



Cistus libanotis from Algeria: Phytochemical analysis by GC/MS, HS-SPME-GC/MS, LC-MS/MS and its anticancer activity

Samiha Ameur^a, Mohamed Toumi^{a,c}, Hamdi Bendif^{b,c}, Larbi Derbak^b, İlyas Yildiz^d, Khellaf Rebbas^b, Ibrahim Demirtas^d, Guido Flamini^e, Maurizio Bruno^f, Stefania Garzoli^{g,*}

^a Department of Natural and Life Sciences, Laboratory REVIECO, University of Alger's 1, Algeria

^b Department of Natural and Life Sciences, Faculty of Sciences, University of M'sila, University Pole, Road Bordj Bou Arreiridj, M'sila 28000, Algeria

^c Laboratory of Ethnobotany and Natural Substances, Department of Natural Sciences, ENS Algiers, Algeria

^d Research Laboratory Application and Research Center (ALUM), Foundation of the Faculty of Health Sciences, Nutrition and Dietetics Department, İgdr University, İgdr 76000, Türkiye

^e Department of Pharmacy, University of Pisa, Via Bonanno 6, Pisa 56126, Italy

^f Department of Biological, Chemical and Pharmaceutical Sciences and Technologies (STEBICEF), University of Palermo, Viale delle Scienze, Ed. 17, Palermo 90128, Italy

^g Department of Chemistry and Technologies of Drug, Sapienza University, Rome 00185, Italy

ARTICLE INFO

Keywords:

HS-SPME

GC-MS analysis

LC-MS-MS analysis

Cytotoxicity

ABSTRACT

In this paper, *Cistus libanotis* (*Cistus clusii* Dunal) from Algeria was investigated. This plant is utilized in numerous industries, mostly in perfumery and, more recently, as a raw material for dietary supplements. For the first time, the present study evaluated the anticancer potential of Algerian *C. libanotis* by performing a comprehensive phytochemical investigation. The volatile fraction of the fresh plant material of *C. libanotis* was investigated using headspace solid-phase microextraction (HS-SPME) coupled to GC-MS, and the chemical composition of the essential oil (EO) of *C. libanotis* was examined using GC-MS technique; additionally, the phenolic compounds were identified and quantified using liquid chromatography coupled with electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS). A healthy cell line (L929) and two cancer cell lines (CAPAN-1 and dld-1) were used to test the ethanolic extract's cytotoxicity. HS-SPME-GC/MS analysis identified sabinene (25.3 %) and α -thujene (23.8 %) as principal components. In EO the major ingredients were γ -terpinene (17.4 %), camphene (16.13 %), α -phellandrene (15.36 %), and 4-carene (13.54 %). Nevertheless, 24 components were identified by LC-ESI-MS/MS analysis and shikimic acid, luteolin and hesperidin were most abundant. Further, the ethanolic extract of *C. libanotis* showed a significant cytotoxic effect against dld-1 and CAPAN-1 cell lines, while it was less active against the healthy cell line L929.

1. Introduction

The Cistaceae family, which includes eight genera and roughly 180–200 species of shrubs, is mainly made up of heliophyte shrubs, subshrubs, and herbs that grow in open spaces with little soil nutrients (Guzmán et al., 2009). Adapted to fires in Mediterranean forests, these plants are pyrophytic and resilient to wildfires, with their seeds able to rapidly repopulate destroyed areas in the subsequent season (Alonso et al., 1992; Ferrandis et al., 1999). Known for their fragrant and sweet-smelling qualities, many members of the Cistaceae family are

highly valued in the perfume industry and as ornamental plants. Some of the genera in this family that are noteworthy are *Cistus*, which has between 16 and 28 species depending on the source, *Helianthemum*, and *Halimium* (Guzmán & Vargas, 2005). *Cistus*, a small yet complex genus, is characterized by its polymorphic species and hybridization between related varieties, with around 20 species of perennial shrubs found in dry or rocky soils across Europe (Tabacik and Bard, 1971; Ellul et al., 2002). Of these, seventeen are common members of the Mediterranean Flora, frequently found in dense numbers close to the coast (Guzmán et al., 2009; Nicoletti et al., 2015). Shrubs within the *Cistus* genus is

* Corresponding author.

E-mail addresses: s.ameur@univ-alger.dz (S. Ameur), m.toumi@univ-alger.dz (M. Toumi), hamdi.bendif@univ-msila.dz (H. Bendif), larbi.derbak@univ-msila.dz (L. Derbak), ilyas.yildiz@igdir.edu.tr (İ. Yildiz), khellaf.rebbas@univ-msila.dz (K. Rebbas), ibrahim.demirtas@igdir.edu.tr (I. Demirtas), guido.flamini@farm.unipi.it (G. Flamini), maurizio.bruno@unipa.it (M. Bruno), stefania.garzoli@uniroma1.it (S. Garzoli).

<https://doi.org/10.1016/j.jfca.2024.106747>

Received 13 July 2024; Received in revised form 12 September 2024; Accepted 12 September 2024

Available online 17 September 2024

0889-1575/© 2024 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).