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## Chemical composition and anti-proliferative activity of the essential oil of *Coriandrum sativum* L

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### Abstract

The aerial parts of *Coriandrum sativum* were collected from the Yovon region of Tajikistan. The essential oil was obtained by hydrodistillation and analyzed by gas- chromatography - mass spectrometry (GC-MS). *In-vitro* cytotoxicity of the essential oil was determined for three different human tumor cell lines using the MTT method. Fifty-five different compounds were identified in the oil accounting for 99.4% of the composition. The main constituents of the essential oil were aliphatic aldehydes and alcohols such as (2*E*)-dodecenal(16.5%), decanol(14.9%), decanal (11.3%), tetradecanol (9.2%), (2*E*)-decene-1-ol (7.4%), (8*Z*)-undecenal (6.2%), and dodecanal (4.4%).The essential oil showed cytotoxic activity against Caco-2, CCRF-CEM and CEM/ADR 5000 tumor cell lines with IC<sub>50</sub> values of 86.8, 16.5 and 38.5 µg/mL, respectively. The hemolytic activity (IC<sub>50</sub>) of the essential oil against red blood cells (RBC) was 2.3 mg/mL.

**Keywords:** Coriandrum sativum; (2*E*)-Dodecenal; Decanol; Essential Oil Composition; Cytotoxicity

### 1. Introduction

*Coriandrum sativum* L. commonly known as coriander or cilantro and Chinese parsley is an annual herb in the family Apiaceae. It is native to the eastern Mediterranean region and western Asia [1]. *C. sativum* has been cultivated as a spice almost worldwide for centuries. In traditional medicine, it is used mainly for the treatment of appetite deficit and digestive problems. The fruits have been used since ancient times for the treatment of wounds and burns [1]. *C. sativum* is an important spice crop, it has antioxidant properties due to containing active phenolic acid compounds, including caffeic and chlorogenic acids [2]. The oil serves as counterirritant in painful joints, rheumatism, and menstrual disorders [1]. The previous pharmacological studies revealed that it possessed anxiolytic, antidepressant, sedative-hypnotic, anticonvulsant, memory enhancement, improvement of orofacial dyskinesia, neuroprotective, antibacterial, antifungal, anthelmintic, insecticidal, antioxidant, cardiovascular, hypolipidemic, anti-inflammatory, analgesic, antidiabetic, mutagenic, antimutagenic, anticancer, gastrointestinal, deodorizing, dermatological, diuretic, reproductive, hepatoprotective, detoxification and many other pharmacological effects [3-5].

The composition of the essential oil of *C. sativum* has been intensively studied and several differences between the oils are apparent. The major oil constituents reported include linalool [6-8], geranyl acetate [9], 2-decenoic acid [7], (2*E*)-dodecenol (17.8%), decanal (15.3%), and (2*E*)-decenol (11.9%) [10]. The content of essential oils can be affected by various factors, including environmental, cultivation, genetic and ontogenetic [7].

Avicenna recommended the combinations of fresh *C. sativum* plant and honey for treatment of tumors [11]. The anticancer, antitumor and immuno modulating activities of aqueous and methanol extracts of *C. sativum* has been investigated *in vitro* [3, 12, 13]. The ethyl acetate extract of *C. sativum* roots showed the highest anti-proliferative activity on MCF-7 cells (IC<sub>50</sub> = 200 µg/mL) [3].

To our knowledge, this is the first report of the chemical composition and anti-proliferative activity of the essential oil of *C. sativum* L. from ornamental plants grown in Central Asia (Tajikistan).

## 2. Materials and methods

### 2.1 Plant material

*C. sativum* plant materials (aerial parts) were collected from a garden in Yovon region, Tajikistan in 10.06.2014, during a harvesting period of the plant. Voucher specimens of *C. sativum* have been deposited in the Institute of Pharmacy and Molecular Biotechnology, Heidelberg University (accession number IPMB P8479).

### 2.2 Essential oil extraction

Fresh plant material of *C. sativum* was used to obtain essential oils by hydrodistillation using Clevenger type apparatus. The yield of the essential oil was 0.67%.

### 2.3 Gas- chromatography – mass spectrometry (GC-MS) analysis

The essential oil of *C. sativum* was analyzed by GC-MS using a Shimadzu GCMS-QP2010 Ultra operated in the EI mode [(electron energy = 70eV), scan range = 3.0 scans/sec], and GC-MS solution software. The GC column was DB-5 fused silica capillary column with a (5% phenyl)-polymethyl siloxane stationary phase a film thickness of 0.25 mm. The carrier gas was helium with a column head pressure 80 psi and flow rate of 1.37 mL/min. Injector temperature was 250 °C, the ion source temperature 200°C, and increase in temperature rate 2 °C/min to 260 °C. The GC oven temperature was programmed for 50 °C initial temperature, increase in rate 2 °C/min to 260 °C. A 5% w/v solution of the sample in CH<sub>2</sub>Cl<sub>2</sub> was prepared and 0.1 µL was injected in splitting mode (30:1).

Identification of the oil components was based on their retention indices determined by reference to a homologous series of *n*-alkanes (Kovats retention index), and by comparison of their mass spectral fragmentation patterns with those reported in the literature [14], and stored in the MS library.

### 2.4 Cytotoxicity assay with 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)

The potential cytotoxic effects of the essential oil of *C. sativum* in three human tumor cell lines (Caco-2, CCRF-CEM and CEM/ADR 5000) were assayed by the MTT assay. The cells were seeded at a density of  $2 \times 10^4$  cells/well (MCF-7, HeLa and Caco-2) and  $3 \times 10^4$  cells/well (CCRF-CEM and CEM/ADR5000). The essential oil was serially double diluted in DMSO from 5 mg/mL to 0.01 mg/mL, and 100 µL liquid of each concentration was applied to the wells of a 96-well plates. Cells were incubated with the samples for 24 h (MCF-7, Caco-2 and HeLa) and 48 h (CCRF-CEM and CEM/ADR5000) before the medium was removed and replaced with fresh medium containing 0.5 mg/mL 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT). The formazan crystals were dissolved in DMSO 4 h later; the absorbance was measured at 570 nm with a Biochrom Asys UVM 340 Microplate Reader. Doxorubicin was used as positive control.

### 2.5 Hemolytic activity of essential oil of *C. sativum*

The hemolytic activity was investigated by incubating 20 µL of serially diluted essential oil of *C. sativum* in phosphate-buffered saline (PBS; 400, 200, 100, 50, 25, 12.5, 6.25, and 3.12 µg/mL) with 80 µL of a suspension of 5% red blood cells

(human O+) for 1h at 37 °C in assay tubes. The reaction was slowed by adding 200 µL of PBS, and then the suspension was centrifuged at 1000 g for 10 min. Cell lysis was then measured spectrophotometrically at 540 nm. The absence of hemolysis (blank control) or total hemolysis (positive control) was determined by replacing the essential oil solution with an equal volume of PBS or distilled water, respectively. The results were determined by the percentage of hemolysis compared to the positive control (100% hemolysis), and the experiments were performed in triplicate.

## 3. Results & Discussion

The aerial parts of *C. sativum* were collected from the Yovon region of Tajikistan. The essential oil was obtained by hydrodistillation with the yield of 0.67%. The essential oil from *C. sativum* was analyzed by gas chromatography - mass spectrometry (GC-MS). The results are presented in Table 1. Fifty-five different compounds were identified in the oil accounting for 99.4% of the composition. The main constituents of the essential oil were aliphatic aldehydes and alcohols such as (2*E*)-dodecenal (16.5%), decanol (14.9%), decanal (11.3%), tetradecanol (9.2%), (2*E*)-decene-1-ol (7.39%), (8*Z*)-undecenal (6.21%), and dodecanal (4.4%). The present study revealed that the oil isolated from Tajikistan *C. sativum* plant is similar to the others in respect of the presence of aliphatic aldehydes and alcohols. Our results are in agreement with previous reported studies [10].

Decanal, (2*E*)-dodecenol and (2*E*)-decenal predominant in coriander volatile oil, as has been reported by Nurzynska-Wierdak, should be considered as important biologically active substances due to their possible toxic activity against tropical mosquitoes transmitting dangerous illnesses [10], nematicidal activity against the pine wood nematode [15].

The essential oil showed cytotoxic activity against Caco-2, CCRF-CEM and CEM/ADR 5000 tumor cell lines with IC<sub>50</sub> values of 86.8, 16.5 and 38.5 µg/mL, respectively (Table 2). Caco-2 and CEM/ADR 5000 overexpress ABC transporters, which would explain the reduced cytotoxicity of these cell lines as compared to the sensitive CCRF-CEM cells. For better understanding the mechanism of action of *C. sativum* essential oil, we have investigated its hemolytic effect. The result of hemolytic activity indicates that the oil is able to lyse the cell membrane. The hemolytic activity of the *C. sativum* essential oil against red blood cells (RBC) was 2.3 µL/mL (IC<sub>50</sub>=2.3 mg/mL). The cytotoxicity is most likely due to the presence of aliphatic aldehydes and alcohols [(2*E*)-dodecenal (16.5%), decanol (14.9%), decanal (11.3%), tetradecanol (9.2%), (2*E*)-decene-1-ol (7.4%), (8*Z*)-undecenal (6.2%), and dodecanal (4.4%)]. Previously, we have reported that *Galagania fragrantissima* oil was rich in unsaturated aldehydes, which accounted for the cytotoxic activity observed [16]. Dodecenal and decanal are very electrophilic and can react with a variety of nucleophiles, such as amino groups either from proteins or DNA [16, 17] or thiol groups of biological molecules [18].

Kano *et al.* [19] noted that alkenals (C10-C16) have anti-deforming activity in Raji cells carrying the genome of Epstein-Barr virus (EBV). The activity is correlated with the length of carbon chain of the unsaturated aldehydes. (2*E*)-dodecenal disappeared immediately from the blood; probably it quickly binds to blood proteins [16].

**Table 1:** Chemical composition of the essential oil of *Coriandrum sativum*

RI	Compounds	Content (%)*
860	2-Methyloctane	0.2
900	Nonane	0.1
902	Santolinatriene	tr
932	$\alpha$ -Pinene	0.4
949	Camphene	0.1
972	Sabinene	0.1
977	$\beta$ -Pinene	0.5
1000	Decane	tr
1003	Octanal	0.4
1024	<i>p</i> -Cymene	0.2
1029	Limonene	0.1
1032	1,8-Cineole	0.1
1069	Octanol	0.1
1100	Undecane	0.1
1105	Nonanal	0.7
1107	1-Octen-3-yl acetate	0.1
1126	$\alpha$ -Campholenal	0.1
1159	(2 <i>E</i> )-Nonenal	0.1
1172	1-Nonanol	0.3
1212	Decanal	11.3
1248	(2 <i>Z</i> )-Decenal	0.4
1271	1-Decanol	14.9
1276	(2 <i>E</i> )-Decene-1-ol	7.4
1277	(2 <i>Z</i> )-Decene-1-ol	0.8
1280	Nonylformate	5.6
1311	(2 <i>Z</i> )-Undecenal	3.0
1324	Hydroxycineoleisomer	0.1
1326	Cyclodecanol	0.1
1331	Undecanol**	0.1
1350	(2 <i>E</i> )-Undecenal	0.2
1370	(8 <i>Z</i> )-Undecenal	6.2
1373	(2 <i>E</i> )-Undecenal	2.0
1376	1-Undecanol	0.9
1385	(6 <i>E</i> )- <i>p</i> -Menthen-2,8-diol	0.2
1400	Tetradecene	0.2
1413	Dodecanal	4.4
1438	Undecanoicacid	0.9
1452	(2 <i>Z</i> )-Dodecenal	0.3
1476	(2 <i>E</i> )-Dodecenal	16.5
1513	Tridecanal	1.1
1572	(2 <i>E</i> )-Tridecen-1-al	2.5
1615	Tetradecanal	2.4
1621	Tridecanolide	0.8
1656	(2 <i>E</i> )-Tetradecenal	0.3
1679	1-Tetradecanol	9.2
1715	Pentadecanal	0.2
1721	Neocnidilide	0.2
1776	(2 <i>E</i> )-Pentadecenal	1.0
1808	Unidentified	0.6
1878	(2 <i>E</i> )-Hexadecenal	0.4
2107	Phytol	0.2
2171	Decyldecanoate	0.3
2223	Heneicosanone	0.1
2255	Heneicosanol	0.1
	TotalIdentified	99.4

\*% of total peak area; \*\*Correct isomer not determined

**Table 2:** Cytotoxicity of *Coriandrum sativum* and *Galagania fragrantissima* essential oils

Species	HeLa	Caco-2	IC <sub>50</sub> , $\mu$ g/ml			Hemolysis of the RBC IC <sub>50</sub> , $\mu$ l/ml
			MCF-7	CCRF-CEM	CEM/ADR 5000	
<i>Coriandrum sativum</i>	n.d.	86.8	n.d.	16.5	38.5	2.3
<i>Galagania fragrantissima</i>	206.2	74.3	58.1	9.26	75.5	0.4
Doxorubicin	4.5	8.1	3.3	2.3	5.2	n.d.

n.d. - not determined

#### 4. Conclusions

This study reports the chemical composition of the essential oil of *C. sativum* L. from ornamental plants grown in Tajikistan dominated with aliphatic aldehydes and alcohols such as (2E)-dodecenal, decanol, decanal, tetradecanol, (2E)-decene-1-ol, (8Z)-undecenal and dodecanal as the major compounds. The essential oil exhibits moderate cytotoxicity in leukemia cells (CCRF-CEM).

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