Bioactive Compounds from Cardoon and Metabolic Disorders

Subjects: Biochemical Research Methods
Contributor: Luís Silva

Cardoon (*Cynara cardunculus* L.) is a Mediterranean plant and member of the Asteraceae family that includes three botanical taxa, the wild perennial cardoon (*C. cardunculus* L. var. *sylvestris (Lamk) Fiori*), globe artichoke (*C. cardunculus* L. var. *scolymus L. Fiori*), and domesticated cardoon (*C. cardunculus* L. var. *altilis DC.*). Cardoon has been widely used in the Mediterranean diet and folk medicine since ancient times. Today, cardoon is recognized as a plant with great industrial potential and is considered as a functional food, with important nutritional value, being an interesting source of bioactive compounds, such as phenolics, minerals, inulin, fiber, and sesquiterpene lactones.

Keywords: Cynara cardunculus L. ; phytochemical composition ; metabolic disorders ; Mediterranean plant ; biological activities

1. Cynara cardunculus L.

Cynara cardunculus L. belongs to the Asteraceae family, one of the largest families of the plant kingdom. Cynara is a relatively small genus, native to the Mediterranean basin [1]. *Cynara cardunculus* comprises three taxa: (i) the wild cardoon (*Cynara cardunculus* L. var. *sylvestris*), (ii) the domesticated cardoon (*Cynara cardunculus* var. *altilis DC*), and (iii) globe artichoke (*Cynara cardunculus* var. *scolymus* L.) [2][3][4]. Studies on the morphology and phytogeography of the *Cynara* genus reported that the referred plants belong to a single species and should consequently be classified as subspecies [1]. With respect to cultivated cardoon, its production is more limited to southern Europe, namely, France, Greece, Italy, Portugal, and Spain. Additionally, *C. cardunculus* L. is distributed across the Mediterranean basin, Macaronesia (Madeira and Canary Islands), North Africa, Cyprus, and Turkey, and it has also colonized Mexico, California, Argentina, Chile, Peru, Australia, China, and West Africa [1]. In these areas, cardoon has revealed its high adaptability to the climate conditions, i.e., a semiarid bioclimate, allowing its cultivation as a perennial crop in marginal lands with low moisture conditions (drylands).

Cardoon is a perennial plant that can reach more than 2 m in height with a thick and rigid stem, often branched in the upper parts; it is longitudinally ribbed and covered in cotton down. This plant has an annual development cycle, which can start with seed germination in autumn or spring, being completed in summer. The above-plant portion of the plant dies down each year, but its large taproot regenerates each year, growing up to 1 m down [5][6].

The seeds are 6–8 mm long, four-sided, and smooth. Their color is light gray, brown, or black, sometimes with longitudinal streaks. A circle of feathery hairs is present at the top of each seed, 25–40 mm in length, that readily falls off.

The leaves form a strong and large basal rosette and can be up to 120 by 30 cm. The upper leaves are comparatively smaller, 10–50 cm in length. Furthermore, they are grayish-green on the upper surface and slightly hairy. On the underside, they are covered in dense hair giving a white woolly appearance. Each leaf is deeply lobed, with each lobe often partly divided again. The tips of the leaves are spiked with yellowish/orange spines, 5–20 mm long [5][6][7].

The inflorescence can be called a capitula or head, and there are hermaphrodites and tubular flowers (florets). The inflorescence occurs singly at the top of a branch on a thick stalk, 1–6 cm long. The flower heads are almost round in shape and grow to be 4–5 cm across. They consist of blue, pink, or purple florets arranged on a fleshy receptacle, enclosed by several large bracts. The bracts are purplish in color and taper to the end in a flattened spine [5][6][7].

Globe artichoke is cultivated for its edible phyllary bases and receptacles of its floral heads. Leaf stalks and leaf bases can be eaten as a cooked vegetable (boiled, braised, or sautéed) and used in salads and soups; they have an artichoke-like flavor. Additionally, artichoke flower extract is used in the food industry as an additive to prevent oil autooxidation and rancidity [8].

On the other hand, cardoon stalks are eaten and their flowers are used as plant rennet for the manufacture of French, Italian, Spanish, and Portuguese cheeses; this is legally required for the production of protected designation of origin (PDO) cheeses from Spain and Portugal, due to their richness in different proteases [5][1][9][10][11]. Additionally, cardoon is utilized by the paper industry due to its high cellulose and hemicellulose contents. It is also applied for biomass and bioenergy production (biogases as bioethanol and biomethane), as it includes 2–3 t·ha^{-1} of seeds, which are a good source of proteins and edible oil [12][13][14][15][16], as well as a good source of oil for biodiesel production [17]. The seeds contain around 25% oil, with good alimentary quality. The seed pomace after the extraction can be used for animal feed [5].

Additionally, cardoon leaf extract proved to have a great inhibitory effect against seed germination from weeds, revealing its potential to be used as a bioherbicide [18]. In a similar line, Restuccia and colleagues [19] combined a biocontrol yeast *W. anomalus* BS91 and three extracts (aqueous, methanolic, and ethanolic) from *C. cardunculus* L. var. *altilis DC*. leaves, the results revealed stronger protection with a combination of the ethanolic extract against green mold decay on oranges and lemons than when used singularly. These results indicate that biocontrol agents and leaf extracts, used in combination, can provide a stronger protection than when used singularly.

Moreover, the cytotoxicity of cardoon has been studied by several authors, reporting that cardoon does not present any toxicity toward noncancer cells; on the contrary, the cytotoxicity against cancer cells can depend on the plant part, maturity stage, and genetic background [20][21].

Cardoon produces a considerable amount of field residues; 590 days after planting, biomass accumulation may reach 3968 g·plant^{-1} [22]. Stalks, capitula, and leaves represent an average of 40%, 35%, and 25% of the aboveground biomass, respectively, and they possess a low moisture content (10–15%) [7][23], with a yield per hectare ranging from 3.64–38.38 t/year, with an average of 19.22 t/year during the first 3 years of production [24][25][26], supporting a good yield as a source of bioactive compounds [5][27][28].

2. Nutritional and Chemical Composition

The edible portion of the cardoon plant is the immature inflorescence (capitula or heads), including the inner bracts and the upper part of the receptacle, which can be eaten as fresh, canned, or frozen vegetal after minimal processing [3][29][30]. Cardoon is extremely nutritive, containing carbohydrates (inulin, sugars, and fiber), proteins and amino acids, fatty acids, organic acids, minerals, and vitamins. It is also an important source of bioactive compounds with pharmaceutical potential, including phenolic compounds, phytosterol, and volatiles [13][2][5][3][22][29][30][31]. The recognized high nutritive value of cardoon heads is attributed to the low content of lipids and high content of minerals, vitamins, and bioactive compounds, which are potent natural antioxidants substances [5][3]. The roots and rhizomes provide a source of inulin [22][31][32], an enhancer of the human intestinal flora, and the leaves provide a source of antioxidants, mainly dicaffeoylquinic acids and luteolin [2][3]. Furthermore, cardoon leaves are traditionally used in popular medicine as diuretics, hepatoprotectors, cholagogues, choleretics, and antidiabetics [33].

The chemical composition has been studied by various researchers in different biomass fractions: root [22][31]; stalks [34]; capitula fractions (receptacle, bracts, hairs, and pappi) [35]; heads [12]; leaves [25][36]; flowers [37]; seeds [12][38][39], as summarized in **Table 1**, **Table 2**, **Table 3**, **Table 4**, **Table 5**, **Table 6**, **Table 7**, **Table 8** and **Table 9**.

Table 1. Nutritional composition of raw cardoon [40].

Nutrient (Unit)	Raw
Basic chemical composition	
Water (g/100 g)	**94**
Energy (kcal/100 g)	**17**
Energy (kJ/100 g)	**71**
Macronutrients	
Total protein (g/100 g)	**0.7**
Total lipids (g/100 g)	**0.1**
Fatty acids, total saturated (g/100 g)	**0.011**

Nutrient (Unit)	Raw
SFA 16:0 (g/100 g)	0.009
SFA 18:0 (g/100 g)	0.002
Fatty acids, total monounsaturated (g/100 g)	0.018
MUFA 16:1 (g/100 g)	0
MUFA 18:1 (g/100 g)	0.018
MUFA 20:1 (g/100 g)	0
Fatty acids, total polyunsaturated (g/100 g)	0.041
PUFA 18:2 (g/100 g)	0.041
Carbohydrates (g/100 g) (by difference)	4.07
Total ash (g/100 g)	1.13
Total dietary fiber (g/100 g)	1.6
Total sugars (g/100 g)	4.07
Micronutrients	
Minerals	
Calcium, Ca (mg/100 g)	70
Iron, Fe (mg/100 g)	0.7
Magnesium, Mg (mg/100 g)	42
Phosphorus, P (mg/100 g)	23
Potassium, K (mg/100 g)	400
Sodium, Na (mg/100 g)	170
Zinc, Zn (mg/100 g)	0.17
Cooper, Cu (mg/100 g)	0.23
Manganese, Mn (mg/100 g)	0.256
Fluoride, F (µg/100 g)	0.2
Vitamins	
Vitamin C (mg/100 g)	2
Thiamin (mg/100 g)	0.02
Riboflavin (mg/100 g)	0.03
Niacin (mg/100 g)	0.3
Pantothenic acid (mg/100 g)	0.338
Vitamin B6 (mg/100 g)	0.116
Folate, total (µg/100 g)	68
Folate, DFE (µg/100 g)	68
Folate, food (µg/100 g)	68
Vitamin A, RAE (µg/100 g)	0
Vitamin A, IU (IU/100 g)	0
Vitamin B12 (µg/100 g)	0
Vitamin D (D2 + D3) IU (IU/100 g)	0
Vitamin D (D2 + D3) (µg/100 g)	0

Table 2. Free sugar composition of cardoon vegetal parts.

Free Sugars (g/100 g d.w.)	Raw A	Roots B	Flowers C	Seeds D	Bracts E	Heads F
Fructose	-	0.1–6.47	-	n.d.–1.94	0.14–1.41	0.013–0.51
Glucose	-	0.07–4.54	2.47–4.69	n.d.–0.78	0.10–0.557	0.0–2.02
Sucrose	-	0.16–4.39	-	0.30–8.77	0.12–4.970	n.d.–2.39
Trehalose	-	-	-	0.16–36.44	0.24–1.16	0.23–0.98
Raffinose	-	-	-	n.d-1.31	n.d.–2.13	0.0–2.62
Rhamnose	0.75–1.1	-	1.10–1.19	-	-	-
Arabinose	1.17–2.7	-	4.23–6.03	-	-	-
Xylose	21.49–27.0	-	2.12–2.61	-	-	-
Mannose	1.1–1.8	-	0.44–0.52	-	-	-
Galactose	1.35–2.5	-	1.27–1.82	-	-	-
Inulin	-	22.4–49.6 *	-	-	-	-

n.d., not detected; * values for roots with 2 years; -, there are no data. A[41][42]; B[22][31]; C[37]; D[12][38][39]; E[35]; F[12].

Table 3. Fiber composition of cardoon vegetal parts.

Fiber (g/100 g d.w.)	Raw A	Stems B	Stalks C	Leaves D	Flowers E
Hemicellulose	12.8–18.19	18.7–19.1	47.3–55.2	4.6–11.3	16.30–17.16
Cellulose	30.52–41.9	50.4–51.7	17.9–27.0	29.0–34.3	10.33–17.73
Lignin	14.21–18.9	10.7–11.9	13.3–28.8	8.7–12.5	7.60–10.73

A[41][43]; B[25]; C[5][42][44][45]; D[25]; E[37].

Table 4. Fatty-acid composition of cardoon vegetal parts.

Fatty Acid (Relative Percentage, %)	Raw A	Flowers B	Seeds C	Bracts D	Heads E
C6:0		n.d.–0.40	0.019–16.3	0.0094–0.05	0.082–3.710
C8:0		-	0.014–3.0	0.0086–0.0429	0.057–1.314
C10:0		-	0.015–0.151	0.00122–0.044	0.186–0.473
C11:0		0.85–1.98	0.027–0.67	0.025–0.092	0.16–0.579
C12:0		-	0.015–0.18	0.0073–0.2502	0.326–2.57
C13:0		1.05–1.17	-	n.d.–0.0105	0.0–0.084
C14:0	0.11	1.08–1.15	0.103–0.59	0.037–0.335	0.58–2.69
C14:1		-	-	n.d.–0.0083	0.0–0.54
C15:0		-	0.032–0.125	0.016–0.092	0.0–0.48
C15:1		-	-	0.0026–1.5197	0.0–1.36
C16:0	0.009–10.8	40.87–45.45	11–55.948	0.0367–6.183	14.62–43.8
C16:1	n.d.–0.02	n.d.–1.46	0.02–0.78	0.0076–0.039	0.317–12.76
C17:0	0.06	-	0.062–0.33	0.0184–0.0915	0.313–0.779
C18:0	0.002–3.6	4.83–6.28	3.289–16.39	0.209–1.775	2.687–6.0
C18:1n9c	0.018–27.3	2.09–3.33	0.58–3.77	0.195–0.903	4.48–46.6

Fatty Acid (Relative Percentage, %)	Raw A	Flowers B	Seeds C	Bracts D	Heads E
C18:2n6c	0.041–56.8	25.10–29.91	1.7–83.3	0.054–2.208	0.748–30.6
C18:3n6	0.17	3.67–7.12	60.15–70.41	-	0.0–0.176
C18:3n3		-	0.037–4.060	0.0076–0.543	0.3675–7.5
C20:0	0.37	3.10–3.76	0.112–1.8	0.0049–0.3693	0.377–3.225
C20:1	0	-	0.08–0.49	0.0042–0.032	0.0–4.52
C20:2		-	0.18–0.24	n.d.–0.022	0.0–0.31
C21:0		-	0.064–0.079	n.d.–0.07	0.070–0.324
C20:3n6		-	0.012–0.015	n.d.–0.1018	0.0–8.6
C20:3n3		-	-	n.d.–0.156	0.0–1.38
C22:0	0.12	-	-	0.063–0.447	0.0–2.6365
C22:1	0.15	-	0.103–0.19	0.0036–0.032	0.12–4.9505
C20:5n3		-	-	0.0039–0.06	0.0–0.6285
C22:2		1.58–2.88	-	n.d.–0.669	0.0–0.30
C23:0		1.32–1.77	0.17–1.51	n.d.–0.06	0.26–1.61
C24:0	0.19	-	0.199–0.66	n.d.–0.128	0.0–7.411
Total variation					
SFA	0.861–15.27	57.07–64.99	15.5–95.5	1.074–9.167	22.9–61.9
MUFA	0.168–27.47	3.33–3.55	0.84–19.39	0.242–2.034	5.61–52.1
PUFA	0.211–56.8	31.66–38.61	1.9–83.7	0.076–2.955	1.895–47.7

Fatty acids are expressed as a relative percentage of each fatty acid. n.d.—not detected; C6:0—caproic acid; C8:0—caprylic acid; C10:0—capric acid; C11:0—undecanoic acid; C12:0—lauric acid; C13:0—tridecanoic acid; C14:0—myristic acid; C14:1—tetradecanoic acid; C15:0—pentadecanoic acid; C15:1—pentadecanoic acid; C16:0—palmitic acid; C16:1—palmitoleic acid; C17:0—heptadecanoic acid; C18:0—stearic acid; C18:1n9—oleic acid; C18:2n6c—linoleic acid; C18:3n6-gamma-linolenic acid; C18:3n3—alpha-linolenic acid; C20:0—arachidic acid; C20:1—gondoic acid; C20:2—eicosadienoic acid; C21:0—heneicosanoic acid; C20:3n6—eicosatrienoic acid; C20:3n3—11,14,17-eicosatrienoic acid; C22:0—behenic acid; C22:1—erucic acid; C20:5n3—eicosapentaenoic acid; C22:2—docosadienoic acid; C23:0—tricosanoic acid; C24:0—lignoceric acid; SFA—saturated fatty acid; MUFA—monounsaturated fatty acid; PUFA—polyunsaturated fatty acid; n-6/n-3: ratio of omega 6/omega 3 fatty acids. -, There is no data. A[40][46]; B[37]; C[12][38][39]; D[35]; E[12].

Table 5. Phytosterol and tocopherol composition of cardoon vegetal parts.

Tocopherols (mg/100 g d.w.)	Stalks A	Leaves B	Flowers C	Seeds D	Bracts and Receptacle E	Heads F
α-Tocopherol	n.d.	39.9–100.7	n.d.	1.210–29.620	n.d.–0.062	0.25–0.619
γ-Tocopherol	-	-	-	n.d.	n.d.–0.120	n.d.
Cholesterol	1.0–1.3	27.6	-	-	n.d.	-
24-Methylenecholesterol	0.7–1.7	n.d.-19.3	-	5.4–6.5	n.d.	-
Campesterol	2.6–5.6	15.1–24.8	-	15.0–17.0	8.1–11.7	-
Stigmasterol	12.9–32.4	33.8–58.8	45.9–46.1	-	52.3–54.2	-
β-Sitosterol	13.1–25.7	63.9–171.6	49.8–70.8	-	39.2–63.7	-
β-Sitostanol	2.5–4.0	n.d.	n.d.	-	nd-10.6	-
Δ5-Avenasterol	n.d.	20.0–32.5	23.9–28.0	-	n.d.	-

n.d., not detected; -, there are no data. A[36];B[36]; C[36]; D[38][39];E[35][36]; F[12].

Table 6. Organic acids composition of cardoon vegetal parts.

Organic Acid (g/100 g d.w.)	Seeds A	Bracts B	Heads C
Oxalic	0.079–0.304	0.093–9.5	0.324–12.1
Quinic	tr–0.07	tr–4.82	0.017–3.3
Malic	tr–0.086	tr–1.87	n.d.–2.31
Citric	n.d.–0.33	n.d.–1.9	n.d.–0.86
Fumaric	tr	n.d.–0.0076	n.d.–0.0542
Total variation	0.03–6.54	1.96–15.6	0.89–15.7

d.w., dry weight; tr, traces; n.d., not detected. A[38][39]; B[35]; C[12].

Table 7. Mineral composition of cardoon vegetal parts.

Minerals (mg/100 g d.w.)	Raw A	Flowers B	Seeds C
K	400	1600–1710	493–880
Na	170	200–300	12–24
Ca	70	580–1010	734–1583
Mg	42	150–170	241–809
Mn	0.256	-	4.21–6.2
Fe	0.7	-	9.2–16
Zn	0.17	-	1.4–5.2

-, there are no data. A[40]; B[37]; C[39].

Table 8. Vitamin content of raw cardoon and raw artichoke.

Vitamins (per 100 g Edible Portion)	Cardoon Raw	Artichoke Raw
Vitamin C (mg)	2.0	11.7
Thiamin (mg)	0.02	0.07
Riboflavin (mg)	0.03	0.07
Niacin (mg)	0.3	0.9
Pantothenic acid (mg)	0.338	0.34
Vitamin B6 (mg)	0.116	0.12
Total folate (µg)	68.0	68.0
Vitamin A µg)	0	8.0
Vitamin E (mg)	-	0.19

Data adapted from [40]. -, There is no data.

Table 9. Volatile organic compounds found in vegetal parts of cardoon.

Volatile Organic Compounds	Vegetal Parts	References
Aromatic compounds		
Benzoic acid	Stalks, receptacles and bracts, florets, leaves	[36]

Volatile Organic Compounds	Vegetal Parts	References
Vanillin	Stalks, receptacles and bracts, leaves	[36]
Syringaldehyde	Stalks, receptacles and bracts, florets, leaves	[36]
2,6-Dimethoxyhydroquinone	Stalks, receptacle and bracts, florets	[36]
3-Vanillylpropanol	Stalks, florets, leaves	[36]
Vanillylpropanoic acid	Florets	[36]
Scopolin	Florets	[36]
Benzaldehyde	Stalks, leaves	[23][47]
Furfural	Leaves	[23][47]
(E)-2-Hexanal	Leaves	[47]
1-Octen-3-one	Leaves	[47]
6-Methyl-5-hepten-2-one	Leaves	[47]
Octanal	Leaves	[47]
Benzene acetaldehyde	Leaves	[47]
(E)-2-Octenal	Leaves	[47]
Acethophenone	Leaves	[47]
(E,E)-3,5-Octadien-2-one	Leaves	[47]
Nonanal	Leaves	[47]
(E)-6-Methyl-3,5-heptadien-2-one	Leaves	[47]
Phenetyl alcohol	Leaves	[47]
Isophorone	Leaves	[47]
3-Nonen-2-one	Leaves	[47]
(E,Z)-2,6-Nonadienal	Leaves	[47]
4-Methyl-Acephenone	Leaves	[47]
Safranal	Leaves	[47]
Decanal	Leaves	[47]
β-Ciclocitral	Leaves	[47]
Neral	Leaves	[47]
β-Homocyclocitral	Leaves	[47]
Geranial	Leaves	[47]
p-Vinylguaiacol	Leaves	[23][47]
Eugenol	Leaves	[23][47]
γ-Nonalactone	Leaves	[47]
(E)-β-Damascenone	Leaves	[47]
Geranyl acetone	Leaves	[47]
β-Ionone	Leaves	[47]
Dicyclohexyl-methanone	Leaves	[47]
Dihydroactinidiolide	Leaves	[47]
Phytone	Leaves	[47]
Fatty acids		

Volatile Organic Compounds	Vegetal Parts	References
Saturated		[36]
Tetradecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Pentadecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Hexadecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Heptadecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Octadecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Nonadecanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Eicosanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Heneicosanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Docosanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Tricosanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Tetracosanoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
Pentacosanoic acid	Stalks, receptacle and bracts, florets	[36]
Hexacosanoic acid	Stalks, florets, leaves	[36]
Octacosanoic acid	Stalks, florets, leaves	[36]
Unsaturated		
cis-9-Hexadecenoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
trans-9-Hexadecenoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
9,12-Octadecadienoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
9,12,15-Octadecatrienoic acid	Stalks, receptacle and bracts, florets, leaves	[36]
cis-9-Octadecenoic acid	Stalks, receptacle and bracts, florets	[36]
trans-9-Octadecenoic acid	Stalks, receptacle and bracts, florets	[36]
Hydroxy fatty acids	Stalks, florets	[36]
2-Hydroxyheptanoic acid	Stalks	[36]
2-Hydroxyundecanoic acid	Florets	[36]
Long-chain aliphatic alcohols		
Hexadecanol-1-ol	Stalks, receptacle and bracts, florets, leaves	[36]
cis-9-Octadecen-1-ol	Stalks, receptacle and bracts, florets	[36]
Octadecan-1-ol	Stalks, receptacle and bracts, florets, leaves	[36]
Eicosan-1-ol	Stalks, receptacle and bracts, florets	[36]
Docosan-1-ol	Stalks, receptacle and bracts, florets, leaves	[36]
Tetracosan-1-ol	Stalks, receptacle and bracts, florets, leaves	[36]
Hexacosan-1-ol	Stalks, receptacle and bracts, florets, leaves	[36]
Octocosan-1-ol	Stalks, florets, leaves	[36]
Sesquiterpene lactones		
Grosheimin	Stalks, leaves	[36]
Deacylcynaropicrin	Stalks, receptacle and bracts, leaves	[36]
Cynaropicrin	Stalks, receptacle and bracts, leaves	[36]
Pentacyclic triterpenes		

Volatile Organic Compounds	Vegetal Parts	References
β-Amyrin	Stalks, receptacle and bracts, florets, leaves	[36]
α-Amyrin	Stalks, receptacle and bracts, florets, leaves	[36]
β-Amyrin-acetate	Stalks, receptacle and bracts, florets, leaves	[36]
α-Amyrin acetate	Stalks, receptacle and bracts, florets, leaves	[36]
Lupenyl acetate	Stalks, receptacle and bracts, florets, leaves	[36]
Ψ -Taraxasterol	Stalks, receptacle and bracts, florets, leaves	[36]
Taraxasterol	Stalks, receptacle and bracts, florets, leaves	[36]
Ψ -Taraxasterol acetate	Stalks, receptacle and bracts, florets, leaves	[36]
Taraxasteryl acetate	Stalks, receptacle and bracts, florets, leaves	[36]
Others		
Inositol	Stalks, receptacle and bracts, florets, leaves	[36]
2,3-Dihydroxypropyl hexadecanoate	Stalks, receptacle and bracts, florets, leaves	[36]
trans-Squalene	Leaves	[36]

3. Cynara carduncculus and Its Effect on Metabolic Disorders

3.1. Hepatoprotective Activity

The in vitro hepatoprotective activity of C. scolymus on a human hepatocellular carcinoma cell line (HepG2 cells) was demonstrated by Youssef and colleagues [48], with the synergic activity resulting from the combination of three extracts (C. cardunculus L. var. scolymus L. Fiori, Ficus carica L. (fig), and Morus nigra L. (blackberry)) which were able to normalize the enzyme levels in the cells after the induction of hepatoxicity using carbon tetrachloride (CCl4), which caused an increase in aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels and a reduction in glutathione (GSH) and superoxide dismutase (SOD).

Furthermore, El Morsy and collaborators [49] studied the potential protective effect of artichoke leaf extract (ALE) against hepatotoxicity triggered by paracetamol overdose in rats. The authors observed that rats pretreated with ALE had lower values of serum ALT and AST, which were previously raised by paracetamol. Furthermore, hepatotoxicity due to paracetamol also causes oxidative damage. For this reason, the ALE effect on enzymatic antioxidants was also studied, and the authors found that ALE increased hepatic GSH, which reversed oxidative stress parameters, DNA damage, and necrosis. Moreover, it is important to emphasize that ALE had a higher impact on the restoration of GSH, nitric oxide, and antioxidant enzyme levels compared to N-acetylcysteine, a reference drug for the treatment of paracetamol overdose [49].

On the other hand, Tang and colleagues evaluated the effect of ALE on the alcoholic liver disease animal model; results showed that the levels of hepatic enzymes were reduced, and there was a suppression of the Toll-like receptor (TLR) 4 and nuclear factor-kappa B (NF-κB) pathway, which ultimately mitigated the oxidative stress and the inflammatory pathway [50].

Additionally, the hepatoprotective effect of bergamont polyphenolic fraction (Citrus bergamia) and C. cardunculus var. scolymus L. Fiori extract was also studied in a clinical trial conducted by Musolino and collaborators. After 16 weeks of supplementation, both extracts alone (300 mg/daily) and in combination (150 mg/kg of each extract) demonstrated the potential to decrease serum ALT and AST; nevertheless, the combination of both extracts exhibited better results [51].

3.2. Hypolipidemic Activity

Ben Salem and collaborators demonstrated the effect of ALE on the lipidic profile, cardiac markers, and antioxidant levels in obese rats [52]. As a result of supplementation of rats with ALE (200 mg/kg and 400 mg/kg), there was an improvement in the lipidic profile due to the decrease in TC, TG, and LDL-c levels and increase in HDL-c levels. In addition, ALE supplementation also reduced the cardiac markers and increased the antioxidant enzyme SOD, GPx, and GSH activities [52]. The effect of artichoke extracts on liver phosphatide phosphohydrolase and lipid profile in hyperlipidemic rats was also evaluated by Heidarian and colleagues. The supplementation with a mix of 10% artichoke in rat pellets for 60 days resulted in a decrease in the lipids in the serum and the phosphatide phosphohydrolase activity, which consequently decreased the levels of TG [53]. Furthermore, Oppedisano and collaborators showed the effect of C. cardunculus var. sylvestris (Lank) Fiori leaf extract in rats fed an HFD. In the animals fed an HFD and supplemented with 10 or 20 mg/kg of C. cardunculus, there was a dose-dependent reduction in TC, TG, and malondialdehyde levels compared with the group that was not supplemented with C. cardunculus var. sylvestris (Lank) Fiori [54].

Furthermore, TC, LDL-c/HDL-c and TC/HDL-c ratio levels suffered a significant reduction in subjects with primary mild hypercholesterolemia and after 8 weeks of supplementation with ALE (2 daily doses of 250 mg). There was a significant increase in HDL-c, which plays an important role in the prevention of cardiovascular diseases [55].

3.3. Antidiabetic Activity

Ben Salem and colleagues studied the in vitro capacity of different extracts (butanolic, ethanolic, and aqueous) of C. cardunculus var. scolymus L. Fiori to inhibit the activity of α-amylase; the results showed that the ethanolic extract exhibited an IC50 value of 72.22 µg/mL (compared to acarbose specific inhibitor (IC50 = 14.83 µg/mL)). Furthermore, the authors investigated the possible anti-diabetic effect of the ethanol leaf extract of C. cardunculus var. scolymus L. Fiori in alloxan-induced stress oxidant Wistar rats. The Wistar rats were supplemented with two daily doses of the ALE extract (200 mg/kg or 400 mg/kg) for 28 days. After the supplementation, ALE decreased the α-amylase levels in the serum of diabetic rats, which consequently lowered the blood glucose rate. Additionally, the administration of ALE also affected the lipidic profile and antioxidative activity in the liver, kidney, and pancreas of diabetic rats [56]. In addition, the antidiabetic activity of infusions (200 mg/L) of Agrimonia eupatoria L. and C. altilis L. was evaluated by Kuczmannová et al., by monitoring the inhibitory effect of α-glucosidase, serum glucose levels, formation of advanced glycation end-products (AGEs), and the activity of butyrylcholinesterase. The artichoke extract did not affect the activity of α-glucosidase, but induced a reduction in the glucose levels and inhibited the formation of AGEs [57]. Similarly, the treatment with an oral administration of ALE (200 and 400 mg/kg) on streptozotocin (STZ)-induced diabetic rats resulted in a significant decrease in serum glucose, TG, and TC levels [58].

In a clinical trial conducted by Ebrahimi-Mameghani and collaborators, the authors examined the effects of supplementation with ALE (1800 mg/daily) in patients with metabolic syndrome for 12 weeks. After the supplementation with ALE, there was a decrease in insulin and in homeostasis model assessment of insulin resistance (HOMA-IR) values [59].

4. Conclusions

Cardoon is a plant used in the Mediterranean diet and traditional medicine, composed of several bioactive compounds, such as dietary fibers, sesquiterpenes lactones, and phenolic compounds. *C. cardunculus* L. is one of the most promising Mediterranean plants, due to its therapeutic potential and industrial applications. Several studies have demonstrated that cardoon has the capacity to act as an anti-inflammatory, antidiabetic, lipid-lowering, antimicrobial, and antitumoral agent due to its phytochemical composition. It is important to exploit cardoon's capacity to be applied as an adjuvant in therapies to prevent or diminish the occurrence of diabetes, as well as cholesterol-related diseases. This yields new insights into the advantages of employing other processing and formulation technologies, such as nanoparticles, microencapsulation, and nanoemulsions, to improve their functionality and to increase the use of nutraceutical products, food supplements, and pharmaceutical formulations. Nevertheless, further studies are needed to fully comprehend the mechanism of action of cardoon metabolites underlying the biological activities stated in this review. It is imperative to conduct more clinical trials to clarify the dose and duration of the therapeutics.

References

1. Conceição, C.; Martins, P.; Alvarenga, N.; Dias, J.; Lamy, E.; Garrido, L.; Gomes, S.; Freitas, S.; Belo, A.; Brás, T.; et al. Cynara cardunculus: Use in cheesemaking and pharmaceutical applications. In Technological Approaches for Novel Ap plications in Dairy Processing; Intech Open: London, UK, 2016; Volume 1, pp. 73–107.
2. Ben Salem, M.; Affes, H.; Ksouda, K.; Dhouibi, R.; Sahnoun, Z.; Hammami, S.; Zeghal, K.M. Pharmacological Studies of Artichoke Leaf Extract and Their Health Benefits. Plant Foods Hum. Nutr. 2015, 70, 441–453.
3. Gostin, A.-I.; Waisundara, V.Y. Edible flowers as functional food: A review on artichoke (Cynara cardunculus L.). Trends Food Sci. Technol. 2019, 86, 381–391.
4. Christaki, E.; Bonos, E.; Florou-Paneri, P. Nutritional and Functional Properties of Cynara Crops (Globe Artichoke and Cardoon) and Their Potential Applications: A Review. Int. J. Appl. Sci. Technol. 2012, 2, 64–70.

5. Gominho, J.; Curt, M.D.; Lourenço, A.; Fernández, J.; Pereira, H. Cynara cardunculus L. as a biomass and multi-purpose crop: A review of 30 years of research. Biomass Bioenergy 2018, 109, 257–275.
6. Pesce, G.R.; Mauromicale, G. Cynara cardunculus L.: Historical and Economic Importance, Botanical Descriptions, Genetic Resources and Traditional Uses. Compend. Plant Genomes 2019, 1–19.
7. Fernández, J.; Curt, M.D.; Aguado, P.L. Industrial applications of Cynara cardunculus L. for energy and other uses. Ind. Crops Prod. 2006, 24, 222–229.
8. Claus, T.; Maruyama, S.A.; Palombini, S.V.; Montanher, P.F.; Bonafé, E.G.; de Oliveira Santos Junior, O.; Matsushita, M.; Visentainer, J.V. Chemical characterization and use of artichoke parts for protection from oxidative stress in canola oil. LWT Food Sci. Technol. 2015, 61, 346–351.
9. Sonnante, G.; Pignone, D.; Hammer, K. The Domestication of Artichoke and Cardoon: From Roman Times to the Genomic Age. Ann. Bot. 2007, 100, 1095–1100.
10. Ben Amira, A.; Besbes, S.; Attia, H.; Blecker, C. Milk-clotting properties of plant rennets and their enzymatic, rheological, and sensory role in cheese making: A review. Int. J. Food Prop. 2017, 20, S76–S93.
11. Gomes, S.; Belo, A.T.; Alvarenga, N.; Dias, J.; Lage, P.; Pinheiro, C.; Pinto-Cruz, C.; Brás, T.; Duarte, M.F.; Martins, A.P.L. Characterization of Cynara cardunculus L. flower from Alentejo as a coagulant agent for cheesemaking. Int. Dairy J. 2019, 91, 178–184.
12. Mandim, F.; Petropoulos, S.A.; Fernandes, Â.; Santos-Buelga, C.; Ferreira, I.C.F.R.; Barros, L. Chemical Composition of Cynara Cardunculus L. var. altilis Heads: The Impact of Harvesting Time. Agronomy 2020, 10, 1088.
13. Zayed, A.; Serag, A.; Farag, M.A. Cynara cardunculus L.: Outgoing and potential trends of phytochemical, industrial, nutritive and medicinal merits. J. Funct. Foods 2020, 69, 103937.
14. Pari, L.; Alfano, V.; Mattei, P.; Santangelo, E. Pappi of cardoon (Cynara cardunculus L.): The use of wetting during the harvesting aimed at recovering for the biorefinery. Ind. Crops Prod. 2017, 108, 722–728.
15. Cajarville, C.; González, J.; Repetto, J.L.; Alvir, M.R.; Rodríguez, C.A. Nutritional evaluation of cardoon (Cynara cardunculus) seed for ruminants. Anim. Feed Sci. Technol. 2000, 87, 203–213.
16. Ferrero, F.; Dinuccio, E.; Rollé, L.; Tabacco, E.; Borreani, G. Suitability of cardoon (Cynara cardunculus L.) harvested at two stages of maturity to ensiling and methane production. Biomass Bioenergy 2020, 142, 105776.
17. Encinar, J.M.; González, J.F.; Rodríguez, J.J.; Tejedor, A. Biodiesel Fuels from Vegetable Oils: Transesterification of Cynara cardunculus L. Oils with Ethanol. Energy Fuels 2002, 16, 443–450.
18. Scavo, A.; Rial, C.; Varela, R.M.; Molinillo, J.M.G.; Mauromicale, G.; Macias, F.A. Influence of Genotype and Harvest Time on the Cynara cardunculus L. Sesquiterpene Lactone Profile. J. Agric. Food Chem. 2019, 67, 6487–6496.
19. Restuccia, C.; Lombardo, M.; Scavo, A.; Mauromicale, G.; Cirvilleri, G. Combined application of antagonistic Wickerhamomyces anomalus BS91 strain and Cynara cardunculus L. leaf extracts for the control of postharvest decay of citrus fruit. Food Microbiol. 2020, 92, 103583.
20. Mandim, F.; Petropoulos, S.A.; Dias, M.I.; Pinela, J.; Kostic, M.; Soković, M.; Santos-Buelga, C.; Ferreira, I.C.F.R.; Barros, L. Seasonal variation in bioactive properties and phenolic composition of cardoon (Cynara cardunculus var. altilis) bracts. Food Chem. 2021, 336, 127744.
21. Mandim, F.; Petropoulos, S.A.; Giannoulis, K.D.; Dias, M.I.; Fernandes, Â.; Pinela, J.; Kostic, M.; Soković, M.; Barros, L.; Santos-Buelga, C.; et al. Seasonal variation of bioactive properties and phenolic composition of Cynara cardunculus var. altilis. Food Res. Int. 2020, 134, 109281.
22. Raccuia, S.A.; Melilli, M. Seasonal dynamics of biomass, inulin, and water-soluble sugars in roots of Cynara cardunculus L. Field Crops Res. 2010, 116, 147–153.
23. Lourenço, A.; Neiva, D.M.; Gominho, J.; Curt, M.D.; Fernández, J.; Marques, A.V.; Pereira, H. Biomass production of four Cynara cardunculus clones and lignin composition analysis. Biomass Bioenergy 2015, 76, 86–95.
24. Ierna, A.; Mauromicale, G. Cynara cardunculus L. genotypes as a crop for energy purposes in a Mediterranean environment. Biomass Bioenergy 2010, 34, 754–760.
25. Francaviglia, R.; Bruno, A.; Falcucci, M.; Farina, R.; Renzi, G.; Russo, D.E.; Sepe, L.; Neri, U. Yields and quality of Cynara cardunculus L. wild and cultivated cardoon genotypes. A case study from a marginal land in Central Italy. Eur. J. Agron. 2016, 72, 10–19.
26. Foti, S.; Mauromicale, G.; Raccuia, S.A.; Fallico, B.; Fanella, F.; Maccarone, E. Possible alternative utilization of Cynara spp.: I. Biomass, grain yield and chemical composition of grain. Ind. Crops Prod. 1999, 10, 219–228.
27. Gouveia, S.C.; Castilho, P.C. Phenolic composition and antioxidant capacity of cultivated artichoke, Madeira cardoon and artichoke-based dietary supplements. Food Res. Int. 2012, 48, 712–724.

28. Pagano, I.; Piccinelli, A.L.; Celano, R.; Campone, L.; Gazzerro, P.; De Falco, E.; Rastrelli, L. Chemical profile and cellular antioxidant activity of artichoke by-products. Food Funct. 2016, 7, 4841–4850.

29. Lattanzio, V.; Kroon, P.A.; Linsalata, V.; Cardinali, A. Globe artichoke: A functional food and source of nutraceutical ingredients. J. Funct. Foods 2009, 1, 131–144.

30. Petropoulos, S.A.; Pereira, C.; Ntatsi, G.; Danalatos, N.; Barros, L.; Ferreira, I.C.F.R. Nutritional value and chemical composition of Greek artichoke genotypes. Food Chem. 2018, 267, 296–302.

31. Pari, L.; Alfano, V.; Stefanoni, W.; Latterini, F.; Liuzzi, F.; De Bari, I.; Valerio, V.; Ciancolini, A. Inulin Content in Chipped and Whole Roots of Cardoon after Six Months Storage under Natural Conditions. Sustainability 2021, 13, 3902.

32. Raccuia, S.A.; Melilli, M. Cynara cardunculus L., a potential source of inulin in the Mediterranean environment: Screening of genetic variability. Crop Pasture Sci. 2004, 55, 693–698.

33. Paris, R.R.; Moyse, H. Matière Médicale; Massons & Cie: Paris, France, 1971.

34. Cavalaglio, G.; Gelosia, M.; Giannoni, T.; Barros Lovate Temporim, R.; Nicolini, A.; Cotana, F.; Bertini, A. Acid-catalyzed steam explosion for high enzymatic saccharification and low inhibitor release from lignocellulosic cardoon stalks. Biochem. Eng. J. 2021, 174, 108121.

35. Mandim, F.; Petropoulos, S.A.; Giannoulis, K.D.; Santos-Buelga, C.; Ferreira, I.C.F.R.; Barros, L. Chemical Composition of Cynara cardunculus L. var. altilis Bracts Cultivated in Central Greece: The Impact of Harvesting Time. Agronomy 2020, 10, 1976.

36. Ramos, P.A.; Guerra, Â.R.; Guerreiro, O.; Freire, C.S.; Silva, A.M.; Duarte, M.F.; Silvestre, A.J. Lipophilic extracts of Cynara cardunculus L. var. altilis (DC): A source of valuable bioactive terpenic compounds. J. Agric. Food Chem. 2013, 61, 8420–8429.

37. Ben Amira, A.; Blecker, C.; Richel, A.; Arias, A.A.; Fickers, P.; Francis, F.; Besbes, S.; Attia, H. Influence of the ripening stage and the lyophilization of wild cardoon flowers on their chemical composition, enzymatic activities of extracts and technological properties of cheese curds. Food Chem. 2018, 245, 919–925.

38. Mandim, F.; Petropoulos, S.A.; Pinela, J.; Dias, M.I.; Giannoulis, K.D.; Kostić, M.; Soković, M.; Queijo, B.; Santos-Buelga, C.; Ferreira, I.C.F.R.; et al. Chemical composition and biological activity of cardoon (Cynara cardunculus L. var. altilis) seeds harvested at different maturity stages. Food Chem. 2022, 369, 130875.

39. Petropoulos, S.; Fernandes, Â.; Pereira, C.; Tzortzakis, N.; Vaz, J.; Soković, M.; Barros, L.; Ferreira, I.C.F.R. Bioactivities, chemical composition and nutritional value of Cynara cardunculus L. seeds. Food Chem. 2019, 289, 404–412.

40. USDA. Available online:https://fdc.nal.usda.gov/ (accessed on 22 September 2021).

41. Fernandes, M.C.; Ferro, M.D.; Paulino, A.F.C.; Mendes, J.A.S.; Gravitis, J.; Evtuguin, D.V.; Xavier, A.M.R.B. Enzymatic saccharification and bioethanol production from Cynara cardunculus pretreated by steam explosion. Bioresour. Technol. 2015, 186, 309–315.

42. Shatalov, A.A.; Morais, A.R.C.; Duarte, L.C.; Carvalheiro, F. Selective single-stage xylan-to-xylose hydrolysis and its effect on enzymatic digestibility of energy crops giant reed and cardoon for bioethanol production. Ind. Crops Prod. 2017, 95, 104–112.

43. Giannoni, T.; Gelosia, M.; Bertini, A.; Fabbrizi, G.; Nicolini, A.; Coccia, V.; Iodice, P.; Cavalaglio, G. Fractionation of Cynara cardunculus L. by Acidified Organosolv Treatment for the Extraction of Highly Digestible Cellulose and Technical Lignin. Sustainability 2021, 13, 8714.

44. Bertini, A.; Gelosia, M.; Cavalaglio, G.; Barbanera, M.; Giannoni, T.; Tasselli, G.; Nicolini, A.; Cotana, F. Production of Carbohydrates from Cardoon Pre-Treated by Acid-Catalyzed Steam Explosion and Enzymatic Hydrolysis. Energies 2019, 12, 4288.

45. Shatalov, A.A.; Pereira, H. Dissolving grade eco-clean cellulose pulps by integrated fractionation of cardoon (Cynara cardunculus L.) stalk biomass. Chem. Eng. Res. Des. 2014, 92, 2640–2648.

46. Mauromicale, G.; Sortino, O.; Pesce, G.R.; Agnello, M.; Mauro, R.P. Suitability of cultivated and wild cardoon as a sustainable bioenergy crop for low input cultivation in low quality Mediterranean soils. Ind. Crops Prod. 2014, 57, 82–89.

47. Saucier, C.; Polidoro, A.d.S.; dos Santos, A.L.; Schneider, J.K.; Caramão, E.B.; Jacques, R.A. Comprehensive two-dimensional gas chromatography with mass spectrometry applied to the analysis of volatiles in artichoke (Cynara scolymus L.) leaves. Ind. Crops Prod. 2014, 62, 507–514.

48. Youssef, F.S.; Labib, R.M.; Eldahshan, O.A.; Singab, A.N.B. Synergistic Hepatoprotective and Antioxidant Effect of Artichoke, Fig, Blackberry Herbal Mixture on HepG2 Cells and Their Metabolic Profiling Using NMR Coupled with Chemometrics. Chem. Biodivers. 2017, 14, e1700206.

49. El Morsy, E.M.; Kamel, R. Protective effect of artichoke leaf extract against paracetamol-induced hepatotoxicity in rats. Pharm. Biol. 2015, 53, 167–173.

50. Tang, X.; Wei, R.; Deng, A.; Lei, T. Protective Effects of Ethanolic Extracts from Artichoke, an Edible Herbal Medicine, a gainst Acute Alcohol-Induced Liver Injury in Mice. Nutrients 2017, 9, 1000.

51. Musolino, V.; Gliozzi, M.; Bombardelli, E.; Nucera, S.; Carresi, C.; Maiuolo, J.; Mollace, R.; Paone, S.; Bosco, F.; Scara no, F.; et al. The synergistic effect of Citrus bergamia and Cynara cardunculus extracts on vascular inflammation and o xidative stress in non-alcoholic fatty liver disease. J. Tradit. Complementary Med. 2020, 10, 268–274.

52. Ben Salem, M.; Affes, H.; Dhouibi, R.; Charfi, S.; Turki, M.; Hammami, S.; Ayedi, F.; Sahnoun, Z.; Zeghal, K.M.; Ksoud a, K. Effect of Artichoke (cynara scolymus) on cardiac markers, lipid profile and antioxidants levels in tissue of HFD-ind uced obesity. Arch. Physiol. Biochem. 2019, 1–11.

53. Heidarian, E.; Rafieian-Kopaei, M. Protective effect of artichoke (Cynara scolymus) leaf extract against lead toxicity in r at. Pharm. Biol. 2013, 51, 1104–1109.

54. Oppedisano, F.; Muscoli, C.; Musolino, V.; Carresi, C.; Macrì, R.; Giancotta, C.; Bosco, F.; Maiuolo, J.; Scarano, F.; Pao ne, S.; et al. The Protective Effect of Cynara Cardunculus Extract in Diet-Induced NAFLD: Involvement of OCTN1 and OCTN2 Transporter Subfamily. Nutrients 2020, 12, 1435.

55. Rondanelli, M.; Giacosa, A.; Opizzi, A.; Faliva, M.A.; Sala, P.; Perna, S.; Riva, A.; Morazzoni, P.; Bombardelli, E. Benefi cial effects of artichoke leaf extract supplementation on increasing HDL-cholesterol in subjects with primary mild hyperc holesterolaemia: A double-blind, randomized, placebo-controlled trial. Int. J. Food Sci. Nutr. 2013, 64, 7–15.

56. Ben Salem, M.; Ben Abdallah Kolsi, R.; Dhouibi, R.; Ksouda, K.; Charfi, S.; Yaich, M.; Hammami, S.; Sahnoun, Z.; Zeg hal, K.M.; Jamoussi, K.; et al. Protective effects of Cynara scolymus leaves extract on metabolic disorders and oxidativ e stress in alloxan-diabetic rats. BMC Complement. Altern. Med. 2017, 17, 328.

57. Kuczmannová, A.; Balažová, A.; Račanská, E.; Kameníková, M.; Fialová, S.; Majerník, J.; Nagy, M.; Gál, P.; Mučaji, P. Agrimonia eupatoria L. and Cynara cardunculus L. Water Infusions: Comparison of Anti-Diabetic Activities. Molecules 2 016, 21, 564.

58. Heidarian, E.; Soofiniya, Y. Hypolipidemic and hypoglycemic effects of aerial part of Cynara scolymus in streptozotocin-induced diabetic rats. J. Med. Plants Res. 2011, 5, 2717–2723.

59. Ebrahimi-Mameghani, M.; Asghari-Jafarabadi, M.; Rezazadeh, K. TCF7L2-rs7903146 polymorphism modulates the eff ect of artichoke leaf extract supplementation on insulin resistance in metabolic syndrome: A randomized, double-blind, placebo-controlled trial. J. Integr. Med. 2018, 16, 329–334.