.1–Fr.12 after pooling according to their TLC profiles. Fr.8 (140 mg), obtained from the elution with n-Hexane–EtOAc–MeOH (10:90:0), was consequently subjected to CC on silica gel using $CHCl_3$, and then on Sephadex LH-20 column using MeOH, gave compound **1** (89 mg, with $R_f = 0.7$ for $CHCl_3$/MeOH: 9/1).

2.3.1. Scillapersicone (*1*)

Yellowish needles from MeOH; mp 102–104 °C; UV (MeOH) λ_{max} (log ε) 214 (sh), 279 (4.88), 350 (4.4) nm; IR (KBr) λ_{max} 3412 (OH), 3196, 1664 (C=O), 1620 (C=C), 1506 (aromatic C=C), 1404, 1332, 1235, 1153, 1111 (C—O) cm^{-1}; EIMS *m/z* 346 $[M]^+$ (50), 224.1 (19), 197.1(17), 154.1 (99), 136.1 (68), 123.1 (22), 79.0 (31), 69.1 (18); HRFAB-MS *m/z* 347.1145 $[M+H]^+$ (calcd for $C_{18}H_{19}O_7$, 347.1131); ^{1}H and ^{13}C NMR spectroscopic data are shown in Table 2.

2.4. X-ray crystal structure analysis of Scillapersicone (*1*)

A single crystal with the dimensions 0.26 mm × 0.17 mm × 0.08 mm of **1** was chosen for X-ray diffraction study. Crystallographic measurements were done at 120 K on a Gemini Atlas CCD diffractometer with mirror collimated Cu Kα radiation. The crystal structure was solved by charge flipping methods [26] and refined with the *Jana2006* program package [27] by full-matrix least-squares technique on F^2. All hydrogen atoms were discernible in difference Fourier maps and could be refined to reasonable geometry. According to common practice, the hydrogen atoms connected to carbon atoms were kept in ideal positions during the refinement. The isotropic atomic displacement parameters of hydrogen atoms were evaluated as $1.2U_{eq}$ of the parent atom. Crystallographic data and details of the data collection and structure solution and refinements are listed in Table 1. Selected bond distances and angles are listed in Tables 3 and 4, respectively. Crystallographic data (excluding structure factors) for the structure reported in this paper has been deposited with the Cambridge Crystallographic Data Center, CCDC 988289. Copies of the data can be obtained free of charge on application to The Director, CCDC,

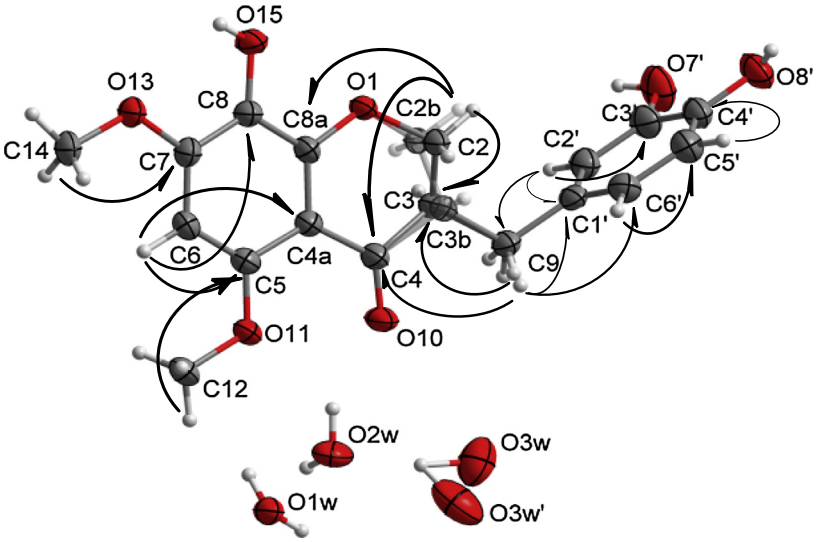

Fig. 2. Key HMBC correlations of Scillapersicone on the ORTEP diagram.

Table 1
Crystallographic data of Scillapersicone (**1**).

Empirical formula	$C_{18}H_{18}O_7{\cdot}3H_2O$
Mr	400.4
Crystal system	Monoclinic
Space group	$P2_1/c$
a, b, c (Å)	11.7676 (2), 20.1174 (4), 7.8645 (2) Å
β (°)	93.544 (2)
V (Å^3)	1858.23 (7)
Z	4
D_{calc} (g cm^{-3})	1.4307
T (K)	120.1 (1) K
μ (mm^{-1})	1.006
F (000)	848
θ (°)	3.76–66.99
Crystal size (mm)	0.26 × 0.17 × 0.08 mm
Measured reflections	30567
Independent reflection	3284
R_{int}	0.041
S	2.21
$R[F^2 > 2\sigma(F^2)]$	0.050
$wR(F^2)$	0.139
$\Delta\rho_{max}$(e Å^{-3})	0.24
$\Delta\rho_{min}$ (e Å^{-3})	−0.29

Table 2
NMR spectroscopic data in CD_3COCD_3 for Scillapersicone (**1**).

Position	δ_c	δ_H (HSQC) (J in Hz)	HMBC
2a	69.17	4.14, dd (8.0 11.2)	H-9a, H-9b
2b		4.33, dd (4.4 11.2)	
3	48.64	2.73, m	H-9a, H-9b
4	190.11	–	H-2a, H-2b, H-9a, H-9b
4a	105.53	–	H-6
5*	152.89	–	H-6, 5-OMe
6	90.49	6.39, s	-
7*	154.67	–	H-6, 7-OMe
8	128.20	–	H-6
8a	150.34	–	H-2a, H-2b
9a	31.77	2.54, dd (10.0 13.6)	H-2b, H-2′, H6′
9b		3.06, overlapped with H_2O	
1′	130.46	–	H-9a, H-9b, H-2′, H-5′
2′	115.23	6.79, d (2.0)	-
3′	145.08	–	H-5′
4′	143.63	–	H-2′, H-6′
5′	116.05	6.78, d (7.6)	H-9a, H-9b, H-6′
6′	120.34	6.61, dd (1.6, 8.0)	H-9a, H-9b, H-5′
C5—OMe	55.60	3.83, s**	–
C7—OMe	55.60	3.94, s**	–
8-OH	–	7.81, broad signal	–
3′-OH	–	7.81, broad signal	–
4′-OH	–	7.81, broad signal	–

*, **: The assignments may be interchanged.

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2.5. Computational procedures

The relaxed geometries, electronic properties, FMO, and quantum molecular descriptor of the crystal were calculated, employing the DFT calculations using Gaussian 98 program package [28]. The structure of Scillapersicone were finally optimized at B3LYP/6-311++G** and HF/6-311++G** level of theory to determine the relative geometric structures, molecular orbital energy, and other electronic properties in its ground state.

2.6. Cell lines and reagents

Two cell lines including WEHI-164 and AGS (both from Pasteur Institute, Tehran, Iran) were grown in DMEM (GIBCO, USA) containing 10% FBS (GIBCO, USA) at 37 °C in a humidified atmosphere of 5% CO_2.

Table 3
Comparison of bond distances of experimental and optimized molecular structure for Scillapersicone.

Atomic bond lengths (Å)	Crystallographic data	Basis sets	
		B3LYP/6-311++G**	HF/6-311++G**
C5′—C4′	1.378 (3)	1.389	1.375
C4′—C3′	1.392 (3)	1.406	1.397
C4′—O8′	1.373 (3)	1.367	1.350
C3′—C2′	1.394 (3)	1.390	1.377
C1′—O7′	1.359 (3)	1.366	1.348
C2′—C1′	1.389 (3)	1.402	1.397
C9—C3	1.528 (7)	1.541	1.535
C9—C3b	1.511 (5)		
C3—C2	1.509 (8)	1.520	1.517
C3b—C2b	1.505 (6)		
C3—C4	1.554 (7)	1.539	1.527
C3b—C4	1.542 (5)		
C2—O1	1.463 (5)	1.432	1.407
C2b—O1	1.449 (4)		
C8a—O1	1.362 (2)	1.354	1.334
C8a—C8	1.383 (3)	1.396	1.386
C8a—C4a	1.406 (3)	1.419	1.404
C8—C7	1.392 (3)	1.394	1.379
C7—O13	1.365 (2)	1.367	1.345
C6—C5	1.385 (3)	1.395	1.384
C5—C4a	1.423 (3)	1.422	1.410
C5—O11	1.359 (2)	1.352	1.331
C4a—C4	1.462 (3)	1.482	1.489
C4—O10	1.225 (2)	1.217	1.190
C14—O13	1.431 (2)	1.425	1.404
C12—O11	1.440 (2)	1.419	1.398

Table 4
Comparison of bond angles of experimental and optimized molecular structure for **1**.

Atomic bond angles (°)	Crystallographic data	Basis sets	
		B3LYP/6-311++G**	HF/6-311++G**
C6′—C5′—C4′	120.00 (2)	121.02	121.11
C1′—C9—C3	116.0 (3)	113.85	113.91
C1—C9—C3b	113.8 (2)		
C9—C3—C2	113.0 (5)	112.66	113.16
C9—C3b—C2b	115.0 (4)		
C9—C3—C4	108.75 (4)	111.94	111.71
C9—C3b—C4	110.37 (3)		
C3—C2—O1	108.01 (4)	111.24	110.65
C3b—C2b—O1	109.7 (3)		
C3—C4—O10	118.3 (3)	120.30	120.63
C3b—C4—O10	120.1 (2)		
C2—O1—C8a	113.4 (2)	116.08	117.25
C2b—O1—C8a	116.18 (18)		
O1—C8a—C8	114.14 (16)	115.22	115.55
C8a—C8—O15	118.12 (17)	119.84	119.60
C8—C8a—C4a	122.74 (17)	121.69	121.91
C7—C8—O15	123.58 (17)	121.46	121.85
C7—O13—C14	117.58 (15)	119.31	120.87
C5—C4a—C4	124.34 (16)	122.98	123.18
C5—O11—C12	117.82 (15)	119.42	121.06
C4a—C4—C3	115.6 (3)	114.98	114.82
C4a—C4—C3b	113.8 (2)		

2.7. MTT cytotoxicity assay

Cell viability was measured by MTT assay according to the manufacturer's instructions (Sigma–Aldrich, USA). Briefly, AGS & WEHI-164 cells were seeded onto 96-well plates and allowed to adhere and grow overnight in 200 μl DMEM medium. The cells were then incubated with fresh medium containing serial concentrations

(0–200 μM) of Scillapersicone dissolved in 1% DMSO for 48 h. Afterward, 20 μl of 5 mg/ml MTT was added to each well and incubated for additional 4 h at 37 °C followed by addition of 200 μl of DMSO [29]. The relative cell viability was determined at 540 nm by a 96-well plate reader (Biorad-USA) and the concentration, at which cell growth inhibition by 50% (IC_{50}) was determined by standard curve method [30]. Each experiment was carried out in triplicate wells and repeated at least three times.

3. Results and discussion

3.1. Structure elucidation of Scillapersicone (1)

Scillapersicone (**1**) was obtained as yellowish needles with molecular formula of $C_{18}H_{18}O_7$, as established by HRFAB-MS (*m/z* 347.1145 $[M+H]^+$; calcd. 347.1131). The IR absorptions at 3412 cm^{-1} and 1664 cm^{-1} implied the existence of hydroxyl and carbonyl groups, respectively. The ^1H and ^{13}C NMR chemical shifts together with the HSQC and HMBC results are summarized in Table 2. The ^1H NMR spectrum together with the HMBC spectrum showed the presence of a singlet aromatic proton signal at δ_H 6.39 (δ_C 90.49) and 1,3,4-substituted benzene ring signals [δ_H 6.61, dd, J = 1.6, 8.0 Hz (δ_C 120.34); δ_H 6.78, d, J = 7.6 Hz (δ_C 116.05); δ_H 6.79, d, J = 2.0 Hz (δ_C 115.23)], two sets of geminal proton signals [δ_H 2.54, dd, J = 10.0, 13.6 Hz and δ_H 3.06 (δ_C 31.77); δ_H 4.13, dd, J = 8.0, 11.3 Hz and 4.33, dd, J = 4.4, 11.2 Hz (δ_C 69.17)], both of which are coupled with the methine proton at δ_H 2.73 (δ_C 48.64), and two methoxy groups at δ_H 3.83 and 3.86 (each 3H, s). The ^{13}C NMR spectrum displayed 17 carbon signals including a carbonyl (δ_C 190.11), six oxygenated aromatic, six aromatic, two methylene (one of them is oxygenated), and a methine carbon signals. However, the two methoxy protons showed HSQC correlations to the same carbon at δ_C 55.60 indicating Scillapersicone has 18 carbons as revealed by HRFAM-MS. These spectral data, especially the presence of oxygenated methylene (δ_C 69.17) – methine (δ_C 48.64) – metylene (δ_C 31.77) sequence, together with the molecular formula indicated that this compound should possess a homoisoflavone structure (16 carbons) with two methoxy groups and three hydroxy groups. The location of the functional groups and the assignment of the NMR signals were achieved by the HMBC spectra. The HMBC correlations are indicated in Table 2 and key correlations were indicated in Fig. 2. The oxygenated methylene–methine–metylene carbons were assigned to C-2 (δ_C 69.17), C-3 (δ_C 48.64) and C-9 (δ_C 31.77) of the homoisoflavone skeleton, respectively, and the carbonyl carbon (δ_C 190.11) was placed at C-4 from the HMBC correlations from H-2 and H-9. The protons and carbons of the ring B were identified starting from the H-9 protons (δ_H 2.54 and δ_H 3.06). For the ring A, the carbon at δ_C 150.34 was placed at C-8a because of the HMBC from H-2, and the proton (δ_H 6.39) bearing carbon at δ_C 90.49 was placed at C-6, which accounted for all the HMBC correlations observed for the ring A. From these spectral data, the structure of **1** was elucidated as 3-(3′,4′-dihydroxybenzyl)-8-hydroxy-5,7-dimethoxychroman-4-one (Fig. 1). As this is the first report of this compound, **1** was named as Scillapersicone. This structure was confirmed by single crystal X-ray analysis. A single crystal of **1** grown from MeOH solution was used for the analysis. The crystal data were summarized in Table 1. The crystal structure of **1** with the atom-numbering scheme is presented in Fig. 2. The crystallographic data were shown in Tables 3–5 in comparison with those from theoretical calculations.

The asymmetric unit consists of one molecule of **1** and three molecules of water. One molecule of lattice water is disordered, as well as the aliphatic part of **1**. The C4—O10 bond length of 1.225 (2) Å matches the value for a double bond C=O, while the C5—O11 (1.359 (2)), C7—O13 (1.365 (2)), C8—O15 (1.361 (2)), C3′—O7′ (1.369 (2)) and C4′—O8′ (1.373 (3)) correspond to the value for single bonds C—O. The dihedral angles between the aromatic rings (C1′—C2′—C3′—C4′—C5′—C6′ and C4a—C5—C6—C7—C8—C8a) is 89.39 (10)°. The structure incorporates a plenty of hydrogen donors and acceptors, forming a well-developed system of hydrogen bonds, with significant impact on structure packing. All three hydroxyl groups serve as donor of hydrogen bonds, but only two of them are acceptors as well. The water molecules play the important role of connecting the molecules of **1** as two of them are forming four hydrogen bonds and the disordered water molecule forms three. The interaction of H1o2w and oxygen atoms O10 and O11 may resemble a bifurcated hydrogen bond but given the unbalanced angles (O2w—H1o2w—O10 = 152° and O2w—H1o2w—O11 = 129°) it is most likely a standard hydrogen bond with a little contribution of a short contact interaction forced by structural geometry.

Table 5
The table of hydrogen bonds of **1**.

D—H···A	*D*—H (Å)	H···A (Å)	*D*···A (Å)	*D*—H···A (°)
O15—H1O15—O1w^{i}	0.86 (2)	1.86 (2)	2.651 (2)	153 (2)
O7′—H1o7′—O3w^{ii}	0.86 (2)	1.85 (3)	2.686 (4)	163 (3)
O7′—H1o7′—O3w′^{ii}	0.86 (2)	1.64 (3)	2.479 (19)	164 (3)
O8′—H1o8′—O2w^{iii}	0.86 (2)	1.86 (2)	2.707 (3)	168 (3)
O1w—H1o1w—O7′^{iv}	0.860 (18)	1.943 (17)	2.786 (2)	166 (2)
O1w—H2o1w—O1^{ii}	0.86 (2)	2.253 (19)	2.8964 (19)	131.6 (18)
O1w—H2o1w—O15^{ii}	0.86 (2)	2.14 (2)	2.900 (2)	147 (2)
O2w—H1o2w—O10	0.860 (9)	1.930 (10)	2.721 (2)	152 (3)
O2w—H1o2w—O11	0.860 (9)	2.37 (2)	2.988 (2)	129 (2)
O2w—H2o2w—O1w	0.86 (2)	1.91 (2)	2.756 (2)	167 (3)

Symmetry code: (i) 1 − *x*, −1/2 + *y*, 1/2 − *z* (ii) *x*, 1/2 − *y*, 1/2 + *z* (iii) 2 − *x*, −1/2 + *y*, 1/2 − *z* (iv) 2 − *x*, 1/2 + *y*, 3/2−.

In conclusion, to the best of our knowledge, this is a first report of isolation and structural elucidation of Scillapersicone (**1**) from an endemic species, *S. persica,* from Iran. Although some other similar structures have been reported from other *Scilla* species like two homoisoflavonoids, 3-(4-hydroxyoxybenzyl)-5,7-dimethoxy-6-hydroxychroman-4-one and 3-(4-methoxybenzyl)-6,7-dimethoxy-5-hydroxychroman-4-one from *S. nervosa* [31], Scillapersicone (**1**) showed new substitutions of oxygenated groups on overall structure.

3.2. Cytotoxic activities

We expected this natural product could affect cancer cells. Thus, we employed two cancerous cell lines, AGS and WEHI-164, to evaluate the toxicity of **1** in a time- and dose-dependent manner. Scillapersicone (**1**) showed significant *in vitro* cytotoxic activity, with IC_{50} values of 25 and 28 μM against AGS and WEHI-164 cells, respectively. These IC_{50} values of **1** were lower compared to that against normal fibroblast cells (120 μM). This indicates the potential usefulness of **1** as a novel anti-cancer therapeutic. Nguyen et al. reported significant cytotoxic activity of homoisoflavonoids [18], and Yen et al. also described that homoisoflavonoids were efficient cytotoxic agents [20].

3.3. Molecular geometry

Theoretical calculations were carried out with the hybrid B3LYP functional and HF level approximation. The high level Gaussian type orbitals (GTOs) basis set, 6-311++G** was performed for all the calculations. The obtained geometrical parameters are listed in Table 3–5 along with the results of single-crystal X-ray crystallography. Molecular structure of **1** obtained by theoretical calculations is shown in Fig. 3.

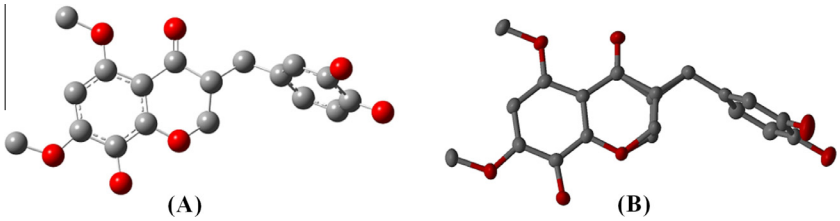

Fig. 3. (A) Theoretical and (B) Experimental molecular structure for Scillapersicone.

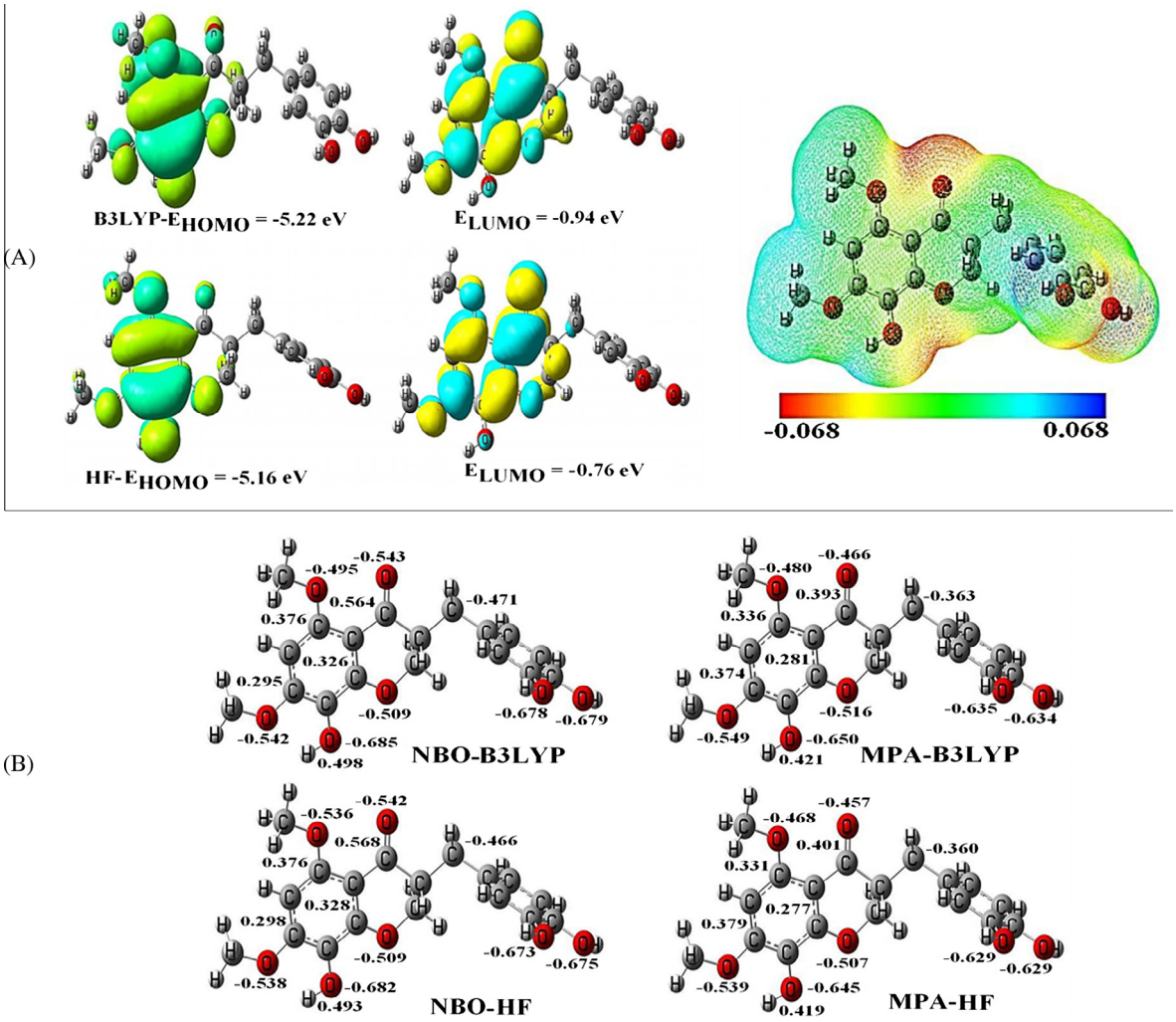

Fig. 4. (A) The HOMO and LUMO, (B) The NBO and MPA calculated for **1** at the B3LYP/6-311++G** and HF/6-311++G** methods.

3.4. HOMO and LUMO analysis

The electronic densities in the HOMO and LUMO for this molecule at the B3LYP/6-311++G** and HF/6-311++G** levels were studied. Our calculation displays that the energy levels of HOMO and LUMO are respectively −5.22 and −0.94 eV at the B3LYP method and −5.16 and −0.76 eV at the HF method. As shown in Fig. 4A, the HOMO in this molecule is primarily located upon the carbon atoms of the phenyl ring containing methoxy groups, while LUMO is situated on the methoxy and carbonyl group atoms and the carbon atoms of the phenyl ring containing C=O bond. The HOMO–LUMO energy separation has been applied as an indicator of kinetic stability of the system [32]. The energy gap (E_{HOMO}–E_{LUMO}) of this natural compound is calculated of as 4.28 and 4.40 eV at the B3LYP and HF methods, respectively. This small energy gap reveals a low kinetic stability and high chemical reactivity because it is energetically unfavorable to append electrons to a high-lying LUMO or to draw out electrons from a low-lying HOMO [32]. The Fermi energy level (E_{FI}) of this molecule at the B3LYP and HF methods are about −3.08 and −2.96 eV, respectively. The MEP and NBO plotted in Fig. 4B shows that oxygen atoms are negatively charged (red color) while the hydrogen atoms of hydroxyl groups are positively charged (blue color) in the molecule. As shown in Fig. 4A, some charge is transferred from H atoms (electropositive atom) to O atoms (electronegative atom) of the molecule.

The quantum molecular descriptors for **1** were determined as follows:

Table 6
The chemistry-physical properties of Scillapersicone computed using DFT at the B3LYP/6-311++G** and HF/6-311++G** basis sets. The parameters are units of eV.

Molecular parameter	ε_{HOMO}	ε_{LUMO}	$\Delta\varepsilon$	D_M (Debye)	E_F (μ)	η	S	ω	χ	ΔN_{max}	HF
B3LYP	−5.22	−0.94	4.28	5.776	−3.08	2.14	1.07	2.22	3.08	1.44	−1223.62430
HF	−5.16	−0.76	4.40	5.733	−2.96	2.20	1.48	1.99	2.96	1.35	−1216.41473

$$\mu = -\frac{I+A}{2}$$

$$\chi = -\mu$$

$$\eta = \frac{I-A}{2} \quad \text{and/or} \quad \eta = \frac{E_{HOMO} - E_{LUMO}}{2}$$

$$S = \frac{1}{2\eta}$$

$$\omega = \frac{\mu^2}{2\eta}$$

$$\Delta N_{max} = -\frac{\mu}{\eta}$$

where I ($-E_{HOMO}$) is the energy of the Fermi level and A ($-E_{LUMO}$) is the first given value of the conduction band. The electronegativity (χ) is determined as the negative of chemical potential (μ), the hardness (η), the global softness (S), the electrophilicity index (ω) and the maximum amount of electronic charge (ΔN_{max}) can be approximated using the Koopmans' theorem. These theoretical values of **1** are given in Table 6 [32–34].

4. Concluding remarks

A homoisoflavonoid, named Scillapersicone (**1**), was isolated from the medicinal plant *S. persica* HAUSSKN. The structure was established by spectroscopic methods and X-ray crystallographic analysis. The molecular geometry was also investigated with theoretical calculations using the B3LYP and HF methods with the 6-311++G** level of theory, yielding results close to the experimental data obtained from X-ray crystallography. Many homoisoflavonoids have been isolated from *Liliaceae* family as well as *Scilla* and *Muscari* species. They may therefore serve as chemical markers for characterization of the *Scilla* genus. The low energy gap of **1** can caused to efficient cytotoxic activity, and this indicates the potential usefulness of **1** as a novel anti-cancer therapeutic. To document this possibility, we are going to study the molecular aspects of its anti-cancer properties in our future research.

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