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The antidiabetic and antioxidant free radical scavenging capacity of wormwood (*Artemisia absinthium*)

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Abstract

Wormwood (*Artemisia absinthium*) is widely used in the middle east in folk medicine for treating many diseases especially those of the digestive system. However, this study was focused on studying its flavonoid and phenolic contents conferring antioxidant activity and free radical scavenging capacity. Fresh wormwood leaves will be collected from the Tabuk region in order to study the bioactive phenols and flavonoids. Wormwood has several economic medicinal properties. uses such as its use as an ingredient in the spirit absinthe as well as some other alcoholic beverages, and aromatic plants, many of which produce essential oils used in folk and modern medicine as well as in the cosmetics and pharmaceutical industry. Wormwood is used for dyspepsia, as a bitter to counteract poor appetite, for various infectious diseases, Crohn's disease, and IgA nephropathy. It is also added to Arabian coffee to confer it a distinct desirable flavor. The total flavonoid and total phenolic content will be determined, and the antioxidants assay will be determined. In addition, DPPH radical scavenging activity, was also assayed. The antidiabetic activity of the wormwood was also reviewed.

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Introduction

Artemisia absinthium (wormwood) is a native herbaceous perennial ornamental plant native to temperate regions of Eurasia and Northern Africa and it can easily be cultivated in dry soil l rich in nitrogen (Rätsch, 2005). It is used as an ingredient in the spirit absinthe as well as some other alcoholic beverages, aromatic plants, many of which produce essential oils used in folk and modern medicine as well as in the cosmetics and pharmaceutical industry and also added to the Arabian coffee to confer it a distinct desirable flavor. (Abad *et al.*, 2012). It is also used for dyspepsia, as a bitter to counteract poor appetite, for various infectious diseases, Crohn's disease, and IgA nephropathy (Algieri *et al.*, 2015).

Artemisia absinthium contain (−)-α- and/or (+)-β-thujone (Nguyen and Németh, 2016), (−)-α-Thujone by itself is a GABAA receptor antagonist that can cause convulsions and death when administered in large amounts to animals and humans (Olsen, 2000), whereas the wormwood extracts have not been shown to cause seizure or other adverse effects at usual doses (Yarnell and Heron, 2000).

Recent investigation showed that the medicinally important natural products used in folk medicine accept their antioxidant activity and their free radical scavenging capacity from their flavonoid and phenolic content (Al-Malki and El-Rabey, 2015; Al-Seeni *et al.*, 2016; Elbakry *et al.* (2019) tested the hepatic protective activity of the methanolic extract of moringa against CCl4 toxicity. Sakran *et al.* (2018) studied the antioxidant enzymatic activity of date palm seedlings under abiotic drought stress. Al-Seeni *et al.* (2018) alleviated the toxic effects of tartrazine toxicity using *Nigella sativa* oil.

Other uses of the role of the antioxidant properties is evidenced in some other studies, (El Rabey *et al.*, 2017) studied the molecular and enzymatic response to drought stress in wheat (*Triticumaestivum* L.). El Rabey *et al.*,2015, 2016 studied the enzymatic and proteomic responses of date palm plants under salinity and drought abiotic stress. Saidi *et al.* (2012) stated that brittle leaf disease induces an oxidative stress and decreases the expression of manganese-related genes in date palm (*Phoenix dactylifera* L.). The wormwood anticancer activity indicated high cytotoxic activity which is attributed to its phenolic content (Olennikov *et al.,* 2018 and Ali *et al.*, 2021).

The aim of this study is reviewing the flavonoid and phenolic content as well as the antioxidant capacity and free radical scavenging capacity of wormwood.

The total Phenolic content of wormwood

The total phenolic content of wormwood was estimated according to the method of Velioglu *et al.* (1998), whereas a modified method of the colorimetric method of Zhishen *et al.* (1999) was used in estimation of the total flavonoid content of wormwood. The average value of extraction yield of wormwood was 29.26 %. Further, the characterization of the phenolic group content was performed (Olennikov *et al.*, 2018).

The phenolic profile of wormwood was constructed after high performance liquid chromatography (HPLC) separation of total methanolic extracts and flavonoid- enriched SPE fractions using diode array detection (DAD) and triple quadrupole electrospray ionization detection (TQ-ESI-MS), with both positive and negative mode. Hbika *et al.* (2022) using HPLC analysis stated that the ethyl acetate and aqueous extracts of wormwood contain caffeic acid and naringenin and as major products in EAE and AQE, respectively. The total polyphenol content in the *A. absinthium* extracts was determined accordingto the Folin–Ciocalteu method, whereas the total flavonoid content of the *A. absinthium* extracts was obtained by using a colorimetric test using aluminum chloride ($AlCl_3$).

The total flavonoid content of wormwood

The values of Total Flavonoid Content (TFC) in A. absinthium was 25.86 ± 0.20 mg of QE /g of extract (Olennikov *et al.*, 2018). Ali *et al.* (2021) evaluated the antioxidant, antibacterial, and anticancer activities of the ethanolic extracts of Artemisia absinthium leaves were investigated. Values of total phenolic contents (TPC), total flavonoid contents (TFC), DPPH-radical scavenging activity, and ferric reducing antioxidant power (FRAP) were measured to explore the antioxidant capacity.

Olennikov *et al.* (2018) quantified 15 phenolic principal compounds in 12 *Artemisia* extracts is presented in Table 1. They found that the 4- *O*-caffeoylquinic acid in the analyzed wormwood extracts ranged from trace amounts (*A. anethifolia*) to 5.64 mg/g (*A. umbrosa*).

They also found that the wormwood content of the monosubstituted phenylpropanoid, 5-*O*-caffeoylquinic acid dominated in the extracts of *A. anethifolia* (78.88 mg/g), *A. sericea* (20.28 mg/g) and A. tanacetifolia (73.71 mg/g). They added that *A. commutata* showed the highest content (127.99mg/g) and *A. desertorum has* the lowest value (21.24 mg/g).

Table 1. Content of 15 phenolic compounds in 12 *Artemisia* extracts (mg/g dry weight ± SD), (From Olennikov *et al.*, 2018).

Artemisia extract	Caffeoylquinic acids					
	1	10	14	44	50	58	Total
A. anethifolia	<0.01	78.88 ± 1.57	<0.01	<0.01	70.76 ± 1.41	6.23 ± 0.12	155.87
A. commutata	3.14 ± 0.06	127.99 ± 2.55	3.75 ± 0.05	4.28 ± 0.08	243.61 ± 4.87	<0.01	382.77
A. desertorum	4.74 ± 0.08	21.24 ± 0.42	1.00 ± 0.02	1.24 ± 0.02	60.51 ± 1.21	3.75 ± 0.07	92.48
A. integrifolia	1.58 ± 0.03	63.73 ± 1.27	0.87 ± 0.02	4.32 ± 0.08	87.02 ± 1.74	22.71 ± 0.45	180.23
A. latifolia	0.61 ± 0.01	35.19 ± 0.70	1.21 ± 0.02	<0.01	58.55 ± 1.17	8.82 ± 0.17	104.38
A. leucophylla	2.57 ± 0.05	48.89 ± 0.98	1.23 ± 0.02	5.35 ± 0.10	108.18 ± 2.16	16.70 ± 0.33	182.92
A. macrocephala	0.81 ± 0.02	47.15 ± 0.94	6.74 ± 0.14	19.83 ± 0.39	13.42 ± 0.26	7.66 ± 0.15	95.61
A. messerschmidtiana	4.14 ± 0.08	53.06 ± 1.06	1.09 ± 0.02	0.82 ± 0.02	125.76 ± 2.51	12.98 ± 0.25	197.85
A. palustris	0.98 ± 0.02	26.59 ± 0.53	1.76 ± 0.03	2.77 ± 0.05	7.35 ± 0.14	3.23 ± 0.06	42.68
A. sericea	1.02 ± 0.02	20.28 ± 0.41	1.19 ± 0.02	<0.01	10.67 ± 0.21	<0.01	33.16
A. tanacetifolia	3.46 ± 0.06	73.71 ± 1.47	1.49 ± 0.03	4.67 ± 0.09	65.17 ± 1.29	1.06 ± 0.02	149.56
A. umbrosa	5.64 ± 0.11	30.05 ± 0.60	0.73 ± 0.01	5.61 ± 0.11	57.74 ± 1.15	10.86 ± 0.21	110.63
				FLAVONOIDS			
Artemisia extract	19		24	25	38		40
A. anethifolia	1.96 ± 0.03		0.00	0.00	9.52 ± 0.19		8.81 ± 0.17
A. commutata	8.40 ± 0.16		8.48 ± 0.16	<0.01	8.73 ± 0.18		1.02 ± 0.02
A. desertorum	0.00		<0.01	<0.01	1.61 ± 0.03		<0.01
A. integrifolia	0.71 ± 0.01		0.00	0.00	<0.01		9.73 ± 0.19
A. latifolia	0.00		0.00	0.00	11.35 ±0.22		15.75 ± 0.28
A. leucophylla	0.00		<0.01	<0.01	6.01 ± 0.12		5.89 ± 0.12
A. macrocephala	0.00		0.00	0.00	<0.01		42.17 ± 0.75
A. messerschmidtiana	0.00		<0.01	<0.01	2.28 ± 0.04		5.87 ± 0.12
A. palustris	0.00		5.90 ± 0.11	16.14 ± 0.32	<0.01		82.31 ± 1.65
A. sericea	0.00		0.00	0.00	<0.01		0.00
A. tanacetifolia	0.00		0.00	0.00	0.41 ± 0.01		1.26 ± 0.03
A. umbrosa	0.00		4.08 ± 0.08	2.82 ± 0.05	7.55 ± 0.15		3.25 ± 0.06
Artemisia extract	42		45	54	78		Total
A. anethifolia	<0.01		<0.01	<0.01	0.00		20.29
A. commutata	2.49 ± 0.05		<0.01	<0.01	<0.01		29.12
A. desertorum	<0.01		0.00	<0.01	0.00		1.61
A. integrifolia	<0.01		<0.01	<0.01	0.00		10.44
A. latifolia	0.00		14.70 ± 0.27	0.00	0.00		41.80
A. leucophylla	0.00		<0.01	<0.01	<0.01		11.90
A. macrocephala	0.00		0.00	7.66 ± 0.15	1.76 ± 0.04		51.59
A. messerschmidtiana	0.00		<0.01	0.00	0.00		8.15
A. palustris	<0.01		17.97 ± 0.35	12.82 ± 0.25	<0.01		135.14
A. sericea	0.00		0.00	0.00	0.00		<0.01
A. tanacetifolia	2.00 ± 0.04		0.00	0.44 ± 0.01	0.00		4.11
A. umbrosa	<0.01		<0.01	<0.01	0.00		17.70

Caffeoylquinic acids: 1, 4-O-caffeoylquinic acid; 10, 5-O-caffeoylquinic acid; 14, 1,3-di-O-caffeoylquinic acid; 44, 3,4-di-O-caffeoylquinic acid; 50, 3,5-di-O-caffeoylquinic acid;"
58, 4,5-di-O-caffeoylquinic acid. Flavonoids: 19, apigenin-6-C-Glc-4 -O-Glc (isosaponarin); 24, quercetin-3-O- RhaGlc (calendoflavobioside); 25, quercetin-3-O- RhaGlc; 38,
quercetin-3-O- RhaGlc (rutin); 40, quercetin-3-O-Glc (isoquercitrin); 42, quercetin-3-O-Gal (hyperoside); 45, kaempferol-3-O-6 RhaGlc (nicotiflorin); 54, isorhamnetin-3-O-Glc; 78,
quercetin.

There were variations in flavonoid and caffeoylquinic acids (CQAs) contents of Artemisia species. (Olennikov *et al.*, 2018).

DPPH radical scavenging activity

The scavenging activity of wormwood was estimated according to the method of Re *et al.* (1999), whereas the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity was assayed using the method of Ao *et al.* (2008). The produced free radicals ions from the DPPH are scavenged by antioxidants of wormwood that appeared from the conversion of the color of DPPH from dark purple to yellow.

Wormwood gave a free radicals scavenging activity of about 74.9 ±0.001 mg of Ascorbic acid/ g of wormwood extract. The antioxidant activity is attributed to free hydrogen produced by wormwood phenolics and flavonoids that reduces DPPH (Olennikov *et al.*, 2018).

Table 2. Effect of the studied herbs on various biochemical parameters in diabetic individuals (from Li *et al.*, 2015).

Group	Biochemical parameters (mg/dL)	Values				
		Day 0	Day 10	Day 20	Day 30	Day 40
Gymnema Sylvestre	Fasting glucose	219 ± 41	159 ± 26	157 ± 24	138 ± 17	181 ± 38
	TGL	218 ± 70	218 ± 75	212 ± 74	208 ± 72	230 ± 87
	Cholesterol	274 ± 70	263 ± 62	261 ± 65	238 ± 56	249 ± 54
	HDL	37 ± 6	39 ± 8	41 ± 11	43 ± 11	37 ± 7
	LDL	191 ± 63	180 ± 57	177 ± 61	154 ± 54	166 ± 51
Citrullus colocynthis	Fasting glucose	215 ± 56	188 ± 49	156 ± 48	140 ± 35	213 ± 69
	TGL	253 ± 76	248 ± 74	242 ± 72	238 ± 69	256 ± 74
	Cholesterol	257 ± 80	249 ± 76	249 ± 71	241 ± 72	253 ± 79
	HDL	38 ± 12	39 ± 11	41 ± 10	40 ± 12	38 ± 11
	LDL	168 ± 83	160 ± 79	158 ± 75	153 ± 77	167 ± 77
Artemisia absinthium	Fasting glucose	211 ± 57	204 ± 262	182 ± 43	143 ± 30	191 ± 26
	TGL	187 ± 65	185 ± 64	181 ± 59	169 ± 64	190 ± 68
	Cholesterol	239 ± 35	237 ± 36	234 ± 34	226 ± 32	238 ± 31
	HDL	39 ± 8	39 ± 8	40 ± 9	40 ± 9	39 ± 8
	LDL	163 ± 36	161 ± 36	157 ± 33	153 ± 32	162 ± 38

(n = 8, the mean ± SD).

The antidiabetic activity of wormwood

Li *et al.* (2015) estimated the antidiabetic effect of *Gymnema sylvestre*, *Citrullus colocynthis* and *wormwood* on blood glucose and lipid profile of diabetic humans. Table 2 shows the Effect of the studied herbs on various biochemical parameters in diabetic individuals.

In addition, Dabe and Kefale (2017) studied the antidiabetic effect of the aqueous and alcoholic extracts of wormwood and found that wormwood extracts reduced the level of blood glucose, so people used it as therapeutic agent in treating diabetes in spite of the presence of many antidiabetic drugs with a relatively less side effects. Moreover, Daradka *et al.* (2014) stated that wormwood extract revealed significant antidiabetic activity on alloxan-induced diabetic rats.

Conclusion

The current review clarified the use of wormwood as a source of bioactive phenolics. The total flavonoid and total phenolic content, and the antioxidants, radical cation decolorization, DPPH radical scavenging activity indicates the possible use of wormwood in other medicinal application as folk medicine or even used as a drug for other diseases that resulted from oxidative stress. In addition, the flavonoid of wormwood is suitable chemotaxonomic tools as other groups of plant phenolics. The 15 principal phenolics showed that the caffeoylquinic acids (CQAs) is the principal constituents. The antioxidant activity of wormwood is a candidate for bioactivity targeting in future research for discovering the hypoglycemic activity machinery of wormwood.

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