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Chemical composition and anticancer activity of the essential oil from *Vicia ochroleuca* Ten., quite rare plant in Kabylia (Algeria)

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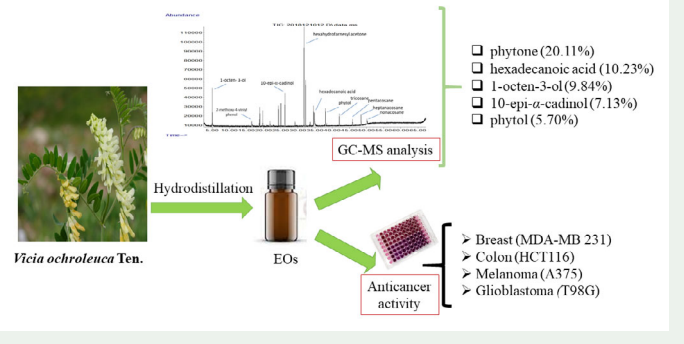
ABSTRACT

The search for new bioactive substances with anticancer activity and the understanding of their mechanisms of action are high priorities in the research effort toward more effective cancer treatments. In this article, we analyzed, for the first time, the chemical composition of the essential oil (EO) hydrodistilled from the aerial parts of *Vicia ochroleuca* Ten. (Leguminosae) by GC–MS. A total of sixteen compounds representing 82.2% of the total composition were identified. The major compounds were phytone (20.11%), hexadecanoic acid (10.23%), 1-octen-3-ol (9.84%), and 10-*epi*-α-cadinol (7.13%). Additionally, using the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) method, the EO was tested *in vitro* against a panel of human cancer cells, including breast (MDA-MB 231), colon (HCT116), melanoma (A375), and glioblastoma (T98G), with corresponding IC_{50} values of 23.07, 47.05, 51.64, and 64.07 μg/mL, respectively. The results demonstrate cytotoxic activity and suggest that *V. ochroleuca* EO could be regarded as a natural bioactive source.



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1. Introduction

The genus *Vicia* L. belongs to the Leguminosae family and includes between 130 and 240 species (Van De Wouw et al. 2001), chiefly located in Europe, Asia, and North America, extending to temperate South America and tropical East Africa. The genus is primarily located in the Mediterranean and Irano-Turanian regions. It is adapted to temperate regions but can also be found at high altitudes in tropical Africa. Endemic species are present on all continents except Australia and Antarctica (Van De Wouw et al. 2001). In Algeria, the genus *Vicia* L. includes 26 species as indicated by the key used by (Quezel and Santa 1962) in the special flora that covers the entire country (Quezel and Santa 1962). While *Vicia* species provide high-quality forage and green manure (Mikić et al. 2009), more than 40 species are economically valuable and are therefore cultivated (El-Bok et al. 2014). *Vicia* plants are used in traditional medicine for treating a broad range of health problems, such as certain cancer types (breast, colon, and prostate), diabetes, and cardiovascular diseases. This genus has several biological activities, in particular, antioxidant, antimicrobial, antidiabetic, antihemolytic, anticoagulant, anti-inflammatory, antinociceptive, anti-Parkinson, anticholinesterase, antidepressant, anticonvulsant, cytotoxic, estrogenic, diuretic, and antihypoxic activities (Salehi et al. 2021). Moreover, *Vicia* seeds are traditionally used as feed additives for farmed animals given their high energy content and represent a low-cost, rich source of proteins and minerals compared to other supplements (El-Bok et al. 2014; Huang et al. 2017). Regarding the chemical composition of *Vicia* genus, many studies have shown that *Vicia* seeds contain phenolic acids, flavonoids, organic acids, hydroxybenzoic aldehyde, as well as amino acids, certain lignans, and terpenoids (Salehi et al. 2021) . The widespread interest in the use of *V. faba* as food attracts more attention to the bioactive metabolites from other species in this genus (Lee et al. 2017; Abozeid et al. 2018). Moreover, a few studies have been conducted on the evaluation of the chemical composition of the EOs of different *Vicia* species and their biological effects, with only four species involved: *V. sativa* L., *V. dadianorum* Sommier & Levier, *V. caroliniana* Walter, and *V. faba* L. In this context, this study aimed to examine the chemical composition of the EO from *Vicia ochroleuca* subsp. *atlantica* (Pomel) Maire (Figure 1), growing in Algeria and known in Arabic as 'Bikia' and which is used as animal feed. Furthermore, the antiproliferative activity of this EO was evaluated against breast (MDA-MB231), colon (HCT116), melanoma (A375) and glioblastoma (T98G) cells. It is important to note that this is the first report on the chemical constituents and cytotoxic activities of *V. ochroleuca* essential oil.

2. Results and discussion

2.1. Chemical composition of essential oil

The hydrodistillation of the aerial parts of *V. ochroleuca* gave a very low yield of EO, 0.0039% (w/w). The EO components were identified and semi-quantified (relative area percentages) by GC–MS and the results are presented in Table 1. In total, sixteen compounds representing 82.2% of the total EO were identified. The EO was characterized by a high content of ketones (21.21%), alkanes (17.95%), alcohols and phenols (13.95%),

Figure 1. Illustration of *Vicia ochroleuca* (top left: plant in its habitat, top right: specimen for the herbarium, down: plant pods), Akfadou (Béjaia), 06.06.2014, Photos: K. Rebbas.

fatty acids (10.23%) and oxygenated sesquiterpenes (8.47%). On the other hand, monoterpene hydrocarbons were not found. If we compare these results with those reported by (Kahriman et al. 2012), the absence of monoterpene hydrocarbons in *V. dadianorum* is confirmed. Furthermore, high levels of alkanes (19.2%) were also observed. In contrary, the volatile EOs from the aerial parts of three populations of *V. caroliniana* were dominated by fatty acids (Vc – 1:44.2%; Vc – 2:51.1%; Vc – 3:73.9%) (Lopez et al. 2017). However, the major components of *V. ochroleuca* EO were phytone (20.11%), hexadecanoic acid (10.23%), 1-octen-3-ol (9.84%), 10-epi-α-cadinol (7.13%), and phytol (5.70%), respectively. These results are in agreement with those reported by (Romeo et al. 2009; Kahriman et al. 2012), who observed the prevalence of phytone (4.7% HD: hydrodistillation and 5.1% MD: microwave distillation) and 1-octen-3-ol as major components of *V. dadianorum* and *V. sativa* EOs, respectively. Likewise, phytol was the major component of *V. caroliniana* EO and was considered to be responsible for the plants' antinociceptive and anti-inflammatory activities (Lopez et al. 2017). The variation in the chemical composition of the EOs can be attributed on the location of the plant, its agroclimatic conditions, the nature of soil, whether the plant material is fresh or dried, the time of collection, the age of the plant and the extraction technique (Abbas et al. 2017, 2022).

Table 1. Chemical composition of the essential oil of the aerial parts of *Vicia ochroleuca*.

Peak	Components[a]	RT[a]	RI[b]	RI_{litt}[c]	%[d]
1	2-Methylbutyl propanoate	4.88	970	968	0.95
2	1-Octen-3-ol	5.00	976	974	9.84
3	2-Methoxy-4-vinylphenol	16.51	1312	1322	4.11
4	(*E*)-*β*-Damascenone	18.73	1379	1383	1.53
5	(*E*)-*β*-Ionone	21.87	1476	1487	1.39
6	10-*epi*-α-Cadinol	26.22	1628	1638	7.13
7	(6*R*,7*R*) -Bisabolone	29.14	1737	1747	1.34
8	Phytone	31.77	1842	1846	20.11
9	(5*E*,9*E*)-Farnesylacetone	33.52	1913	1913	1.10
10	Methylhexadecanoate	33.80	1931	1921	0.88
11	Hexadecanoic acid	34.78	1966	1968	10.23
12	Phytol	38.04	2102	2113	5.70
13	Tricosane	42.05	2300	2300	4.03
14	Pentacosane	45.91	2500	2500	3.22
15	Heptacosane	48.39	2700	2700	5.55
16	Nonacosane	50.13	2900	2900	5.15
Total identified					82.26
Grouped compounds					
Aliphatics					
Alcohols					9.84
Esters					1.83
Ketones					21.21
Fatty acids					10.23
Alkanes					17.95
Aromatics					
Phenols					4.11
Terpenoids					
Norisoprenoids					2.92
Oxygenated sesquiterpenes					8.47
Oxygenated diterpenes					5.70

[a]Compounds are listed according to their elution from a HP-5MS (30 m × 0.25 mm, 0.25 μm) capillary column.
[b]Retention index experimentally determined using a mixture of C8–C30 *n*-alkanes (Sigma-Aldrich).
[c]Retention index values taken from Adams (2007) and NIST17 (2008).
[d]Peak are percentages are means of three determinations ± SD.

Table 2. *In vitro* cytotoxic activity of *V. ochroleuca* EO.

	Cell line (IC_{50} μg /mL)[a]			
	A375[b]	T98G[c]	MDA-MB 231[d]	HCT116[e]
Compound				
Essential oil	51.64	64.07	23.07*	47.05
95% C.I.[f]	46.49–57.36	52.08–78.83	19.83–26.83	41.63–53.18
Positive control				
Cisplatin	0.47	7.07	3.20	2.71
95% C.I.	0.35–0.55	6.23 – 7.80	2.95–3.36	2.45–3.04

[a]IC_{50}= The concentration of compound that affords a 50% reduction in cell growth (after 72h of incubation).
[b]Human malignant melanoma cell line.
[c]Human glioblastoma multiforme cell line.
[d]Human breast adenocarcinoma cell line.
[e]Human colon carcinoma cell line.
[f]Confidence interval.
*Statistical analysis was performed by One-way analysis of variance ($p < 0.001$).

2.2. Evaluation of the anticancer activity

Cytotoxic effects of *V. ochroleuca* EO were evaluated on melanoma (A375), glioblastoma (T98G), breast (MDA-MB 231), and colon (HCT116) human tumor cell lines. Tumor

cells were treated with various concentrations (1.56–200 μg/mL) of EO for 72 h and then submitted to the MTT assay. Cisplatin was used as a positive control. The results are given in Table 2. The EO of the aerial parts of *V. ochroleuca* exhibited significant cytotoxicity against MDA-MB 231 (IC_{50} = 23.07 μg/mL). It also exhibited a significant cytotoxic activity against A375 (IC_{50} = 51.64 μg/mL), T98G (IC_{50} = 64.07 μg/mL), and HCT116 (IC_{50} = 47.05 μg/mL) cell lines in a concentration-dependent manner. In addition, the cytotoxic activity of the EO against MDA-MB 231 cell line was found significantly higher than that against A375, HCT116 and T98G cell lines ($p < 0.001$).

Of the major components of the oil, phytone and *n*-hexadecanoic acid have been reported showing no antiproliferative activity against human cervical cancer cell line (HeLa), human colon carcinoma cell line (HCT116) and human osteosarcoma cell line (U2OS), at least, at lower concentrations. The IC_{50} values for phytone were above 4 mg/mL and for *n*-hexadecanoic acid much lower, but still high enough not to inhibit proliferation of cancer cells (IC_{50} > 1 mg/mL) (Nazlić et al. 2021). *n*-hexadecanoic acid has shown cytotoxicity to human leukemic cells, MOLT-4, and also shows *in vivo* antitumor activity in mice (Harada et al. 2002). (*E*)-phytol has been reported to have cytotoxicity against HT-29 human colon cancer cells, MG-63 osteosarcoma cells and AZ-521 gastric cancer cells (Yuenyongsawad and Tewtrakul 2005). In literature, also 1-octen-3-ol results low toxic at list on human lung carcinoma epithelial cell line A549 with IC_{50} values of 3.4 mM (Kreja and Seidel 2002). Therefore, the cytotoxic activities of *V. ochroleuca* EO may be attributed to the specific chemical constituents and/or synergies between various components.

According to the criteria established by the U.S. National Cancer Institute on cytotoxicity of crude extracts, the IC_{50} values of *V. ochroleuca* EO lie close to the cut-off value (30 μg/mL) between an 'active' and 'moderately active' compound (Suffness and Pezzuto 1991). In light of these data, *V. ochroleuca* EO might be considered as 'active' against MDA-MB 231 cell line and as 'moderately active' against A375, HCT116, and T98G cell lines.

3. Conclusion

In conclusion, the EO of *V. ochroleuca* has been investigated for the first time for chemical composition and cytotoxic activity against tumor cell lines. Since *V. ochroleuca* is generally utilized as animal's food, the information acquired on its EO, particularly for the presence of isoprenoid ketones and fatty acids, is of great interest for the traceability of dairy items (Romeo et al. 2009). This study adds scientific support to ethnopharmacological information on the health benefits of *V. ochroleuca* and suggests that this EO contains potential anti-cancer compound(s). Further studies to elucidate the mechanisms of action and the possible compounds involved in these activities will be undertaken.

Disclosure statement

No potential conflict of interest was reported by the authors.

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