Bioactive Compounds from *Artemisia campestris* L. Subsp. *Campestris*

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Artemisia campestris L. (field wormwood) is a known medicinal plant used mainly in Asian medicine and most often overlooked in the western world, despite its cosmopolitan distribution. The aim of this study was to investigate the phytochemical composition of A. campestris from Romanian spontaneous flora in order to determine the bioactive molecules and to assess the antioxidant effect of the plant extract. For this purpose, we applied LC-MS methods for the analysis of phytosterols and polyphenols and developed new methods for the analysis of methoxylated flavones and sesquiterpene lactones, specific compounds in Artemisia genus. The paper is the first to report the concentration of these compounds in the indigenous plant and also to identify some new compounds, previously not reported in this species, such as eupatolin, casticin, and acacetin. The plant extract showed significant antioxidant activity in both radical scavenging and reducing power assay, well correlated with the polyphenolic profile.

Keywords: LC-MS, methoxylated flavonoids, phytosterols, polyphenols.

Artemisia genus includes over 400 species, many of which are well-known medicinal and aromatic plants, used for their analgesic, anti-inflammatory, anti-spasmodic, antimalarial, antimicrobial, anthelmintic, hepatoprotective, antidiabetic, antilulcer, anticancer properties [1]. The importance of *Artemisia* genus is still discovered, new therapeutic approaches are investigated and the area of therapeutic potential is extended. Recently, it was proved that some *Artemisia* sp. inhibit acetylcholinesterase activity, a target for treatment of myasthenia gravis (an autoimmune disease), glaucoma, Parkinson’s disease, dementia [2, 3].

*Artemisia campestris* L. is a perennial plant distributed to Eurasia, North Africa and North America. Romanian flora contains three subspecies: *alpina, campestris* and *lednicensis*, from which *campestris* is frequently encountered [4]. A. *campestris* flowers and leaves were traditionally used as hypoglycaemic, cholagogue, choleric, antivenin, anti-inflammatory, anti-rheumatic, antimicrobial, diuretic, antithiastis, for the treatment of obesity and to decrease cholesterol levels [5, 6]. Most phytochemical studies carried out to date analyzed the composition of volatile oil that differs according to plant source and variety [7-9]. Other studies mention the presence of alkaloids, saponins, coumarins, terpenes, flavonoids [1, 6] and fatty acids [10]. The only information regarding the chemical composition of Romanian plants refers to the quantity (0.05 mL/100 g) and components of essential oil [8]. Numerous studies confirm the biological activities of *A. campestris* such as antimicrobial, anthelmintic, antioxidant, antitumor, antidiabetic, hepatoprotective, nphroprotective, insecticidal, anti-tumor, antilulcer and allelopathic [5, 11-13].

Considering the therapeutic potential, the large distribution in the spontaneous flora and the scarcity of chemical information regarding the Romanian species, we attempted a phytochemical screening of *A. campestris* subsp. *campestris* using LC-MS analysis. The study was focused on the following bioactive compounds: polyphenols - with emphasis on methoxylated flavones, phytosterols and sesquiterpene lactones. The antioxidant activity of the extract was also assessed through two antioxidant tests.

Experimental part

**Materials and methods**

Plant material and extraction procedure

The aerial parts of *Artemisia campestris* subsp. *campestris* were harvested at the flowering stage from the countryside around Iasi, Romania in September 2014. The species was identified by a specialist (biologist C. Mardari, PhD) from the Botanical Garden A. Fatu Iasi and a voucher specimen was deposited in the Herbarium of Pharmaceutical Botany Department from Grigore T. Popa University of Medicine and Pharmacy. The plants were air-dried at room temperature and grounded to a fine powder. 10 g of plant material was extracted three times with 200 mL methanol for 1 hour, at room temperature, using a magnetic stirrer. The extract was appropriately diluted before injection in HPLC.

Chromatographic conditions for polyphenols analysis

Polyphenols were quantified using a HPLC-UV-MS method, previously described [14]. Eighteen polyphenolic standards were used: caffeic acid, chlorogenic acid, p-coumaric acid, kaempferol, apigenin, rutin, quercetin, quercitrin, isoquercitrin, fisetin, hyperoside, myricetin (Sigma, Germany), ferulic acid, gentisic acid, sinapic acid, patuletin, luteolin (Roth, Germany), caftaric acid (Dalton, USA). Calibration curves in the 0.5 - 50 µg/mL range with...
good linearity ($R^2 > 0.999$) were used to determine the concentration of polyphenols in plant samples. Samples were analyzed before and after hydrolysis in order to identify the flavonoidic glycosides and also flavonoid aglycones released after hydrolysis. Four polyphenols cannot be quantified in current chromatographic conditions due to overlapping (caffaric acid with gentisic acid and caffeic acid with chlorogenic acid). However, all four compounds can be selectively identified in MS detection (qualitative analysis) based on differences between their molecular mass and MS spectra.

**Chromatographic conditions for the analysis of caffeic and chlorogenic acids.**

Seeing that caffeic and chlorogenic acids, important antioxidants, could only be identified, but not quantified in the previous chromatographic conditions, we carried out a new analysis in order to determine the quantity of these two hydroxycinnamic acids. The compounds were separated using a Zorbax SB-C18 reversed-phase analytical column (100 x 3.0 mm i.d., 3 µm particles) fitted with a guard column Zorbax SB-C18, both operated at 42°C. The separation was achieved under isocratic conditions using a mobile phase consisting of 0.1% acetic acid and acetonitrile (v/v). The flow rate was 0.8 mL/min and the injection volume was 5 µL. Mass spectrometry analysis was performed on an Agilent Ion Trap 1100 VL mass spectrometer with electrospray ionization (ESI) interface in negative mode. Operating conditions were optimized in order to achieve maximum sensitivity values: gas (nitrogen) temperature 60°C at a flow rate of 12 L/min, nebulizer pressure 60 psi and capillary voltage + 3500 V. The full identification of compounds was performed by comparing the retention times and mass spectra with those of standards in the same chromatographic conditions. To avoid or limit the interference from background, the multiple reactions monitoring analysis mode was used instead of single ion monitoring (e.g., MS/MS instead of MS). Calibration curves of the hydroxycinnamic acids in the range of selected concentrations (0.06 - 4 µg/mL) showed a good linear correlation coefficient ($R^2 > 0.99$).

**Chromatographic conditions for the analysis of methoxylated flavones.**

Methoxylated flavonoid aglycones were quantified through high-performance liquid chromatography coupled with mass spectrometry (LC-MS), using six standards: jaceosidin, eupatilin (ALB Technology, China), casticin, acacetin, eupatorin, hispidulin (Sigma, Germany). The separation of the methoxylated flavones was achieved using a Zorbax SB-C18 reversed-phase analytical column (100 x 3.0 mm i.d., 5 µm particle) fitted with a guard column Zorbax SB-C18, both operated at 48°C. The mobile phase consisted in 0.1% (v/v) acetic acid and methanol for 8 min with a flow rate of 0.9 mL/min and an injection volume of 5 µL. For the MS analysis the following optimized conditions were used: electrospray ionization (ESI) interface operating in negative mode, gas (nitrogen) temperature 325°C at a flow rate of 7 L/min, nebulizer pressure 60 psi and capillary voltage - 3500 V. The full identification of compounds was performed by comparing the retention times and mass spectra with those of standards in the same chromatographic conditions. To avoid or limit the interference from background, the multiple reactions monitoring analysis mode was used instead of single ion monitoring (e.g., MS/MS instead of MS). Calibration curves of the lactones in the range of selected concentrations (0.02 - 3 µg/mL) showed a linear correlation coefficient ($R^2 > 0.99$).

**Results and discussions.**

The antioxidant activity of extracts was evaluated by high-performance liquid chromatography coupled with mass spectrometry (LC-MS), using six standards: quercetin, ß-sitosterol, stigmasterol, campesterol, brassicasterol and ergosterol, acquired from Sigma (Germany). Calibration curves of the sterols in the range of selected concentrations (0.06-6 µg/mL) showed a linear correlation coefficient ($R^2 > 0.99$).

**Chromatographic conditions for the analysis of sesquiterpene lactones.**

The analysis of sesquiterpene lactones was carried out by high-performance liquid chromatography coupled with mass spectrometry (LC-MS), using six standards: ß-sitosterol, stigmasterol, campesterol, brassicasterol and ergosterol. The analysis of sesquiterpene lactones was carried out by high-performance liquid chromatography coupled with mass spectrometry (LC-MS), using six standards: ß-sitosterol, stigmasterol, campesterol, brassicasterol and ergosterol. Quantification of sterols was performed by a LC-MS method previously described [15], using five standards: ß-sitosterol, stigmasterol, campesterol, brassicasterol and ergosterol, acquired from Sigma (Germany). Calibration curves of the sterols in the range of selected concentrations (0.06-6 µg/mL) showed a linear correlation coefficient ($R^2 > 0.99$).
Aglycones) have been investigated in *A. campestris* subsp. *campestris* extract using a previously developed HPLC method [15]. This method allows a simultaneous analysis of different classes of polyphenols by a single column pass. The separation of examined compounds was performed in 35 min. Figures 1 and 2 show the HPLC chromatogram of the non-hydrolyzed and hydrolyzed extract of *A. campestris*. The concentrations of identified polyphenolic compounds in *A. campestris* extract are presented in table 1 in order of the compounds' retention time, expressed as µg/g dry weight plant material.

The results show the presence of phenolic acids in the samples: p-coumaric acid is found in free form and in higher quantity in esterified form, gentisic and ferulic acid are only present in the hydrolyzed extract, caffeic and chlorogenic acid are both present in extracts. Caffeic acid and sinapic acid, hyperoside, myricetin, fisetin, quercitrin, patuletin and kaempferol were not identified in the tested extracts.

Among the analyzed flavonoids, isoquercitrin is found in high amounts in the crude methanol extract of *A. campestris*, followed by rutin and moderate quantities of luteolin, apigenin and quercetin. As expected, higher amounts of quercetin are present in the hydrolyzed extract, seeing that its glycosides were found in the crude extract. Luteolin is also present in the hydrolyzed extract.

![Figure 1](image1.png)

**Fig. 1. HPLC chromatogram of *A. campestris* extract (non-hydrolyzed): p-coumaric acid (1), isoquercitrin (2), rutoside (3), quercetin (4), luteolin (5), apigenin (6)**

![Figure 2](image2.png)

**Fig. 2. HPLC chromatogram of *A. campestris* extract (hydrolyzed): p-coumaric acid (1), ferulic acid (2), quercetin (3), luteolin (4)**

<table>
<thead>
<tr>
<th>Phenolic Compounds</th>
<th>m/z value</th>
<th>Rt (min)</th>
<th><em>A. campestris</em> extract (non-hydrolyzed)</th>
<th><em>A. campestris</em> extract (hydrolyzed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentisic acid</td>
<td>153</td>
<td>3.5</td>
<td>-</td>
<td>*</td>
</tr>
<tr>
<td>Caffeic acid</td>
<td>179</td>
<td>5.6</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Chlorogenic acid</td>
<td>233</td>
<td>5.6</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>p-Coumaric acid</td>
<td>163</td>
<td>8.7</td>
<td>18.44</td>
<td>38.92</td>
</tr>
<tr>
<td>Ferulic acid</td>
<td>193</td>
<td>12.2</td>
<td>-</td>
<td>224.50</td>
</tr>
<tr>
<td>Isoquercitrin</td>
<td>463</td>
<td>19.6</td>
<td>1974.80</td>
<td>-</td>
</tr>
<tr>
<td>Rutin</td>
<td>609</td>
<td>20.2</td>
<td>364.52</td>
<td>-</td>
</tr>
<tr>
<td>Quercetin</td>
<td>301</td>
<td>26.3</td>
<td>7.88</td>
<td>36.50</td>
</tr>
<tr>
<td>Luteolin</td>
<td>285</td>
<td>29.1</td>
<td>46.68</td>
<td>50.1</td>
</tr>
<tr>
<td>Apigenin</td>
<td>269</td>
<td>33.1</td>
<td>21.38</td>
<td>-</td>
</tr>
</tbody>
</table>

*Only MS qualitative determination was done; UV signal <LoQ (limit of quantification) or interferences/peak overlapping from other compounds does not allow the quantitative determination of these substances.*
The data available in the scientific literature reports the presence of luteolin and apigenin glycosides in the ethanolextract and the presence of quercetin and its glycosides in the aqueousextract of A. campestris from Tunisia [12]. Karabegovic et al. [20] identified in the methanol extracts of A. campestris from Bulgaria apigenin, quercetin, rutin, hyperoside and their glycosides and also glycosides of kaempferol and luteolin. Megdiche-Ksouri et al. [11] have found rutin in the methanol crude extract and the aqueous fraction and quercetin in the methanol crude extract of A. campestris subsp. maritima.

**Caffeic and chlorogenic acids analysis**

In the previous polyphenols analysis, caffeic and chlorogenic acids - both powerful antioxidants, could not be quantified due to co-elution, so a new LC-MS method was used for their determination in plant extract.

In the aforementioned chromatographic conditions, the retention time of the chlorogenic was 2.2 min and of caffeic acid 3.3 min, as shown in figure 3. Because in the ionization conditions both acids lose a proton, the ions monitored by the mass spectrometer are always in the form \([M-H]^-\), so the ions recorded have \(m/z = 353\) for chlorogenic acid and \(m/z = 179\) for caffeic acid. Anyway, in order to increase the selectivity and sensitivity of the method, for each compound, a second ion was monitored from the MS/MS spectrum: \(m/z = 191\) for chlorogenic acid and \(m/z = 135\) for caffeic acid.

These ions were further used for the quantitative determination of these compounds, seeing that the intensity of ions in the mass spectrum is proportional to the concentration of the substance in the sample. The native species contains higher amounts of chlorogenic acid (8197.2 µg/g dw) than caffeic acid (61.6 µg/g dw) in accord to the findings of Pereira et al. who reported the presence of both hydroxycinnamic acids in A. campestris subsp. maritima [6].

To the best of our knowledge, our study identified and quantified for the first time isoquercitrin, caffeic acid, chlorogenic acid, ferulic acid and p-coumaric acid in A. campestris subsp. campestris samples. It also qualitatively identified gentisic acid in the hydrolyzed extract.

**The analysis of methoxylated flavones**

Considering the fact that methoxylated flavones, found generally as aglycones in the epicuticular wax, are bioactive compounds frequently identified in species from Asteraceae family [21], their determination is of interest from the point of view of a medicinal plant.

Thus, a new LC-MS method was developed in order to assess the presence of six methoxylated flavones in the plant extract: jaceosidin, hispidulin, eupatilin, eupatorin, casticin and acacetin. The analytes eluted in less than 10 min in the chosen chromatographic conditions, as shown in figure 4. In the process of MS analysis, the pseudo-molecular ions of the flavones have been fragmented, and based on their daughter ions from the MS spectrum (table 2) the extracted chromatograms of each compound were constructed for quantification.

![Fig. 4. MS chromatograms of analyzed flavones: jaceosidin (1), hispidulin (2), eupatilin (3), eupatorin (4), casticin (5) and acacetin (6) (image)](image)

**Table 2**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Kt (min)</th>
<th>M</th>
<th>[M-H]^-</th>
<th>Monitored ions/fragments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaceosidin</td>
<td>2.9</td>
<td>330.3</td>
<td>325.3</td>
<td>314</td>
</tr>
<tr>
<td>Hispidulin</td>
<td>4.2</td>
<td>300.2</td>
<td>296.2</td>
<td>284</td>
</tr>
<tr>
<td>Eupalitin</td>
<td>7.05</td>
<td>344.3</td>
<td>343.3</td>
<td>328</td>
</tr>
<tr>
<td>Eupatorin</td>
<td>7.6</td>
<td>344.3</td>
<td>343.3</td>
<td>328</td>
</tr>
<tr>
<td>Casticin</td>
<td>8.03</td>
<td>374.3</td>
<td>373.3</td>
<td>338</td>
</tr>
<tr>
<td>Acacetin</td>
<td>9.8</td>
<td>284.3</td>
<td>283.3</td>
<td>268</td>
</tr>
</tbody>
</table>

All six compounds selected for this analysis are known for their pharmacological properties, mainly antitumor, anti-inflammatory, antioxidant, antimicrobial and anti-ulcer [22, 23]. Eupatilin, casticin and acacetin were determined for the first time in A. campestris, while jaceosidin was not present in the plant extract. Eupatilin and hispidulin were previously reported in Tunisian and Bulgarian plants, respectively [1, 20]. The compounds were identified in moderate amounts, eupatorin having the highest concentration in plant (100.90 µg/g dw) and acacetin the lowest (1.89 µg/g dw). The eupatilin content in plant was 40.33 µg/g, hispidulin 27.58 µg/g and casticin 24.39 µg/g dw. Methoxylated flavonoids are promising therapeutic candidates due to their lipophilic nature and increased metabolic stability that results in high oral bioavailability compared to other polyphenols [23].

**The analysis of phytosterols**

In order to identify the sterols present in the plant extract, a previously reported method LC-MS method was used.
The ions monitored in the MS assay are presented in Table 3. The ions detected by the mass-spectrometer are in the form \([\text{M-H}_2\text{O}+\text{H}]^+\) because in the ionization conditions all sterols have lost a water molecule. The specific ions of the five standard sterols have been fragmented and the extracted chromatograms of each compound were drawn. The method was also applied for the quantification of phytosterols, because the intensity of major ions in the mass spectrum is proportional to the concentration of the substance in the sample.

Stigmasterol, \(\beta\)-sitosterol and campesterol were quantified in \(A.\ campestris\) extract, while brassicasterol and ergosterol were not present. None of the sterol compounds were previously reported for \(A.\ campestris\). \(\beta\)-Sitosterol was the dominant sterol (159.84 \(\mu\text{g/g dw}\)), followed by stigmasterol (27.38 \(\mu\text{g/g dw}\)) and low amounts of campesterol (4.10 \(\mu\text{g/g dw}\)). Plant sterols have cholesterol-lowering effect and offer protection against cardiovascular diseases; they also exhibit a potent anti-inflammatory activity and manifest anticancer properties [24].

The analysis of sesquiterpene lactones

Sesquiterpene lactones are an important class of secondary metabolites specific to \(Artemisia\) species, structurally divers and synthesized in response to biotic or abiotic stress [25]. For that reason, we attempted the identification of some compounds in this group by developing a new LC-MS method in order to assess the presence of six sesquiterpene lactones: vulgarin, \(\alpha\)-santonin, dehydroeleucodine, artemisinin, costunolide and alantolactone. The analytes eluted in less than 7 minutes in the selected chromatographic conditions, as presented in Figure 5.

MS detection showed the parent-ions of analyzed lactones. Apart for vulgarin, in each case the expected ion was observed (Table 4). Vulgarin suffers dehydration during the ionization process, so the scanned ion has \(m/z\) 247.3 and not 265.3, as expected. In this case, the ion with \(m/z\) 247.3 was further fragmented in order to obtain the MS/MS spectrum.

The specific ions of the six standard lactones have been fragmented and the extracted chromatograms of each compound were constructed for quantification.

From the six standards used in analysis of sesquiterpene lactones, only \(\alpha\)-santonin was found in small amounts in \(A.\ campestris\) (0.24 \(\mu\text{g/g dw}\)). \(\alpha\)-Santonin is a known anthelmintic drug, fallen out of used due to severe side effects and development of modern safer de-worming drugs. It also manifests anti-inflammatory, analgesic, antipyretic and mild anticancer effect and in recent years has become the parent molecule for the synthesis of new anticancer compounds [26].

Table 3

<table>
<thead>
<tr>
<th>Compound</th>
<th>(R_t) (min)</th>
<th>(M)</th>
<th>Specific ions for identification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ergosterol</td>
<td>3.2</td>
<td>396</td>
<td>(379&gt; 138.9; 184.9; 199; 213; 223; 239; 273; 309; 323)</td>
</tr>
<tr>
<td>Brassicasterol</td>
<td>3.9</td>
<td>398</td>
<td>(381; 201.3; 203.3; 215.3; 217.3; 241.2; 255.3; 257.4; 271.1; 297.3; 299.3)</td>
</tr>
<tr>
<td>Stigmasterol</td>
<td>4.9</td>
<td>412</td>
<td>(395; 255; 297; 283; 311; 241; 201)</td>
</tr>
<tr>
<td>Campesterol</td>
<td>4.9</td>
<td>400</td>
<td>(383; 147; 149; 161; 176; 138; 203; 213; 229; 233; 237)</td>
</tr>
<tr>
<td>(\beta)-Sitosterol</td>
<td>5.7</td>
<td>414</td>
<td>(397; 160.9; 174.9; 188.9; 202.9; 214.9; 243; 257; 287.1; 315.2)</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Compound</th>
<th>(R_t) (min)</th>
<th>(M)</th>
<th>(M+H^+)</th>
<th>Monitored ions/fragments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulgarin</td>
<td>1.45</td>
<td>264.3</td>
<td>265.3 / 247.3</td>
<td>173.2</td>
</tr>
<tr>
<td>(\alpha)-Santonin</td>
<td>2.00</td>
<td>245.3</td>
<td>247.3</td>
<td>173.2</td>
</tr>
<tr>
<td>Dehydroeleucodine</td>
<td>2.70</td>
<td>244.3</td>
<td>345.3</td>
<td>199.2; 208.2; 217.2; 227.2</td>
</tr>
<tr>
<td>Artemisinin</td>
<td>5.50</td>
<td>282.3</td>
<td>283.3</td>
<td>247.2; 265.2</td>
</tr>
<tr>
<td>Costunolide</td>
<td>6.40</td>
<td>232.3</td>
<td>233.3</td>
<td>187.3; 215.2</td>
</tr>
<tr>
<td>Alantolactone</td>
<td>6.85</td>
<td>232.3</td>
<td>233.3</td>
<td>151.2; 187.3; 215.2</td>
</tr>
</tbody>
</table>

Fig. 5. MS chromatograms of analyzed lactones: vulgarin (1), \(\alpha\)-santonin (2), dehydroeleucodine (3), artemisinin (4), costunolide (5), alantolactone (6)
**Total phenols and total flavonoids content**

*Artemisia campestris* extract contains significant amounts of phenolic compounds, having a total phenolic content of 114.61 mg/g dw. This result is comparable to levels of polyphenols found in *A. campestris* subsp. *maritima* (119 - 134 mg/g dw) [6] and superior to those reported for North-African plants [9, 27]. Total flavonoid content, expressed as quercetin equivalents, was 17.99 mg/g dw, similar to values reported in literature [9, 13].

**Antioxidant activity**

The radical scavenging activity of *A. campestris* extract varied depending on concentration (fig. 6). Thus, the extract exhibited a scavenging activity of 9.87 ± 0.18% at a concentration 5.20 µg/mL; at the same concentration, quercetin inactivated the DPPH radical in high percentage (75.64 ± 0.46%). At a concentration 83.33 µg/mL, the activity increased, reaching similar values for both extract (92.64 ± 0.07%) and quercetin (96.34 ± 0.31%). The *A. campestris* extract (*EC₅₀ = 28.0 ± 0.2 µg/mL) was less active than quercetin (*EC₅₀ = 3.1 ± 0.04 µg/mL) as scavenger of DPPH radicals. Still, taking into account the *EC₅₀* values and the fact that quercetin is a pure compound known for its antioxidant properties, we can estimate that the field wormwood extract shows a very good scavenging activity against DPPH radicals.

The ability of *A. campestris* extracts to scavenge free radicals is also supported by other studies, as shown in literature. The *EC₅₀* values vary widely depending on the type of extract, subspecies and pedoclimatic conditions varied depending on concentration (fig. 6). Thus, the radical scavenging activity of *A. campestris* plants confirm the fact that it has antioxidant activity and could be used as a potential therapy in oxidative stress related diseases.

**Conclusions**

Our study reports for the first time the presence of eupatorin, acacetin, casticin, stigmatosterol, â-sitosterol, campesterol, and gentisic acid in *A. campestris*. All the above-mentioned compounds and others already acknowledged manifest different pharmacological activities that contribute to the therapeutic effect of the plant extract. The phytochemical study was carried out through LC-MS analyses and two new methods were developed for the analysis of methoxylated flavones and sesquiterpene lactones. Antioxidant tests carried out *in vitro* on *A. campestris* plants confirm the fact that it has antioxidant activity and could be used as a potential therapy in oxidative stress related diseases.

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