



It has been used as a dietary and medicinal product since 4th century B.C.



Artichoke leaf extract was one of the few herbal remedies which the clinical and experimental trials have complemented each other.

Both experimental and clinical effects have been verified through extensive biomedical herbal remedy research. Specifically, antioxidant, choleretic, hepatoprotective, bile-enhancing and lipid-lowering effects have been demonstrated, which corresponded with its historical use.

## **Chemical components:**

Phytochemical Analysis of Cynara scolymus Leaves Extracts revealed the presence of flavonoid, cardiac glycosides, saponin, tannin, terpenoid, and alkaloids.

The phytochemical screening also has been found to be a rich source of polyphenolic compounds including Quercetin, apigenin-7-glucoside, and verbascoside.<sup>1</sup>

Elemental analysis in (mg/100 g of dry weight basis) indicated that leaves of artichoke contained the following order of essential minerals compounds:

potassium	2886.80	manganese
sodium	1762.94	zinc
calcium	1359.34	copper
magnesium	433.21	chromium
iron	16.17	

Artichoke is found to be rich source of **inulin** which is considered prebiotic, also known as "food for probiotics" that are major factor for strong immune system.<sup>2</sup>

13.05

7.37

1.300.12

<sup>1</sup> Maryem Ben Salem, 1 Hanen Affes, 1, \* Khaled Athmouni, 2 Kamilia Ksouda, 1 Raouia Dhouibi, 1 Zouheir Sahnoun, 1 Serria Hammami, 1 and Khaled Mounir Zeghal 1 Chemicals Compositions, Antioxidant and Anti-Inflammatory Activity of Cynara scolymus Leaves Extracts, and Analysis of Major Bioactive Polyphenol

<sup>2</sup> Ramnani 1, E Gaudier, M Bingham, P van Bruggen, K M Tuohy, G R Gibson Prebiotic effect of fruit and vegetable shots containing Jerusalem artichoke inulin: a human intervention study

## **Pharmacological effects:**

Pharmacological experiments have demonstrated the health promoting effects of artichoke extracts including: **hepatoprotective**, **cholagogic** and **choleretic** properties.

**Hepatoprotective** effect of Cynara extract is reported with reducing the cholesterol biosynthesis and the oxidation of LDL. Artichoke has been found to decrease the production of reactive oxygen species, the oxidation of low-density lipoproteins, lipid peroxidation, and protein oxidation and increase the activity of glutathione peroxidase.<sup>3-4</sup>

Serum ALT and AST are effective biomarkers in the diagnosis of hepatic damage. Severe liver damage was demonstrated by remarkable elevation of serum ALT and AST levels. This elevation may be attributed to the release of these enzymes from the cytoplasm in to the blood circulation after rupture of the plasma membrane and cellular damage.

The study showed significant changes in serum ALT and AST levels in intervention group in comparison with the placebo group that could be attributed to antioxidant ingredients in Cynara scolymus extract.<sup>7</sup>

Several in vitro and animal studies assessed the antioxidative and free radical scavenging potential of artichoke extracts in protection hepatocytes from oxidative stress.<sup>5,6</sup>

**Choleretic** properties are demonstrated in many studies and approved as an indication in world's pharmacopeas. The artichoke performs a "amphocholeretic" role, regulating the biliary flow by either decreasing an exceedingly high biliary secretion or increasing it whenever it is reduced by toxic factors. The whole phytocomplex enhances choleresis through the simultaneous stimulation of the enzymatic, functional and antitoxic activities of the liver, liver regeneration and blood flow increase.

In fact, it joins the biliary activity to the liver activity, thus justifying its indication against dyspepsia accompanied by a sensation of a full stomach, abdominal pain, meteorism, nausea and vomiting. This means that the artichoke can be recommended for treatment of dyspepsia, especially when the cause can by ascribed to dyskinesia of biliary ducts or fat absorption disorders.<sup>15</sup>

Results of another study indicate increased bile synthesis after 30 minutes of use and concludes that artichoke extract can be recommended for the treatment of **dyspepsia**, especially when the cause may be attributed to dyskinesia of the bile ducts or disorder in the assimilation of fat.<sup>7</sup>

The efficacious HYPOLIPIDEMIA effect, published in many studies, is due to cynarin and luteolin components that play a crucial role in inhibiting cholesterol and triglycerides synthesis by regulation of HMG-CoA reductase activity and by increasing the fecal excretion of bile acids that follows a significant decrease in LDL cholesterol.

Cholesterol metabolism is also associated with liver fat content independent of body weight, implying that the more the fat the liver contains, the higher the cholesterol synthesis is.<sup>8</sup>

<sup>8</sup> P. Simonen, A. Kotronen, M. Hallikainen et al., "Cholesterol synthesis is increased and absorption decreased in non-alcoholic fatty liver disease independent of obesity," Journal of Hepatology, vol. 54, no. 1, pp. 153–159, 2011.



<sup>3</sup> D. Zapolska-Downar, A. Zapolski-Downar, M. Naruszewicz, A. Siennicka, B. Krasnodbska, and B. Kolodziej, "Protective properties of artichoke (Cynara scolymus) against oxidative stress induced in cultured endothelial cells and monocytes," Life Sciences, vol. 71, no. 24, pp. 2897–2908, 2002.

<sup>4</sup> A. Jim'enez-Escrig, L. O. Dragsted, B. Daneshvar, R. Pulido, and F. Saura-Calixto, "In vitro antioxidant activities of edible artichoke (Cynara scolymus L.) and effect on biomarkers of antioxidants in rats," Journal of

<sup>5</sup> N. S.Metwally, T. E. Kholeif, K. Z. Ghanem, A. R.H. Farrag, N. M. Ammar, and A. H. Z. Abdel-Hamid, "The protective effects of fish oil and artichoke on hepatocellular carcinoma in rats," European Review for Medical and Pharmacological Sciences, vol. 15, no. 12, pp. 1429–1444, 2011.

<sup>6</sup> G. Mehmetc, İk, G. "Ozdemirler, N. Koc, ak-Toker, U. C, evikbas,, and M. Uysal, "Effect of pretreatment with artichoke extract on carbon tetrachloride-induced liver injury and oxidative stress," Experimental and Toxicologic Pathology, vol. 60, no. 6, pp. 475–480, 2008.

 $<sup>7\</sup> R. Kirchhoff CH. Beckers G. M. Kirchhoff H. Trinczek-G\"{a}rtner O. Petrowicz H. J. Reimann* Increase in choleresis by means of artichoke extract the contract of the cont$ 

Cellular cholesterol synthesis is regulated by specific sterol binding proteins that are mostly found in the liver and the excess of cellular cholesterol is esterified by the ACAT enzyme. It is suggested that the effects of Cynara scolymus may appear by inducing and involving these two metabolic pathways in the liver.<sup>9</sup>

To date, many studies confirmed significant reduction in TG and LDL-C in patients used Artichoke leaves extract. The dose was 2700mg/day for 2 months and the reduction was 20% for TG and 11% for LDL. On the other hand, positive effect on liver enzymes, blood pressure and blood sugar were noted. Therefore, artichoke could be a good choice in patient with statins intolerance who exhibits elevated liver enzymes or experience side effects leading to statin therapy contraindication.

#### **Product:**

Sloth MD Artichoke (Cyanara Scolymus leaf) 500mg, vegetarian capsules.

#### Dose

Take 1 capsule 3 times a day with meals or as prescribed by health practitioner.

## **Cautions:**

Stop using the product if allergy or hypersensitivity occurs. Do not use the product if you have bile duct obstruction. No known side effects were observed as per drug monograph.

# Other potential use

## Role in diabetes

Diabetes mellitus is a chronic disease manifested mainly by disorders of carbohydrate metabolism. Researches have shown lowering in postprandial hypoglycemia and overall improvement in fasting blood sugar with Artichoke consumption.

The proposed mechanisms were: by affecting glucose absorption and as an antioxidant it delays depletion of stomach and bowels which inhibited alpha-amylase and alpha-glucosidase enzymes in bowels and blocked glucose transportation to blood.

Human pancreatic amylase and intestinal glucosidase are responsible for hydrolyzing carbohydrates into absorbable monosaccharides.

Artichoke content of polyphenolic compounds and chlorogenic acid had the greatest influence on the antidiabetic activity.<sup>11</sup>

On the other hand antioxidants have insulin-like effect and increase glucose absorption in peripheral tissue. Another probable mechanism is influencing beta-cells, repairing damaged cells, and stimulating these cells to secrete insulin.<sup>9</sup>

<sup>11</sup> Igor Piotr Turkiewicz 1, AnetaWojdyło 1,\*, Karolina Tkacz 1, Paulina Nowicka 1 and Francisca Hernández 2 Anticholinesterase and Antioxidant Activity vs. Terpenoids and Phenolic Compounds in Selected New Cultivars and Hybrids of Artichoke Cynara scolymus





<sup>9</sup> Vajiheh Rangboo,1 Mostafa Noroozi,2 Roza Zavoshy,3 Seyed Amirmansoor Rezadoost,4 and AsgharMohammadpoorasl5 The Effect of Artichoke Leaf Extract on Alanine Aminotransferase and Aspartate Aminotransferase in the Patients with Nonalcoholic Steatohepatitis

<sup>10</sup> Sahebkar A, Pirro M, Banach M, et al. Lipid-lowering activity of artichoke extracts: a systematic review and meta-analysis. Crit Rev Food Sci Nutr. 2017; Advance Access published June 13, doi:10.1080/10408398.2017.1332572

The study proposed the anti-inflammatory effect of ALE by means of inhibiting the synthesis and the release of inflammatory mediators like histamine, serotonin, and prostaglandins that are involved in acute inflammation, inhibitory effect on PN migration and decreasing the levels of fibrinogen and CRP.<sup>12</sup> Obesity is related to increase in inflammatory markers which characterized a low grade chronic inflammation.

The administration of antioxidant-rich Cynara extract ameliorates the undesirable effect of a high fat diet on lipid accumulation and hepatic disorders in rats fed with high fat diet.<sup>13</sup>

#### **Antioxidant**

Artichoke extracts possess efficacious properties against the oxidative stress induced by inflammatory process mediators and LDL oxidation.

The radical scavenger properties of the extract, documented by in-vitro copper-induced oxidative prevention of LDLs, are due to the presence of flavonoids and, in particular, luteolin.

Flavonoids act as hydrogen donors (reducing action) and as chelating substances capable of binding to catalyzing metals.

In practice, they act as antioxidants because they seize reactive oxygen species (ROS) and transform them into less aggressive radicals, thus sacrificing themselves and, at the same time, saving physiological antioxidants (carotenoids, glutathione, vit. C and vit. E).<sup>14</sup>

# Neurodegenerative

Pathogenesis of Alzheimer's disease correlates with deficiency of acetylcholinesterase (AChE) in the brain. Several clinical trials confirmed that AChE inhibitors may be used to treat this pathology.

AChE catalyzes the hydrolysis of acetylocholine (Ach) to choline in order to terminate nerve impulses.

Besides AChE, butyrylcholinesterase (BuChE) plays an important role in ACh hydrolysis, especially when a selective anticholinesterase inhibits AChE.<sup>15</sup>

Multiple studies have proved strong antioxidant and anti-inflammatory activities of polyphenolic compounds (especially flavonoids) that slow down neurodegenerative processes. In addition, in vivo studies on carotenoid and retinoid supplementation revealed their beneficial effect in Alzheimer's disease.<sup>16</sup>

The results from another study demonstrated high potential of any cultivar of artichoke as a diet supplement supporting therapy of patients suffering from carbohydrate metabolism disorders and aging adults with neurodegenerative disorders.<sup>11</sup>

<sup>16</sup> Honarvar, N.M.; Saedisomeolia, A.; Abdolahi, M.; Shayeganrad, A.; Sangsari, G.T.; Rad, B.H.; Muench, G. Molecular anti-inflammatory mechanisms of retinoids and carotenoids in Alzheimer's disease: A review ofcurrent evidence. J. Mol. Neurosci. 2017, 61, 289–304.





<sup>12</sup> Maryem Ben Salem, 1 Hanen Affes, 1, \* Khaled Athmouni, 2 Kamilia Ksouda, 1 Raouia Dhouibi, 1 Zouheir Sahnoun, 1 Serria Hammami, 1 and Khaled Mounir Zeghal 1 Chemicals Compositions, Antioxidant and Anti-Inflammatory Activity of Cynara scolymus Leaves Extracts, and Analysis of Major Bioactive Polyphenol

<sup>13</sup> Ben Salem M1 Ksouda K1, Dhouibi R1, Charfi S2, Turki M3, Hammami S1 Ayedi F3,Sahnoun Z1, Zeghal KM1, Affes H1 LC-MS/MS Analysis and Hepatoprotective Activity of Artichoke (Cynara scolymus L.) Leaves Extract against High Fat Diet-Induced Obesity in Rats.

<sup>14</sup> Mariangela Rondanelli, Francesca Monteferrario, Simone Perna, Milena Anna Faliva, Annalisa Opizzi Health-promoting properties of artichoke in preventing cardiovascular disease by its lipidic and glycemic-reducing action

<sup>15</sup> Choi, D.-Y.; Lee, Y.-J.; Hong, J.T.; Lee, H.-J. Antioxidant properties of natural polyphenols and theirtherapeutic potentials for Alzheimer's disease. Brain Res. Bull. 2012. 87. 144–153.