# Cistus sp.

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Cistusis a Mediterranean native genus of shrubs belonging to the familyCistaceae. Species of this genus can grow during hot summers and after wildfires.Cistusspecies are most widespread in the Mediterranean region, whilst some of them are endemic.Cistusplants can grow under slightly different environmental conditions. Most species are very fragrant and sweet-smelling.

sp. phytochemicals microorganisms antimicrobials multidrug resistance

## 1. Introduction

Nature is the source of natural remedies widely used by 80% of the world population [1]. In North America, Europe, and other developed regions, over 50% of the population has used traditional medicine at least once [2].

The World Health Organization (WHO) has a keen interest in documenting medicinal plants used by indigenous people from different parts of the world [3][4]. The use of plant derivatives as medicinal treatments gained popularity in the late 1990s [5].

The screening of phytochemical composition in medicinal and aromatic plants plays a significant role in many areas, such as the human diet, animal feed, pharmaceuticals, fragrances, and cosmetics, etc. [6][7][8][9].

The Mediterranean basin, one of the hot spot biodiversity in the world [10][11], is rich in vegetation, including medicinal plants [12][13][14]. One example is Cistus L. sp., which was intensively studied in terms of medicinal properties along with its chemical composition. In this sense, this work was conducted to gather data on Cistus L. regarding antimicrobial potential and chemical profiles.

## 2. Biological Potent of Cistus Species

Considering the importance of developing pharmaceutical products with lesser side effects for inflammation and pain treatments. The current study proposed by [15] reports the anti-inflammatory and analgesic potent of Moroccan C. salviifolius aqueous extracts, an important reduction of inducing paw edema (97.57%), and significant inhibition of writhes for a dose of 500 mg/Kg of body weight. In a recent paper published by I. Chiocchio, the authors demonstrated for the first time the skin protection effect of C. salviifolius hydro-methanolic extracts [16]. Trials aimed to test the in vitro inhibition of two enzymes which are cosmetic targets (tyrosinase and elastase), showed the

inhibition of 51% against elastase and 61% against tyrosinase at a concentration of 50 µg/mL. Also, a correlation was established between inhibition enzymatic potency and the total phenolic and flavonoids content.

Ethnopharmacological data revealed the use of C. albidus flowering top in decoction against respiratory disorders by the North-West of Morocco population [17]. In this regard, a study was carried to support the traditional pharmacopeia in Morocco. A high value of total phenolic content and total flavonoid content was registered from ethanolic extract (TPC 112.48 ± 1.78 mg GAE/g extract; TFC 24.55 ± 0.58 mg QE/g extract). Those compounds are secondary metabolites that could act as antibacterial responsible for respiratory infections [18].

In contrast, a study carried out with C. clussi on the role of a secondary metabolic pathway in responses to stress such as summer drought, reported the increased syntheses of many phenolic compounds and the maximum efficiency of photosystem II. The induced drought may be due to the compound's action to protect the plant from oxidative damage [19].

The C. populifolius aqueous extract from Spain have demonstrated for the first time a high polyphenol (especially ellagitannins) content and high antioxidant capacity observed in many analysis, data reported in this study suggests the use of this species in the food industry and biological systems [20].

## 3. Antiparasitic Activity of Cistus Extracts

Each year diseases caused by parasites lead to hundreds of millions of infected people, particularly in tropical and subtropical regions, resulting in one million deaths [21]. At first report about the potential of Cistus against parasites, Fokialakis have demonstrated the significant antileishmanial activity of raw extract of C. monspeliens is and C. creticus [22][23]. Also, the authors tested pure and semisynthetic compounds from the same species against L. donovani promastigote (causative agent of visceral leishmaniasis). Obviously, among the eight natural compounds from C. monspeliensis , 18-acetoxy-cis-clerod-3-en-15-ol was the most active with an IC 50 value of 3.3 µg/mL, while C. creticus compounds were less sensitive ent-3b-acetoxy-13-epi-manoyl oxide active with an IC 50 value of 17 µg/mL. As far as we could observe, semisynthetic derivatives showed variable responses, ranging from inactivated to more active than the parent compound. As it is commonly acknowledged that the fundamental concepts of activity are about selective toxicity against the target without any toxicity to the host cell, none of all compounds tested in this study was cytotoxic to mammalian cells up to the highest concentration of 47.6 µg/mL.

A recent report by Bouyahya on macerated extracts from C. crispus leaves against three Leishmania species tests at the promastigote stage have demonstrated that among the solvent used, methanol and ethanol, n-hexane showed the best anti-promastigote activity regarding L. major , L. tropica , and L. infantum . Moreover, L. Infantum was the most sensitive IC 50 47.29 µg/mL. Also, it should not be forgotten that all results obtained with C. crispus extracts were lower than the control used (Glucantime ®® IC 50 > 500 µg/mL) [24]. However, no toxicity tests were performed. Unfortunately, there is a high probability that the products that have been classified as active against a particular parasite in vitro are likely to be known toxins to host cells ( **Table 1** ).

**Table 1.** Antiparasitic potent of *Cistus* extracts.

| *Cistus* Species | Collection Area | Part of Plant | Type of Extract | Parasite | Technique | Concentration µg/mL | $IC_{50}$ µg/mL | Mechanism | References |
|---|---|---|---|---|---|---|---|---|---|
| *C. monspeliensis* *C. creticus* | Greece | Aerial parts Resin | Pure compounds from Dichloromethane extracts and semisynthetic derivatives | *L. donovani* | In vitro culture of promastigote and Alamar blue assay | 1.6–8–40 | From 3.5 to 37 | ND | [23] |
| *C. crispus* | Ouezzane, Morocco | Leaves | Methanolic, Ethanolic and *n*-hexane extracts | *L. major* *L. tropica* *L. infantum* | MTT assay | ND | *n*-hexane against *L. major* = 47.29 | ND | [24] |

ND: Not determined; *L*: *Leishmania*.

The in vivo screen should assess activity against an intracellular stage of parasite development to be genuinely representative for an antiparasitic product suitable for development. Nevertheless, no screening system is perfect because of the lack of correlation between tests in vitro and in vivo in all areas of drug discovery. We cannot emulate the complex situation in vivo.

# 4. Antifungal Activity of Cistus Extracts

In search for antifungal drugs in the Cistus genus, rockrose is also known as C. creticus = C. villosus = C. incanus , was widely investigated. First, by Demetzos et al., in both reports about EO's composition and its effect against C. albicans which had almost the same effect [25][26]. Comparative MIC analyses of Moroccan and Turkish rockrose against C. glabrata and C. albicans show respectively significant MIC values with methanol extract from Moroccan species 0.19–6.25 mg/mL and 8–32 mg/mL with aqueous extract from Turkish samples. Interestingly the bio-guided extraction (fractionation with increasing polarity solvent) of Bouamama allowed a better activity localization. Butanol fraction and remaining aqueous layer were more active than the raw extract. It also should be noticed that C. glabrata was the most sensitive while C. krusei was the most resistant to extracts [27][28]. However, the highest anti-candida activity was reported with phenolic extract of C. ladaniferus . MIC was lower 0.05 mg/mL for C. albicans , C. glabrata , and C. parapsilosis [29]. This extract was mainly made of phenolic compounds, which might explain its activity.

Karim did similar investigations to demonstrate the effectiveness of eight Cistus varying types of extracts. Obviously, for anti- G. citri-aurantii , water was the best extraction solvent, followed by methanol and chloroform. In both studies at a concentration of 5 mg/mL aqueous and methanolic, extracts of C. creticus , C. albidus , C.

laurifolius , C. monspeliensis , C. crispus , C. salviifolius , and C. populifolius exhibited a total inhibition of arthrospore germination. However, among all extracts, aqueous ones of C. salviifolius and C. monspeliensis have strongly inhibited the fungi with MIC values low than 0.625 mg/mL.

To the best of our knowledge, little is shown about post-harvest citrus fungal pathogens. These studies have pointed out that Cistus extracts will widen the list of allelopathic plants to G. citri-aurantii growth.

A recent Moroccan report about the ethanolic extract from rockrose against P. expansum and P. digitatum : the research was done using agar dilution, and the results revealed the sensitivity of P. digitatum MIC 1 mg/mL while P. expansum was more resistant with MIC of more than 10 mg/mL. Also, the same study has evaluated the effect against unusual fungi such as C. versicolor , G. trabeum , P. placenta , and C. puteana , which is known to be wood decomposition. Most of them presenting a resistance against ethanolic extract. However, they were more sensitive against EO [30].

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