Natural products from *Dittrichia Viscosa* (Mini-Review)

M. Zaki¹*, M. Loubidi¹, A. Oukhrhib², S. Mallouk³

¹ Laboratoire de Chimie Physique & Chimie Bioorganique, Département de Chimie, URA C 22, Pole RePAM, F. S. T. Université Hassan II de Casablanca, B.P. 146 Yasmina, 28800, Mohammedia, Morocco
² Laboratoire de Chimie Biomoléculaire, substances naturelles et Réactivité (URAC 16), Faculté des Sciences Semlalia, Université Cadi Ayyad, B.P. 2390, Marrakech, Morocco.

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**ABSTRACT**

During the last two decades, natural products and their biological activities have been the focus of numerous phytochemical, pharmacological and synthetic studies. There has also been much interest in relating the structure and oxygenation patterns of these products to their function. This review covers the structures of different compounds from *Dittrichia vicsosa*.

**Corresponding Author:**
Adress: Laboratoire de Chimie Physique & Chimie Bioorganique, Département de Chimie, URA C 22, Pole RePAM, F. S. T. Université Hassan II de Casablanca, B.P. 146 Yasmina, 28800, Mohammedia, Morocco
Email: mohamed.zaki@etu.univ-orleans.fr

**1. INTRODUCTION**

Plants are considered among the main sources of biologically active chemicals. It has been estimated that about 50% of the prescription products in Europe and the USA originate from natural products or their derivatives [1]. Out of the 250,000-500,000 plant species on earth, only 1-10% have been studied chemically and pharmacologically for their potential
medicinal value [2]. The Mediterranean climate encourages the development of plants. Unfortunately, among the plant species endemic to the Mediterranean, only a few have been studied. The valorization of these natural resources is based on the extraction of their essential oils, which are used in the pharmaceutical, cosmetic and food industries. *Dittrichia viscosa* belongs to Asteraceae family and is widely used in traditional medicine in many Mediterranean countries, especially in rural areas, for the treatment of various diseases such as bronchitis, diabetes.

2. DISTRIBUTION AND BOTANICAL ASPECT OF *DITTRICHIA VISCOSA*

The genus *Inula* belong to the Asteraceae family. It is an important family of dicotyledonous plants which comprises 20,000 species. The genus *Inula* includes a variety of 90 species (*inula viscasa*, *inula helvetica*, *inula montana*, *inula salicina*, *inula ensifolia* ...). Those are herbaceous, perennials, with alternate leaves, yellow flowering heads, containing both of flowers tubular and ligulate, bracts in several series of flowers with pistillated peripherals, with tridentate ligules, sagitted anthers at the base, with chains fitted with coasts and simple egrets. The *Inula* are widely used in traditional medicine. They have antiseptic, antibiotic, antispasmodic, anti-inflammatory and anti-diabetes properties [3-6].

The *Inula* genus is widely distributed in the Mediterranean basin [7], in Europe (Spain, Italy, France, Greece ...), Asia (China, Japan ...) and in Africa (Morocco, Algeria, Tunisia ...). It is found in salty soils, prairie wetlands and on the edges of rivers and roads. *Dittrichia viscosa* grows in uncultivated soils including at the edges of paths, amongst rubble, abandoned lands, summer fallow, and dunes. It likes environments where soils have been freshly disturbed by farming activities or other work related activities, and often grows after the passage of fire. It also grows well on clay soils and sand [8].

*Dittrichia viscosa* is a perennial plant [9], with a taproot, that grows up to 1.50 meter) and can form a rather large populations (picture 1). Its stems provide dense foliage. With age, they become woody and dark on the base. The plant is sticky and very fragrant, with a camphor-like odor. The leaves alternate from elongated to lanceolate, and are inserted directly on the stem, without petioles. The base of the leaf of the rod seems to partly encircle (leaves embrassantes). Their margin is smooth or toothed, and the acute summit. The whole plant is covered with glandular hairs that liberate an odoriferous and sticky resin.
Flowering begins from the month of September and as among all the Asteraceae, the flowers are grouped in capitula (approximately 10-20 mm in diameter), surrounded by an involucre of bracts, which may be in part and membranous ciliate. Among *Dittrichia viscosa*, there are two types of flowers: flowers to petals welded in yellow tabs (ligulate flowers) to the outside of the flower head, and flowers in tubes (tubular flowers), orange-yellow in the center of the flower head (picture 2).

**Picture 2: The two types of flowers of *Dittrichia viscosa***

3. **PHYTOCHEMICAL DESCRIPTION OF *DITTRICHIA VISCOSA***

The species of *Dittrichia viscosa* is rich in secondary metabolites. These have been the subject of several studies. We report here the different constituents of *Dittrichia viscosa* grouped according to the following structural categories: terpenoids, flavonoids, phenylpropanoid and polyketides.
3.1. TERPENOIDS

Terpenes are naturally occurring hydrocarbons with a cyclic or open-chain structure. Their empirical formula is \((C_5H_x)_n\), where \(x\) is variable depending on the degree of unsaturation of the molecule and can take values (1-8) except polyterpenes where it can reach over 100 (rubber). The basic molecule is isoprene formula \(C_5H_8\).

The term terpenoid refers to a set of substances having the skeleton terpenes with one or more chemical function (alcohol, aldehyde, ketone, acid, lactone, etc.)

3.1.1. Monoterpenes

Shtacher et al. successfully isolated for the first time monoterpane derivatives of 3-methoxy-p-cymen-7-ol: 1, 2 and 3 from the root extract of *Dittrichia viscosa* [10]. Then Bohlmann et al. isolated a thymol derivative 4 from the same extracts (Figure 1) [11]. Fresh leaves of *Dittrichia viscosa* contain eucalyptol 5, which is explains the soothing and antiseptic properties attributed to the plant (Figure 1) [12].

![Monoterpenes extracted from the roots and leaves of *Dittrichia viscosa*](image)

The essential oil of the aerial part of *Dittrichia viscosa* was also studied and the main molecules isolated from this oil were: borneol 6 (25.2%), bornylacetate 7 (19.5%), isobornylacetate 8 (22.5%) [13] and carvacrol 9 (18.6%) (Figure 2) [14]. Mueller-Riebau [15] and Grande [16] also studied the essential oils of *Dittrichia viscosa*, and their studies have shown that this oil also contains the following structures.
3.1.2. Sesquiterpenes

This is the most diverse class of terpenes since it contains more than 3000 molecules. Sesquiterpenes are divided into several structural categories: non-cyclic, monocyclic, bicyclic, tricyclic, polycyclic.

3.1.2.1. Non-cyclic sesquiterpenes

The essential oil of the aerial part of *Dittrichia viscosa* is rich in sesquiterpene products as nerolidol 19, the esters 20 - 24, diols 25 and 26 [16]. Other sesquiterpene derivatives have been isolated such as the β-farnesene 27 [17] and fōkienol 28 [18] (Figure 3).
3.1.2.2. Bicyclic sesquiterpenes

Several studies have shown that the essential oil of *Dittrichia viscosa* contains also bicyclic sesquiterpenes, as globulol 29 (15.0%) extracted using the supercritical CO$_2$ method under the conditions of 90 bar pressure and a temperature of 50 °C [19], the chamazulene 30 and 1,4-dimethylazulene 31 (Figure 4) [20].

Furthermore, other bicyclic sesquiterpenes were also isolated from the essential oil of *Dittrichia viscosa* (Figure 6) [11, 17, 21].
3.1.2.3. Sesquiterpenic acids

The α-costic acid [22] is considered the first product isolated from the extract of petroleum ether from leaves of *Dittrichia viscosa*, and this product showed antiparasitic activity [23-24]. Other sesquiterpene acids were also isolated (Figure 5) [15, 25-35].
3.1.2.4. Sesquiterpene lactones

The aerial part of *Dittrichia viscosa* contains also the sesquiterpene lactone family (Figure 6) [31,33, 36-37].
The germacranolides derivatives were also extracted from the roots of *Ditrichia viscosa*. The ineupatorolides 76-80, iso-butyrate, valerate and iso-2-methyl butyrate ditrichiolide 81-83 [21]. In contrast, the tayunine 84 was isolated from the leaves and exhibits antifungal activity (Figure 7) [38].
Other sesquiterpene lactones have been also isolated from *Dittrichia viscosa* as santonin 85, helenine 86 [39] and naphtho [2,3-b] furan-2 (3H) -one 87 (Figure 8) [17].

![Figure 8: Other sesquiterpene lactones from *Dittrichia viscosa*](image)

3.1.2.5. Other sesquiterpenic derivatives

In 1987 Rustaiyan et al. [31] have isolated the ketoacide 88 from *Dittrichia viscosa*, while Chahboun et al. [17] described his isomer ciperanique 89, and other sesquiterpenes as germacrene 90 and the (-) - ciperene 91 (Figure 9).

![Figure 9: Other sesquiterpenic derivatives from *Dittrichia viscosa*](image)

3.1.3. Triterpenes and sterols

Studies made by the team of Grande and Cum showed that the acetone extract of the aerial part of *Dittrichia viscosa* consists of several triterpene compounds as acetate damaradienile 92, friedelin 93, 3β-hydroxyfriedelane 94, 3β -mono acetate triterpenoids 95, faradiols esters 96 and calenduladiol esters 97 (Figure 10) [21, 40].
Meanwhile, research carried out previously on the leaves of *Dittrichia viscosa* resulted in the isolation of a series of sterols (Figure 11): \(\psi\)-taraxasterol 98, \(\psi\)-taraxasterolacetate 99 [41], taraxasterol 100 and its acetate 101 [41], (\(-\)) - \(\beta\)-sitosterol 102 and its glucoside 103 [32], stigmastanol 104 and stigmasterol 105 [42].
3.2. FLAVONOIDs

The term "flavonoid" refers to a very wide range of natural compounds belonging to the family of polyphenols. They are considered the almost universal pigments of plants. All flavonoids (more than 4000) have the same basic structural element, namely the sequence 2-phenylchromane (Figure 12).

![Figure 12: 2-phenylchromane](image)

Flavonoids such as terpenoids, are responded in *Ditrichia viscosa*, particularly in the extracts obtained from the aerial part of the plant. In the 1977 Oksuz et al. successfully isolated quercetin 106, 3-methoxyquercetine 107 and 3-methoxyquercetin-7-glucoside 108 from the extract of flowers of *Ditrichia viscosa* [43]. This was followed by the work of Taillade who succeeded in extracting the 4-methoxykaenferol 109 [44]. A few years later, the Chiappini et al. isolated 3,3'-dimethoxyquercetine 110 and 2,3-dihydro-7-methoxykaenferol 111 [45] (Figure 13).

![Figure 13: First flavonoids isolated from Ditrichia viscosa](image)

In 1985, Grande et al. extracted from the aerial part of *Ditrichia viscosa* six flavonoid compounds: 3-*O*-acetyl padmatine 112, padmatine 113, apigenin 114, 7-
methoxylapigenine 115, naringenin 116 and 3-\(O\)-acetyl-7-\(O\)-methylaromadendrine 117 (Figure 14) [46].

Other studies have characterized many of flavonoid derivatives (Figure 15) [30, 32, 47].
Figure 15: Other flavonoids isolated from *Dittrichia viscosa*
Other flavonoid derivatives have been purified and characterized from the ethylacetate extracts of the aerial part of *Dittrichia viscosa* [8]: 6,3′-dimethoxyuteolin 136, tomentin (3,7-dimethoxiquercetagenin) 137, 3,6,3′-tri-methoxyquercetagenin 138, 3-\(O\)-glucoside of quercetin 139 and 7-\(O\)-\(\beta\)-D-glucoside of quercetin 140 (Figure 16).

3.3. PHENYLPROPANOIDS

Phenylpropanoids derivatives have been isolated from the extract of inflorescences of *Dittrichia viscosa*: cinnamaldehyde 141 by Grande et al. [46] and caffeic acid 142 and chlorogenic acid 143 by Alarcon et al. [48] (Figure 17).

3.4. POLYKETIDES

Several polyketides have been characterized in the extracts of *Dittrichia viscosa* such as 4-hydroxyphenylethanol 144 [41], myristic, palmitic, stearic, oleic and linoleic acid [49-50] and resorcinol 145 (Figure 18) [51].
4. CONCLUSION
This review provides an overview of the chemical constituents of *Dittrichia viscosa*. The starting point for many investigations is the use of plants in traditional medicine, followed by the isolation and biological testing of their active components. The broad and often very promising biological properties of natural products are well known. Studies on the semi-synthesis, total synthesis and biotransformation of these compounds derivatives have been described and are increasing in number.

REFERENCES