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Health effects of wormwood (*Artemisia absinthium* L.): From antioxidant to nutraceutical

Maria-Evelina Bordean[1], Sevastița Muste[2*], Georgiana Smaranda Marțiș[3], Vlad Mureșan[4], Bettina-Cristina Buican[5]

[1]*University of Agricultural Science and Veterinary Medicine Cluj-Napoca, 400372, Doctoral School of Agricultural and Engineering Sciences, Field: Agronomy, Calea Mănăștur, no. 3-5, Cluj-Napoca, Romania*
[2]*University of Agricultural Science and Veterinary Medicine Cluj-Napoca, 400372, Calea Mănăștur, no. 3-5, Faculty of Agriculture, Department of Plant Science, Calea Mănăștur, no. 3-5, Cluj-Napoca, Romania*
[3]*University of Agricultural Science and Veterinary Medicine Cluj-Napoca, 400372, Calea Mănăștur, no. 3-5, Faculty of Food Science and Technology, Department of Food Engineering, Calea Mănăștur, no. 3-5, Cluj-Napoca, Romania*
[4]*University of Agricultural Science and Veterinary Medicine Cluj-Napoca, 400372, Calea Mănăștur, no. 3-5 Faculty of Food Science and Technology, Department of Food Engineering, Calea Mănăștur, no. 3-5, Cluj-Napoca, Romania*
[5]*Hochschule Geisenheim University (HGU), Von-Lade-Straße 1, 65366, Geisenheim, Germany*

Abstract

Wormwood, scientifically called *Artemisia absinthium* L., is one of the largest and most widespread species in the genus *Artemisia*.

Known as a medicinal and aromatic plant, wormwood has many beneficial effects on the body, some of which have already been proven and some are still under study. The purpose of this review is to evaluate these studies in order to elucidate the possible health-beneficial effects of the antioxidant present in wormwood. Among the therapeutic properties of wormwood can be listed the digestive, tonic, antiparasitic, hepatoprotective, antioxidant activities, antimicrobial, diuretic, antipyretic, etc. The important active constituents, essential oil, and flavonoids drew attention due to the potential use of this antioxidant as a nutraceutical.

Keywords: wormwood, health effects, antioxidant activity, nutraceuticals

1. Context

Globally, there is a growing interest in identifying those natural antioxidant compounds that can be used safely in the food industry and preventive medicine, with significant pharmacological effects and, if possible, with very few or no side effects. Antioxidant-producing plants (in a considerable amount) are the most tender in this respect due to the fact that they can prevent oxidative stress. Thus, they can be natural sources of new antioxidant compounds.

More recently, antioxidant capacity has become a new parameter for characterizing healthy foods due to bioactive compounds.

2. Introduction

In recent years there has been a lot of interest in studying bioactive compounds from *Artemisia* species. *Artemisia absinthium* L. is a medicinal and aromatic plant, which is part of the *Asteraceae* / *Compositae* family and has antibacterial, anti-inflammatory, hepatoprotective, antidepressant, antioxidant, etc. effects [1].

The purpose of this article review is to highlight the importance of antioxidant compounds found in *Artemisia absinthium* L. for use in the food and pharmaceutical industries. In order to design this article, we used the databases of the following scientific journals: Science Direct, PubMed, and Google Scholar, from which we extracted bibliographic sources from 2005 to 2020.

3. Antioxidant activity of *Artemisia absinthium* L.

Why is antioxidant capacity important? The interest in finding natural antioxidants to replace synthetic ones is growing day by day because antioxidant capacity is considered to be a parameter that measures bioactive compounds in healthy food or plants.

Corresponding authors: sevastita.muste@usamvcluj.ro

Oxidative damage occurs in all aerobic organisms, including humans, and is stopped by natural antioxidant mechanisms. As they become ineffective at some point, a diet rich in antioxidants becomes essential. Lipid peroxidation in food can be caused by free radicals, and thus food spoils. Although foods contain synthetic antioxidants such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) prove to have various side effects. Thus, the research is aimed at discovering natural sources of antioxidants and capitalizing on plants for their antioxidant potential [2].

Wormwood (*Artemisia absinthium* L.) has been recognized in numerous studies as a vital and natural source of compounds with antioxidant activity [3]. In the following, we will be able to observe what this statement is based on.

A study on the essential oil extracted from the aerial parts of *Artemisia absinthium* L. from Turkey shows that this essential oil has antioxidant activity, except for camphor and 1,8-cineole compounds [4].

Lopes-Lutz, D. et al. (2008) state that in terms of reducing DPPH radicals and preventing the oxidation of linoleic acid, *Artemisia* essential oils are characterized by a poor antioxidant capacity. The antioxidant activity of two oils from Turkey, containing *A. absinthium* and *A. dracunculus*, was investigated and it was found that their antioxidant activity is medium to weak [5].

Another study conducted by *Kharoubi, O. et al.* (2008) questioned the effect of the aqueous extract of *Artemisia absinthium* L. against oxidative stress that occurs in rats exposed for a long time to Pb. The results showed that the aqueous extract of *Artemisia absinthium* L. has antioxidant effects against lipid peroxidation [6].

In 2009, in India, it was conducted a study by *Mahmoudi, M et al*. regarding the antioxidant capacity of wormwood methanolic extract obtained in the flowering stage of the plant. Five tests were performed to determine the antioxidant activity of the extract. Although the test results were different, they showed good antioxidant activity and a high content of phenols and flavonoids. Thus these natural antioxidants could be used as food additives in the food industry [7].

Another study conducted in Turkey on three local medicinal plants compared the antioxidant, antimicrobial activity, and total phenolic compounds.

The methanolic extract (aerial part of the plant) of *Artemisia absinthium* L. showed that it possesses the highest total antioxidant activity (71.78%). Regarding the total content of phenolic compounds of wormwood, using Folin-Ciocalteu assay the content was determined o be: 8.86 µgGAE / mg dry weight basis [8].

In Pakistan Asghar, *M. N. et al.* (2011) conducted a study aimed at quantifying the antioxidant capacity *in vitro* for extracts (methanolic, n-hexane, and ethyl acetate) of two species, including *Artemisia absinthium* L. The research results are positive and attest to the strong effect of eliminating free radicals and the ability to prevent lipid peroxidation for both plant extracts. These extracts can be used both against various chronic diseases and in the food industry [9].

Another study conducted in 2011 in India studied *in vitro* (free radical scavenging) and *in vivo* (antioxidant activity) the effects of the methanolic extract of *Artemisia absinthium* L. The methanolic extract proved neuroprotective (*in vivo*) properties, being reduced the level of lipid peroxidation due to the decrease of thiobarbituric acid. The test results showed that the plant has strong antioxidant effects and can be used against oxidative stress [10].

In 2012, in Anatolia, another study investigating the antioxidant activity of the genus *Artemisia* (essential oil and extract), showed that *Artemisia absinthium* L. extract is among the top 3, with the most important high results (α-tocopherol equivalent: 5.87 ± 0.17) [11].

In Romania, a research conducted on Romanian wormwood demonstrates that ethanolic wormwood extract contains a high percentage of phenolic acids and flavonoids. The antioxidant capacity of wormwood extract is high, it has a fibroblast protective effect against oxidative stress. Also, the use of wormwood in the treatment of various skin conditions can be explained by its antioxidant and cytoprotective effect, and it will be discovered which are the chemical compounds responsible for these effects [12].

A study conducted in Tunisia, which aimed at the chemical characterization of essential oil and methanolic extract from wormwood flowers and leaves, showed important antioxidant effects. It was thus found that the yield of essential oil from flowers 2.98% is higher than that from leaves 1.87%.

Chemazulenes and b-thujones are the chemical compounds with the highest weight in both oils. The highest antioxidant capacity (*in vitro*) was identified in the methanolic extract from leaves and flowers, but also the essential oil from leaves and flowers has an important antioxidant capacity. Comparing the antioxidant capacity of the essential oil and the extract from different parts of the plant, the leaf extract has the highest antioxidant capacity. The chemical composition and especially the presence of chamazulene in wormwood essential oil is responsible for such significant antioxidant activity [13].

In 2013, in Pakistan, *Ali M. et al*. conducted research on antioxidant capacity and total phenolic compounds in suspension cultures. The phenolic compounds found are: gallic acid (maximum level: 104 g g^{-1} (control: 21.3 g g^{-1})) - antiapoptotic, neuroprotective, anticarcinogenic properties, caffeic acid (maximum level: 27.40 g g^{-1} (control: 28.5 g g^{-1})) - pharmacological antioxidant, anticancer, and catechin (maximum level: 92.0 g g^{-1} (control: 68.10 g g^{-1})) - prevents oxidative damage in the epithelial cells of the digestive system. Because the relationship between phenolic compounds and antioxidant activity is directly proportional, the results showed that *in vitro* cultures (cell suspension culture of *A. absinthium* L.) are worth of commercial study due to phenolic compounds with a positive impact in the pharmaceutical industry [14].

Another study conducted in 2013 aims to evaluate the total antioxidant capacity of wormwood extract using ultrasonic-assisted extraction. The conditions (control factors) for maximum extraction of antioxidants and phenolic compounds, must have the following ranges: HCl concentrations 0.41–0.44 mol / L, methanol concentration 55–59% (v/v), extraction temperature 64–70 C, extraction time 101–107 min. Thus totally phenolic content was 57.83 mg GAE / g dried plant and total antioxidant activities were 70.29 mg TE / g dried plant for ABTS and 296.05 mg TE / g dried plant for CUPRAC. Using ultrasonic-assisted extraction, the following acids were discovered in wormwood extracts: protocatechuic, chlorogenic, caffeic, ferulic, and rosmarinic. The share of ferulic, caffeic, and chlorogenic acids was higher than in the study of Crăciunescu et al. made in 2012. This study confirms that *Artemisia absinthium* L. is a perfect candidate with antioxidant effect and can be used in the food industry [15].

Lee, Y.-J. et al., 2013 studied the possibility of using wormwood in the food industry, and for this, it was necessary to analyze phenolic compounds and antioxidant activity. Phenolic compounds were evaluated by UHPLC and a number of 20 were discovered, of which in decreasing amounts: salicylic acid, myricetin, caffeic acid, gallic acid, and ferulic acid. The three extracts were tested by three different methods and it was concluded that in terms of antioxidant activity the aqueous extract has higher antioxidant activity than methanolic extract, and the methanolic extract has higher antioxidant activity than ethyl acetate extract. The highest antioxidant capacity has been shown by the aqueous extract, capable of reducing phosphomolybdic power. The highest phenolic content was aqueous extract (134.47 mg equivalent gallic acid 100g DW-1), and the highest flavonoid content was ethyl acetate extract (87.04 mg quercetin equivalent 100g DW-1). According to the results obtained, we find that these compounds offer health benefits, so *Artemisia absinthium* L. can be used as an antioxidant in the food industry [16].

Msaada, K. et al. (2015), in a study conducted in Tunisia regarding wormwood extracts from four different regions, have evaluated the phenolic antioxidants and found their quantitative and qualitative changes, depending on the geographic origin of the plant, resulting in changes that are nutritionally significant (antiradical activity of methanolic extract was region-dependent). The largest amount of chamazulene (monoterpene hydrocarbons) was identified in wormwood essential oils, and phenolic acids predominated in the methanolic extract. The methanolic extract from the Bou Salem region had the highest antioxidant activity compared to the other regions: (9.38 ±0.82 mg / mL). Following the results obtained, wormwood can be considered a true source of antioxidant compounds and can be used in the food industry due to its phenolic composition [17].

A research conducted in India in 2017 showed the increased antioxidant capacity of wormwood and its property to reduce free radicals (*in vitro*). Moreover, the extracts are promising cytotoxic and may have antitumor activity. Most phenolic and flavonoid compounds have been identified in the hydroalcoholic extract. The total antioxidant capacity varied among the extracts. It is considered that this plant would be important to use in various pharmaceutical preparations to treat diseases caused by oxidative stress [18].

Another research conducted in Romania by *Moacă E.A. et al*., 2019, aims at the phytochemical analysis of two ethanolic extracts of wormwood (leaf systems). Regarding the antioxidant capacity of the two extracts, it was compared with an ascorbic acid control solution. Both extracts showed antioxidant effects, slightly higher the values of the extract obtained from stems. It was also found that the antioxidant effect of the leaves is directly proportional to the concentration of the extract. As for the antioxidant activity of the extract of the stem, it does not depend on the concentration. Regarding the total phenolic content evaluated for both extracts, which is very important for the evaluation of the antioxidant effects of the plant, the results highlighted the following: the leaf extract showed a higher content of phenolic compounds compared to the stem extract (54.68 ± 1.93 mg GAE / g respectively, 44.15 ± 1.12 mg GAE / g). It is very important to specify that the phenol content depends on the area from which the plant is collected. The stems extract has an anti-inflammatory effect tested *in vivo* on a model of inflammation [19].

The main compounds with antioxidant activity and there structures found *in Artemisia absinthium* L. is presented in Table 1.

Table 1. The main compounds with antioxidant activity in *Artemisia absinthium* L.

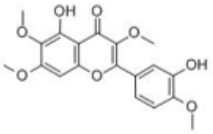
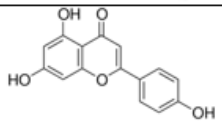
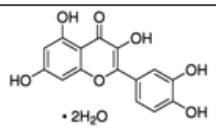
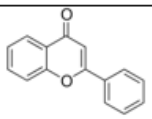
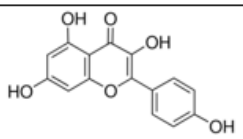
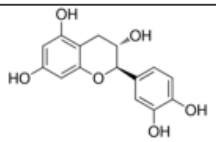
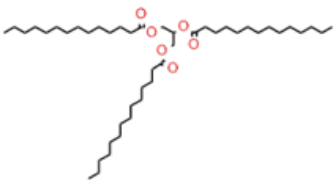
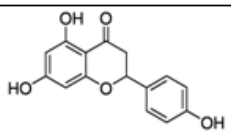
Antioxidant compound	Structure	Source
casticin		[20]
apigenin		[17]
quercetin dihydrate		
flavone		
kaempferol		
catechin		
myristin		
naryngenin		

Table 1. The main compounds with antioxidant activity in *Artemisia absinthium* L (*continued*)

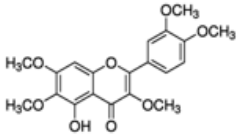
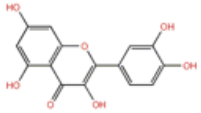
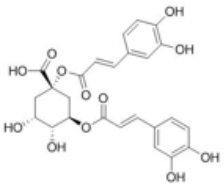
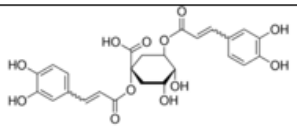
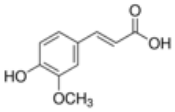
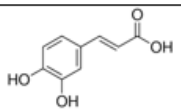
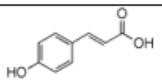
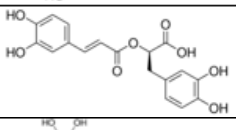
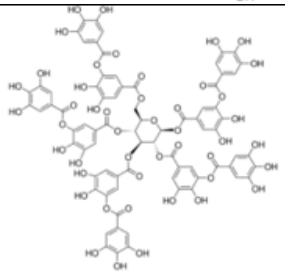
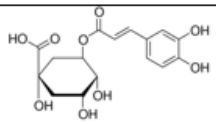
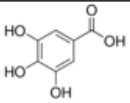
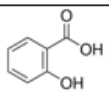
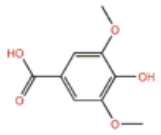
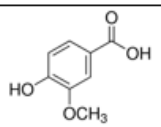
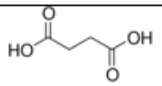
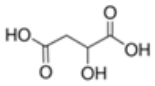
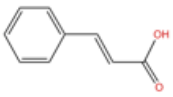
artemetin		[20,21,22]
quercetin		[23]
1',3'-O-dicaffeoylquinic acid		[24]
1',5'-O-dicaffeoylquinic acid		
ferulic acid		[17, 25]
caffeic acid		[14, 17, 21, 23, 25]
p-coumaric acid		[17]
rosmarinic acid		
tannic acid		[17]
chlorogenic acid		[26, 21, 23, 24]
gallic acid		[14, 17]
salicylic acid		

Table 1. The main compounds with antioxidant activity in *Artemisia absinthium* L (*continued*)

syringic acid		[17, 23]
vanillic acid		
succinic acid		[17, 25]
malic acid		
(E)-cinnamic acid		

4. Nutraceutics

Recent studies have shown a growing interest among researchers in nutraceuticals of plant or animal origin. This interest has increased greatly due to the curiosity about the mechanism of action of nutraceuticals. The recognition of these beneficial effects of certain substances in food on health depends on the recognition by evidence of the clinical efficacy of these substances. The definition of nutraceuticals is still unclear and this is the biggest problem: the term is confusing. Very often the term is confused with prebiotics, probiotics, functional foods, etc. Why is it so important to give them a clear definition? Some patients are not compatible with conventional medical treatments, and in this case, nutraceuticals would be a solution, behind everything that means diet, drugs. Nutraceuticals could prevent and treat pathological conditions. Consumers have become more selective and are beginning to put more emphasis on quality: the quality of their lives and the products they consume. So they try to treat themselves rather through food and safely natural origin products, to bring more health, as opposed to the offers of synthetic drugs promoted by pharmacies Nutraceutical research is a goal of the future in terms of preventing and treating various diseases. Although nowadays therapy is based only on pharmaceuticals, it is desired that nutraceuticals become at least complementary in different treatment schemes.

In the absence of clinical trials and without following their mechanism of action, nutraceuticals can not be used safely. For them to be helpful, they must meet two conditions: to prevent chronic diseases for people who cannot follow a pharmaceutical treatment and to complete a pharmacological therapy [27].

At the same time, the nutraceuticals market is expanding, and their sources are becoming more and more tender. The launch of the idea of nutraceuticals based on active substances of unconventional plants is a tender one. One such example is wormwood, *Artemisia absinthium* L., a popular plant in traditional medicine, which must keep its current popularity. Due to its antimicrobial and antioxidant actions, wormwood can become a real candidate for obtaining nutraceuticals [28].

In Lithuania, a study was carried out to obtain nutraceuticals from food by-products and essential oil and aqueous wormwood extract. It was found that after the addition of the essential oil and the extract, the antioxidant capacity of the nutraceuticals increased [28].

6. Conclusions

According to the studies presented above, it can be stated that wormwood *Artemisia absinthium* L. has biologically active compounds that maintain homeostasis of the body. As natural compounds are being sought to replace synthetic ones, applications of wormwood compounds may take other forms, such as pharmacology and the food industry.

These statements reinforce the words of Hyppocrates: "Let the food be the medicine and medicine be the food" [29].

Compliance with Ethics Requirements. Authors declare that they respect the journal's ethics requirements. Authors declare that they have no conflict of interest and all procedures involving human or animal subjects (if exist) respect the specific regulation and standards.

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